ANNOVIS BIO, INC.

FORM S-1
(Securities Registration Statement)

Filed 07/03/19

Address	1055 WESTLAKES DRIVE, SUITE 300 BERWYN, PA, 19312
Telephone	610-727-3913
CIK	0001477845
Symbol	ANVS
SIC Code	2834 - Pharmaceutical Preparations
Industry	Biotechnology & Medical Research
Sector	Healthcare
Fiscal Year	12/31

Table of Contents

As filed with the Securities and Exchange Commission on July 2, 2019

Registration No.

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-1

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

ANNOVIS BIO, INC.

(Exact name of registrant as specified in its charter)

Delaware	**2834**	(I.R.S. Employer
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	Identification No.) 26-2540421

1055 Westlakes Drive, Suite 300
Berwyn, PA 19312
Attention:
(610) 727-3913
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Maria Maccecchini, Ph.D.
President and Chief Executive Officer
Annovis Bio, Inc.
1055 Westlakes Drive, Suite 300
Berwyn, PA 19312
(610) 727-3913
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Kathleen M. Shay, Esq.	**William N. Haddad, Esq.**
John W. Kauffman, Esq.	**Carmen M. Fonda, Esq.**
Duane Morris LLP	**Venable LLP**
30 South 17 th Street	**Rockefeller Center**
Philadelphia, Pennsylvania 19103	**1270 Avenue of the Americas, 24th Floor**
(215) 979-1227	**New York, New York 10020**
	(917) 287-1580

Approximate date of commencement of proposed sale to the public:
As soon as practicable after this Registration Statement is declared effective.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. ☐

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer" "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐	Accelerated filer ☐	Non-accelerated filer ☒	Smaller reporting company ☒ Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. ☒

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to Be Registered	**Proposed Maximum Aggregate Offering Price(1)**	**Amount of Registration Fee(2)**
Common Stock, $0.0001 par value per share	$11,500,000	$1,393.80
Total		

(1) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended (the "Securities Act").

(2) Calculated pursuant to Rule 457(o) based on an estimate of the proposed maximum aggregate offering price.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become

effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

Table of Contents

The information contained in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

PRELIMINARY PROSPECTUS SUBJECT TO COMPLETION DATED JULY 2, 2019

Shares

Common Stock

ANNOVIS BIO, INC.

This is a firm commitment initial public offering of shares of common stock of Annovis Bio, Inc. No public market currently exists for our shares. We anticipate that the initial public offering price of our shares will be between $ and $ and for calculation purposes herein, we assume a mid-point of $ per share.

We intend to apply to list our shares of common stock for trading on the Nasdaq Capital Market under the symbol "ANVS." No assurance can be given that our application will be approved.

We are an emerging growth company under the Jumpstart our Business Startups Act of 2012, or JOBS Act, and, as such, may elect to comply with certain reduced public company reporting requirements for future filings.

Investing in our common stock is highly speculative and involves a high degree of risk. See " *Risk Factors* " beginning on page 13 of this prospectus for a discussion of information that should be considered in connection with an investment in our common stock.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

	Per Share	Total
Initial public offering price	$	$
Underwriting discounts and commissions(1)	$	$
Proceeds to us, before expenses	$	$

(1) Underwriting discounts and commissions do not include a non-accountable expense allowance equal to % of the public offering price payable to the underwriters. We refer you to " *Underwriting* " beginning on page 146 for additional information regarding underwriters' compensation.

We have granted the underwriters a 30-day over-allotment option to purchase up to additional shares of common stock at the initial public offering price less underwriting discounts and commissions.

The underwriters expect to deliver our shares to purchasers in the offering on or about , 2019

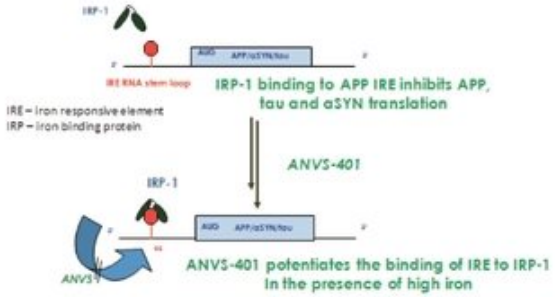
ThinkEquity

a division of Fordham Financial Management, Inc.

The date of this prospectus is , 2019

Our Solution to Reverse Neurodegeneration

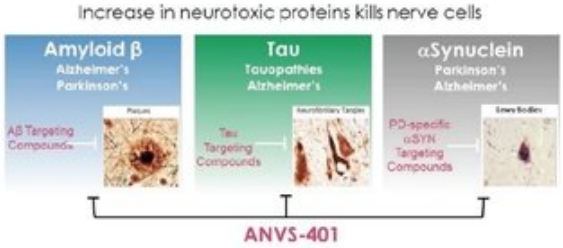
ANVS-401 Mechanism of Action



In our studies we saw that the mechanism of action of our lead compound, ANVS-401, inhibits over-expression of neurotoxic proteins by binding to the IRE-IRP1 complex and preventing its opening, thereby inhibiting the release of the mRNAs and their translation.

Brain injuries and stresses lead to increases in neurotoxic proteins, impaired axonal transport and nerve cell death – they lead to neurodegeneration.

To date, all approaches have targeted one or the other neurotoxic protein with negative outcomes. We believe ANVS-401 is the only drug in development that targets multiple neurotoxic proteins.



By targeting multiple neurotoxic proteins, ANVS-401 resembles a combination therapy approach, with the added convenience of being a single drug with a single drug target.

	DISEASE	NEUROTOXIC PROTEIN TARGET	PRECLINICAL	PHASE 1	PHASE 2
ANVS-401	AD	APP, tau, αSYN			
ANVS-401	AD-DS	APP			
ANVS-401	PD	αSYN, APP			
ANVS-405	TBI	Tau, APP, αSYN			
ANVS-301	Advanced AD	BChEI			

Our pipeline consists of oral drugs for chronic neurodegeneration. ANVS-401 is being developed for Alzheimer's disease, its orphan indication Alzheimer's in Down Syndrome and for Parkinson's disease.

Additionally, our intravenous drug, ANVS-405, is being developed for acute indications, such as traumatic brain injury and stroke.

Our third drug, ANVS-301, is in Phase 1 clinical studies for advanced Alzheimer's disease and dementia.

ANNOVIS

TABLE OF CONTENTS

We have not authorized anyone to provide you with different information, and we take no responsibility for any other information others may give you. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the front of this prospectus.

No action is being taken in any jurisdiction outside the United States to permit a public offering of our common stock or possession or distribution of this prospectus in that jurisdiction. Persons who come into possession of this prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus applicable to that jurisdiction.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our financial statements and the related notes thereto and the information set forth in the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." Unless the context otherwise requires, we use the terms "Annovis," "company," "we," "us" and "our" in this prospectus to refer to Annovis Bio, Inc.

ANNOVIS BIO, Inc.

Our Company

Annovis is a clinical stage, drug platform company addressing neurodegeneration, such as Alzheimer's disease in Down syndrome (AD-DS), Alzheimer's disease (AD) and Parkinson's disease (PD). We have an ongoing Phase 2a proof-of-concept study in AD patients and have planned to commence a second Phase 2a study in PD patients. We are developing our lead compound, ANVS-401, for chronic neurodegenerative diseases, such as AD-DS, AD and PD. In a number of studies, ANVS-401 inhibited the synthesis of neurotoxic proteins—APP/A β (APP), tau/phospho-tau (tau) and α -Synuclein (α -SYN)—that are the main cause of neurodegeneration. High levels of neurotoxic proteins lead to impaired axonal transport, which is responsible for the communication between and within nerve cells. When that communication is impaired, the immune system is activated and attacks the nerve cells, eventually killing them. Through our patented product platform, in clinical studies in mildly cognitive impaired (MCI) patients, ANVS-401 normalized levels of neurotoxic proteins and inflammatory factors. In preclinical studies, the lowering of neurotoxic proteins also led to the restoration of axonal transport, lowering of inflammation and prevention of nerve cell death.

The industry has encountered challenges in targeting specifically one or the other neurotoxic protein, be it APP, tau or α SYN, indicating that targeting one neurotoxic protein alone does not change the course of neurodegeneration. Our goal is to develop a disease modifying drug (DMD) for patients with neurodegeneration by leveraging our clinical and animal evidence in inhibiting at least the three most relevant neurotoxic proteins.

We believe that we are the only company developing a clinical stage proof-of-concept drug for AD-DS, AD and PD that inhibits more than one neurotoxic protein and has a mechanism of action designed to restore nerve cell axonal and synaptic activity. By restoring axonal transport and homeostasis in the brain we expect to treat memory loss and dementia associated with AD-DS and AD as well as body and brain function in PD.

We believe that ANVS-401 has the potential to be the first drug to interfere with the underlying mechanism of neurodegeneration. ANVS-401 is a small, once a day, orally administered, brain penetrant inhibitor of neurotoxic proteins. The biological activity of ANVS-401 has been evaluated in 19 animal studies conducted in leading institutions such as the Karolinska Institute, Columbia University and Harvard University. 16 of the studies are published and three are presently manuscripts in preparation. We also conducted three clinical trials with 125 humans including two safety studies in 120 healthy volunteers and a proof-of-concept study in five MCI patients with Parexel, an international clinical research organization. In these studies, we showed that ANVS-401 was well tolerated and we saw promising clinical signals: ANVS-401 reduced and normalized the levels of APP, tau and α SYN (α SYN is an unpublished observation) back to the levels seen in healthy volunteers and statistically lowered inflammation.

We are presently conducting a Phase 2a study in AD patients in collaboration with the Alzheimer Disease Cooperative Study (ADCS) group and plan to initiate a second Phase 2a proof-of-concept

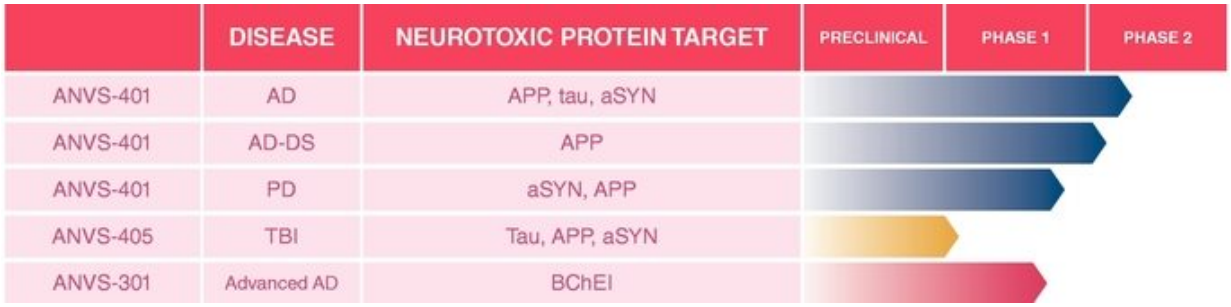
study of ANVS-401 in the first quarter of 2020 with 50 PD patients. The study being conducted by ADCS is expected to enroll a total of 24 persons at three dose levels plus placebo in a double-blind, placebo controlled fashion. To date, the study has enrolled and treated six early to moderate AD patients and has enrolled two additional patients. We have designed the two Phase 2a studies with Parexel by applying our understanding of the underlying disease states in neurodegeneration and by measuring not just target, but also pathway validation in the spinal fluid of these patients. By showing both target and pathway validation in two patient populations, we believe that our opportunity for successful Phase 3 studies is better than if we merely demonstrated target validation in one patient population.

We believe AD and PD are two of the largest medical needs of the aging U.S. population, and two potentially large markets, once a DMD has been developed and approved. Therefore, we desire to demonstrate ANVS-401's efficacy in both indications. However, since AD studies are very large and time and capital consuming, we plan to focus on an orphan population that is substantially similar to AD, but in a very controlled and limited setting. We intend to focus on AD in the DS population; in DS the APP gene is triplicated, leading to early onset AD with similar pathology as sporadic AD. In accordance with our animal studies in DS mice, lowering their high levels of APP is expected to restore axonal transport and homeostasis in the brain of DS patients and normalize their memory loss and dementia. This will allow us to obtain human data for AD in an orphan subpopulation much faster than in the regular AD population. Concomitantly, our goal is to also conduct a Phase 3 pivotal study in early PD patients. By the end of 2024, we expect to have conducted two pivotal studies for ANVS-401, one in AD-DS and one in PD, and to have filed a new drug application (NDA) with the U.S. Food and Drug Administration (FDA).

Innovation

Pipeline

Our Pipeline is focused primarily on drugs for chronic neurodegeneration—AD, its orphan indication AD-DS and PD. Additionally, we have a compound to treat acute neurodegeneration—traumatic brain injury (TBI) and stroke—and a third compound for advanced AD.



ANVS-401

Our lead compound, ANVS-401 is being developed for AD-DS, AD and PD, because in preclinical studies it normalized axonal transport in these diseases by inhibiting neurotoxic proteins that kill nerve cells. The compound was tested in three Phase 1 clinical studies that showed it to be well tolerated. This safety data is applicable to the clinical development of ANVS-401 for AD-DS, AD, PD and other chronic neurodegenerative disorders.

ANVS-405

For acute indications, we are developing ANVS-405, focused on protecting the brain after TBI and/or stroke. In a preclinical study, TBI rats that were treated with ANVS-405 after the insult exhibited normal memory and learning, normalized inflammation and re-established homeostasis in the brain.

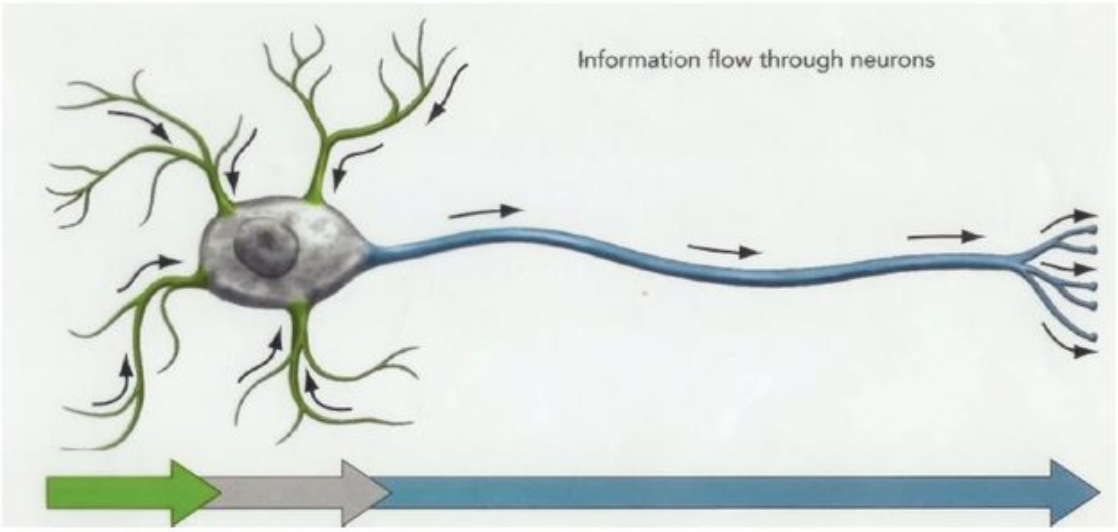
ANVS-301

Our compound ANVS-301 is expected to increase cognitive capability in later stages of AD and dementia. In preclinical studies, ANVS-301 fully restored memory and learning in very old rats and made the old rats cognitively equivalent to young rats. ANVS-301 is in a Phase 1 clinical trial that is being conducted and financed by the National Institutes of Health (NIH).

Background—What is Neurodegeneration?

A normal nerve cell receives signals, processes them in the cell body and transports them through the axon, a long-arm nerve fiber that extends out from the cell body and connects to the synapses, or fingers. These fingers then touch the successive nerve cell(s), where the signals are relayed further.

Nerve Cell with Axon and Synapse



When brain cells become injured or stressed their first response is reduction and impairment of axonal transport. If the insult persists, axonal vesicle transport remains impaired resulting in decreased levels of neurotransmitters and leading to depression (serotonin), anxiety and insomnia (GABA), AD (acetylcholine) and PD (dopamine). It also results in lower levels of neurotrophic factors and in nerve cells getting sick. When the immune system sees a sick cell, it proceeds to remove it, which leads to inflammation in the brain. Eventually, the sick cell is then killed by the immune system.

ANVS-401—Our Solution to Reverse Neurodegeneration

ANVS-401 is a small lipophilic molecule that is orally available and readily enters the brain, as demonstrated by pharmacokinetics analyses showing brain concentrations approximately 6 to 8 times higher than plasma concentrations. In preclinical studies, ANVS-401 showed a mechanism of action we believe to be unique, in that it inhibited the translation and, therefore, the levels of several key neurotoxic aggregating proteins both *in vitro* and *in vivo* including APP, tau and α SYN. Three Phase 1 clinical studies demonstrated that ANVS-401 was well tolerated. The third proof-of-concept study showed that it normalized levels of APP, tau and α SYN in the cerebrospinal fluid (CSF) of MCI patients. Additionally, we now have preclinical data that showed that ANVS-401 restored memory and learning in two AD animal models—AD transgenic (tg) mice and DS trisomic mice. ANVS-401 also restored colonic motility in a PD tg mouse model of PD.

By targeting multiple neurotoxic aggregating proteins, ANVS-401 resembles a combination therapy approach, with the added convenience of being a single drug with a single drug target. Therefore, we have worked to understand how ANVS-401 is able to inhibit the translation of more than one neurotoxic protein.

Novel Mechanism of Action and Target Engagement

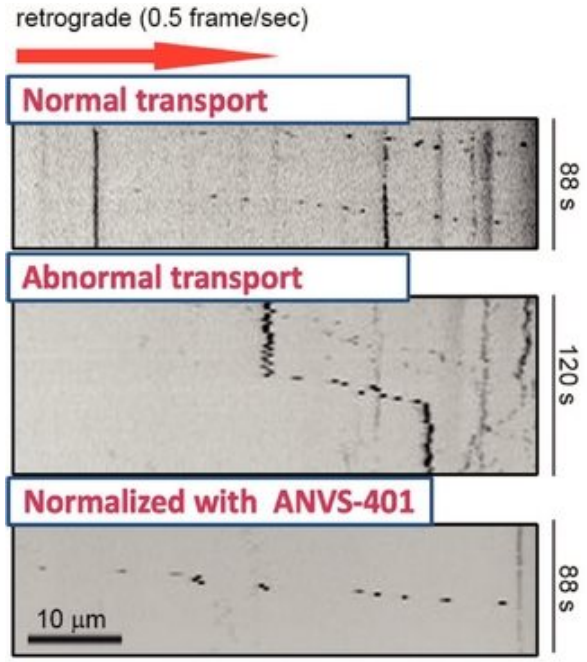
We undertook an extensive exploration of the mechanism of action of ANVS-401 on APP and α SYN synthesis and determined that ANVS-401 specifically inhibits translation of mRNAs coding for neurotoxic proteins only. Using five different methods we produced overlapping results *in vitro* . mRNAs of neurotoxic proteins have a conserved stem loop in the 5' untranslated region (5'UTR) called an iron-response element (IRE) type II stem loop. These IREs bind to an RNA binding protein, specifically to iron regulatory protein 1 (IRP1). When the mRNAs are bound, they are not translated. When the iron levels in the cytoplasm go up, IRP1 releases its mRNAs and they are translated.

Target Engagement

ANVS-401 specifically binds to the IRE/IRP1 complex of mRNAs coding for neurotoxic proteins and stops the release of the mRNAs under high iron conditions. It does not bind to IRE/IRP1 complexes of mRNAs coding for iron carrying or shuttling proteins, such as ferritin, transferring or ferroportin.

Axonal Transport and Pathway Engagement

When axonal transport and synaptic transmission are impaired, the cell releases lower levels of neurotransmitters, leading to neuropsychopharmacological disorders. Abnormal axonal transport also lowers levels of neurotrophic factors, which are responsible for the health of nerve cells. When the immune system sees a sick nerve cell, it gets activated and attacks the nerve cell, eventually killing it. Therefore, impairment in axonal transport leads to inflammation and, finally, leads to nerve cell death. Through several studies, we have found that, by reducing APP, tau and α SYN levels, ANVS-401 treatment restored normal axonal transport and prevented or restored those events all the way to preserving nerve cell health.



ANVS-401 normalized anterograde and retrograde vesicle transport in fully differentiated Down syndrome nerve cells;

On top: 2N normal nerve cells show a linear and smooth movement of vesicles carrying the neurotrophic factor BDNF.

In the middle, Down syndrome nerve cells show a disturbed, erratic and slowed transport of the vesicles carrying BDNF.

At the bottom: When the Down Syndrome nerve cells were treated with ANVS-401, their transport was fully restored and the vesicles carrying BDNF again move smoothly and expeditiously along the axon.

In preclinical trials, by normalizing axonal transport, ANVS-401 and/or ANVS-405 normalized all the functions that are negatively affected by disturbances of the transport.

Pathway Engagement:

- Studies showed that ANVS-401 lowered and normalized levels of neurotoxic proteins:
  - AD tg mice—restored normal levels of APP and its fragments with full recovery of memory, learning and brain function. The AD tg mice on placebo never learned to find their way in the 7-arm water maze with less than 3 to 4 mistakes, whereas the ANVS-401 treated mice found their way with one mistake, just like the normal wild-type mice.
  - DS trisomic mice—restored normal levels of APP and fully recovered memory and learning. The trisomic mice moved 38% less and made 68% more mistakes in the maze, whereas the ANVS-401 treated mice performed like normal wild-type mice.
  - PD tg mice—restored normal levels of α SYN in brain and gut with full recovery of gut motility. The PD tg mice at 4 months had 4 times slower and at 7 months 7 times slower gut motility than normal wild-type mice. ANVS-401 restored colonic motility.
  - MCI patients—restored normal levels of APP, tau and α SYN.
- Studies showed that ANVS-401 normalized retrograde and anterograde transport:
  - DS trisomic mice nerve cells—in studies conducted at UCSD, inhibition and normalization of APP levels led to restoration of anterograde and retrograde vesicle transport. ANVS-401 treatment of the DS nerve cells resulted in an increase in velocity of 70%, a value comparable to the velocity seen in normal neurons. ANVS-401 also decreased the pause time by 29%, again bringing it to the same pause time as in healthy normal cells. This was measured *in vitro* in isolated fully differentiated nerve cells.

- Studies showed that ANVS-401 normalized impaired synaptic transmission in:
  - AD tg mice—A Columbia University study showed that the AD tg mice treated with ANVS-401 had normal long-term potentiation, whereas long-term potentiation of the placebo treated AD tg mice was reduced by 66%.
- Studies showed that ANVS-405 increased neurotransmitter release in:
  - Rat striatum after TBI—A UCLA study showed that after TBI animals treated with placebo had 31% less dopamine than animals treated with ANVS-405.
- Studies showed that ANVS-401 increased levels of neurogenesis and brain derived neurotrophic factor (BDNF) in:
  - DS trisomic mice—A UCSD study, *in vivo* , was able to show a 60% increase in BDNF in DS trisomic animals treated with ANVS-401 compared to placebo.
  - AD tg mice brains—The Karolinska Institute measured BDNF and found that after ANVS-401 treatment, old AD tg mice showed increased levels of BDNF.
- Studies showed that ANVS-401 and/or ANVS-405 lowered inflammation in:
  - MCI patients—In a proof of concept clinical trial, 5 MCI patients treated with ANVS-401 had inflammatory factors that were statistically reduced.
  - TBI rats—rats with traumatic brain injury had much larger microglia than normal rats. Enlarged microglia means that the microglia is activated and shows inflammation. After treatment with ANVS-405, the size of the microglia shrank back to the size seen in healthy normal rat brain.
- Studies showed that ANVS-405 protected nerve cells in:
  - TBI rats—A UCLA study stained the rat substantia nigra for dead cells and found after TBI that 15% of the cells had died in placebo treated TBI rats. In ANVS-405 treated rats the nerve cells did not die.
  - Retina rats—In a Hershey Medical Center unpublished study in which saline was injected into one eye to increase the pressure, which kills retinal cells, ANVS-405 protected 67% of the retina.

By normalizing levels of neurotoxic proteins, ANVS-401 normalized the affected functions in all diseases we tested. These functions are: memory, learning, fear conditioning and long-term potentiation in AD mice and gut and gait function in PD mice. ANVS-405 restored memory and learning in TBI rats and sight in acute glaucoma rats.

Collectively, we believe these effects make ANVS-401 a very promising drug for the treatment of memory loss and dementia in AD-DS and AD and bodily and brain functions in PD.

Impact: Our goal, in our Phase 2a studies in AD and PD patients, is to demonstrate that ANVS-401 is well tolerated and is able to normalize the CSF levels of neurotoxic proteins (at least APP, tau, and α SYN) and inflammatory markers, as previously seen in preclinical studies. In these studies, we are also planning to analyze the CSF levels for additional neurotoxic aggregating proteins, control proteins lacking the conserved mRNA sequence of neurotoxic aggregating proteins, as well as neurotransmitters, neurotrophic factors, degeneration markers, and cognitive outcomes. Thus, we expect that we will be able to identify potential biomarkers for use in later studies.

Plans for the Two Phase 2 studies in AD and PD Patients

Our goal is to replicate the same target and pathway validation in our two Phase 2a studies in AD and PD patients as we saw in preclinical studies. In the spinal fluid of AD and PD patients we plan to show a decrease in levels of neurotoxic proteins and show the reversal of the toxic cascade back to normal. Once these two studies are fully analyzed, we will be able to better understand the similarities and differences between early AD and PD patients, as well as the effect of ANVS-401 on all endpoints. If the two studies are successful, we expect to expand the clinical proof of mechanism of ANVS-401 in the case of AD and PD, thereby enabling the start of pivotal late phase clinical studies for these diseases.

To date, we have submitted all our animal and human data to the FDA as well as our plans for doing the two Phase 2a studies in AD and PD patients. The FDA has raised no objections to our plans and protocols to date, however, the results of preclinical studies and early clinical trials are not necessarily predictive of future results.

Our Team

We have assembled a highly experienced management team, board of directors and scientific advisory board to execute on our mission to develop disease modifying therapies for the treatment of neurodegenerative disorders. Our Founder and Chief Executive Officer, Maria Maccecchini, Ph.D., is a business leader, drug developer and neuroscientist, with over 30 years of expertise in neurodegeneration. Our Chairman, Michael Hoffman, has extensive experience in investing in successful businesses as well as growing and leading companies. Our Chief Medical Officer, Jeffrey Cummings, M.D. is one of the most respected clinical Alzheimer scientists; he was Director of Neurology at the Cleveland Clinic before becoming our CMO. Our Chief Financial Officer is Jeffrey McGroarty; he has extensive experience as CFO of public companies.

Our scientific advisory board is composed of scientists known for their work in the area of neurodegeneration. Our scientific advisory board provides us with advice and guidance on scientific and industry matters. We believe our team, with its deep scientific background, drug development experience and industry-leading business capabilities, positions us to become a leading company developing therapies for neurodegenerative disorders. We do not have rules or procedures governing our scientific advisory board. However, the universities they are associated with may have rules regarding outside activities of faculty members.

Our Strategy

Our objectives are to develop and gain regulatory approval for ANVS-401 for the treatment of AD-DS, which is an orphan indication of Alzheimer's disease, AD and PD and leverage our discovery platform to treat other neurodegenerative disorders.

The key elements of our strategy are:

We expect the funds we are raising in this offering to be sufficient to complete the following:

- ***Advance clinical development of ANVS-401 to two Phase 2a clinical studies—one in AD and one in PD.***

  - Accelerate recruitment of the ongoing Phase 2a study in AD patients run by ADCS to achieve full recruitment within one year.
  - Start Phase 2a PD trial in the United States and, possibly, internationally, for the treatment of PD in the first quarter of 2020.
  - Complete both studies by the end of 2020.

- ***Prepare for a Phase 3 pivotal study in AD-DS***

  - Commence the planning of the AD-DS phase 3 study in collaboration with Professor William Mobley.

- ***Conduct chronic toxicology studies in rats and dogs*** —in order to test a drug in humans for extended lengths of time, it has to first be tested for safety for 6 months in rats and 9 months in dogs.

- ***Manufacture adequate quantities of ANVS-401*** to conduct the Phase 2a study in PD patients as well as Phase 3 studies in AD-DS and early PD patients.

Upon completion of a future subsequent financing, we intend to undertake the following:

At the end of the two Phase 2a studies, we will evaluate the data, discuss the animal toxicology and the two studies with the FDA and move to one Phase 3 in AD-DS and one in early PD patients.

- ***Conduct a Phase 3 study in AD-DS,*** an orphan indication that fully follows the course of AD, including memory loss and dementia, in a well characterized genetic predisposed group of people.

- ***Conduct a Phase 3 study in early PD patients,*** who show symptoms of PD, but are not taking L-dopa or agonist.

Assuming the successful conduct of the two Phase 3 studies, we intend to:

- ***Commercialize ANVS-401 in collaboration with one or more pharmaceutical companies.*** To commercialize ANVS-401, when approved, we intend to establish one or more marketing collaborations with pharmaceutical or biotechnology companies. We expect to seek separate development and commercialization collaborators in Japan and other parts of Asia.

- ***Evaluate the development of ANVS-401 for other PD populations.*** After our initial focus on early PD, we plan to test ANVS-401 in advanced PD as well as a prophylaxis for PD

- ***Evaluate ANVS-401 for early AD populations.*** Conduct a Phase 3 study in early AD.

- ***Evaluate the development of ANVS-401 for other AD populations.*** After our initial focus on early AD, we plan to test ANVS-401 in advanced AD as well as a prophylaxis for AD

- ***Evaluate ANVS-401 in other neurodegenerative disorders.***

Summary of Risks Associated with Our Business

Our business is subject to numerous risks and uncertainties, including those highlighted in the section titled "Risk Factors" immediately following this prospectus summary. Some of these risks are:

- We have incurred significant net losses since inception and anticipate that we will continue to incur net losses for the foreseeable future and may never achieve or maintain profitability.

- Even if this offering is successful, we will require additional capital to fund our operations, and if we fail to obtain necessary funding, we may not be able to complete the development and commercialization of ANVS-401.

- Our independent registered public accounting firm has expressed substantial doubt about our ability to continue as a going concern.

- We are heavily dependent on the success of ANVS-401, our lead product candidate, which is still under clinical development, and if it does not receive regulatory approval or is not successfully commercialized, our business may be harmed.

- We have concentrated our research and development efforts on the treatment of AD and PD, two diseases that have seen limited success in drug development.
- Clinical trials are expensive, time-consuming, difficult to design and implement, and involve an uncertain outcome.
- Results of preclinical studies, early clinical trials or analyses may not be indicative of results obtained in later trials.
- If we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our target markets.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in 2008. Our principal executive offices are located at 1055 Westlakes Drive, Suite #300, Berwyn, PA 19312. Our telephone number is 610 727 3710.

Our website address is *www.annovisbio.com* . The information contained in, or accessible through, our website does not constitute a part of this prospectus.

Implications of Being an Emerging Growth Company

As a company with less than $1.07 billion in revenue during our last fiscal year, we qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act, or JOBS Act, enacted in April 2012. An emerging growth company may take advantage of reduced reporting requirements that are otherwise applicable to public companies. These provisions include, but are not limited to:

- being permitted to present only two years of audited financial statements and only two years of related Management's Discussion and Analysis of Financial Condition and Results of Operations in this prospectus;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended;
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may take advantage of these provisions until the last day of our fiscal year following the fifth anniversary of the completion of this offering. However, if certain events occur prior to the end of such five-year period, including if we become a large accelerated filer, our annual gross revenue exceeds $1.07 billion or we issue more than $1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to the end of such five-year period.

We have elected to take advantage of certain of the reduced disclosure obligations in the registration statement of which this prospectus is a part and may elect to take advantage of other reduced reporting requirements in future filings. As a result, the information that we provide to our stockholders may be different than you might receive from other public reporting companies in which you hold equity interests.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

THE OFFERING

Common stock offered by us	shares
Common stock to be outstanding after this offering	shares (or shares if the underwriters exercise their over-allotment option in full)
Over-allotment option	shares
Use of proceeds	We intend to use the net proceeds of this offering to advance the preclinical and clinical development of ANVS-401 and for working capital and general corporate purposes. See "Use of Proceeds" in this prospectus for a more complete description of the intended use of proceeds from this offering.
Risk factors	See "Risk Factors" beginning on page and the other information included in this prospectus for a discussion of factors you should consider carefully before deciding to invest in our common stock.
Proposed Nasdaq Capital Market symbol	"ANVS"

The number of shares of our common stock to be outstanding after this offering is based on shares of our common stock outstanding as of , 2019, which includes shares of restricted stock subject to repurchase, and excludes:

- 495,025 shares of common stock issuable upon exercise of stock options outstanding as of , 2019, at a weighted-average exercise price of $0.13 per share; and
- 533,746 shares of our common stock that are available for future issuance under our 2018 Incentive Award Plan, or shares that will become available under our 2019 Plan, which will become effective in connection with this offering.

Unless otherwise indicated, this prospectus reflects and assumes the following:

- the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 5,763,881 shares of our common stock upon the closing of this offering;
- the issuance of shares of our common stock upon conversion of the $530,000 principal amount of our convertible promissory notes upon the closing of this offering into shares of our common stock at a 20% discount to the public offering price;
- no exercise of outstanding options described above after March 31, 2019;
- a 1-for- reverse stock split of our common stock prior to the effectiveness of the registration statement of which this prospectus forms a part;
- the filing of our restated certificate of incorporation and the adoption of our amended and restated bylaws, which will occur upon the closing of this offering; and
- no exercise by the underwriters of their over-allotment option or the warrants to purchase shares of our common stock at an exercise price per share equal to % of the initial public offering price per share or $, based on an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, that may, under certain circumstances, be issued to the representatives of the underwriters in connection with this offering.

SUMMARY FINANCIAL DATA

You should read the following summary financial data together with our financial statements and the related notes appearing at the end of this prospectus and the "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of this prospectus. We have derived the statement of operations data for the years ended December 31, 2018 and December 31, 2017 from our audited financial statements appearing at the end of this prospectus. We have derived the statement of operations data for the three months ended March 31, 2019 and 2018 and the balance sheet data as of March 31, 2019 from our unaudited interim financial statements appearing at the end of this prospectus. The unaudited interim financial statements have been prepared on the same basis as the audited financial statements and reflect, in the opinion of management, all adjustments of a normal, recurring nature that are necessary for a fair presentation of the unaudited interim financial statements. Our historical results are not necessarily indicative of results that should be expected in any future period, and our results for any interim period are not necessarily indicative of results that should be expected for any full year.

In thousands, except share and per share data	Year Ended December 31, 2018	Year Ended December 31, 2017	Three Months Ended March 31, 2019	Three Months Ended March 31, 2018
			(Unaudited)	
Statement of Operations Data:				
Operating expenses:				
Research and development	$ 111.6	$ 273.4	$ 6.0	$ 57.8
General and administrative	602.3	409.0	180.8	132.1
Total operating expenses	713.9	682.4	186.8	189.9
Loss from operations	(713.9)	(682.4)	(186.8)	(189.9)
Other income (expense):				
Interest income (expense), net	—	0.1	(4.1)	—
Income tax expense (benefit)	—	—	—	—
Net loss	$ (713.9)	$ (682.3)	$ (190.9)	$ (189.9)
Net loss per common share—basic and diluted(1)	$ (1.84)	$ (1.90)	$ (0.48)	$ (0.51)
Weighted average common shares outstanding—basic and diluted(1)	388,612	358,599	395,653	375,653
Pro forma net loss per common share—basic and diluted (unaudited)(2)	$ (0.12)		$ (0.03)	
Pro forma weighted average common shares outstanding (unaudited)(2)	6,152,493		6,159,534	

	As of March 31, 2019		
	Actual (Unaudited)	Pro Forma(2) (Unaudited)	Pro Forma As Adjusted(3) (Unaudited)
Balance Sheet Data:			
Cash and cash equivalents	$ 336.6	$ 336.6	
Working capital	$ (207.6)	$ (207.6)	
Total assets	$ 431.3	$ 431.3	
Convertible debt, net of unamortized deferred financing fees and debt discount	$ 495.9	$ 495.9	
Redeemable convertible preferred stock	$ 7,077.0	$ —	
Stockholders' equity (deficit)	$ (7,775.9)	$ (699.0)	

(1) See note 9 to our audited financial statements and note 10 to our unaudited interim financial statements appearing at the end of this prospectus for further details on the calculation of basic and diluted net loss per common share.

(2) Reflects the automatic conversion of all outstanding shares of our preferred stock into 5,763,881 shares of our common stock upon the closing of this offering.

(3) Reflects the effect of our issuance and sale of shares of our common stock in this offering at an assumed initial public offering price of $ share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us and the issuance of shares of our common stock upon conversion of the $530,000 principal amount of our convertible promissory notes upon the closing of this offering into shares of our common stock at a 20% discount to the public offering price.

A $1.00 decrease in the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would decrease the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' equity by approximately $, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. At an initial public offering price of $ per share, the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' equity would increase by approximately $, assuming the number of shares offered by us, as set forth on the cover page of the prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. A $1.00 increase in the initial public offering price above $ per share would increase the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' equity by approximately $, assuming the number of shares offered by us, as set forth on the cover of the prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offer expenses payable by us. A decrease of shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would decrease the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' equity by approximately $, assuming no change in the assumed initial public offering price per share and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase of shares in the number of shares offered by us, as set forth on the cover page of this prospectus, to shares would increase the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' equity by approximately $, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us and assuming the assumed initial public offering price stays the same. An increase in the number of shares offered by us, as set forth on the cover page of this prospectus, to shares would increase the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' equity by approximately $, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us and assuming the assumed initial public offering price stays the same. Each increase of in the number of shares offered by us above would increase the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' equity by approximately $, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us and assuming the initial public offering price stays the same.

RISK FACTORS

You should carefully consider the risks and uncertainties described below and the other information in this prospectus before making an investment in our common stock. Our business, financial condition, results of operations or prospects could be materially and adversely affected if any of these risks occurs, and as a result, the market price of our common stock could decline, and you could lose all or part of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred losses since inception and anticipate that we will continue to incur losses for the foreseeable future. We are not currently profitable, and we may never achieve or sustain profitability.

We are a clinical stage biopharmaceutical company with a limited operating history and have incurred losses since our formation. We incurred net losses of $0.7 million for each of the years ended December 31, 2018 and 2017, and $0.2 million for each of the three month periods ended March 31, 2019 and 2018. As of March 31, 2019, we had an accumulated loss of $8.0 million. We have not commercialized any products and have never generated revenue from the commercialization of any product. To date, we have devoted most of our financial resources to research and development, including our preclinical and clinical work, and to intellectual property.

We expect to incur significant additional operating losses for the next several years, at least, as we advance ANVS-401 and any other product candidate through clinical development, complete clinical trials, seek regulatory approval and commercialize the drug or any other product candidate, if approved. The costs of advancing product candidates into each clinical phase tend to increase substantially over the duration of the clinical development process. Therefore, the total costs to advance any of our product candidates to marketing approval in even a single jurisdiction will be substantial. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to begin generating revenue from the commercialization of any products or achieve or maintain profitability. Our expenses will also increase substantially if and as we:

- commence our two Phase 3 trials in AD-DS and in early PD, or conduct clinical trials for any other product candidates;
- are required by the U.S. Food and Drug Administration, or FDA, to complete two Phase 3 trials to support a New Drug Application, or NDA, for ANVS-401 in AD-DS or in PD;
- establish a sales, marketing and distribution infrastructure to commercialize our drug, if approved, and for any other product candidates for which we may obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, scientific and commercial personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts, as well as to support our transition to a public reporting company; and
- acquire or in-license or invent other product candidates or technologies.

Furthermore, our ability to successfully develop, commercialize and license any product candidates and generate product revenue is subject to substantial additional risks and uncertainties, as described under "—Risks Related to Development, Clinical Testing, Manufacturing and Regulatory Approval" and "—Risks Related to Commercialization." As a result, we expect to continue to incur net losses and negative cash flows for the foreseeable future. These net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. The amount of

our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. If we are unable to develop and commercialize one or more product candidates, either alone or through collaborations, or if revenues from any product that receives marketing approval are insufficient, we will not achieve profitability. Even if we do achieve profitability, we may not be able to sustain profitability or meet outside expectations for our profitability. If we are unable to achieve or sustain profitability or to meet outside expectations for our profitability, the value of our common stock will be materially and adversely affected.

Even if this offering is successful, we will require additional capital to fund our operations, and if we fail to obtain necessary financing, we may not be able to complete the development and commercialization of ANVS-401.

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts to advance the clinical development of ANVS-401 and launch and commercialize ANVS-401, if we receive regulatory approval. We will require additional capital for the further development and potential commercialization of ANVS-401 and may also need to raise additional funds sooner to pursue a more accelerated development of ANVS-401. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We believe that the net proceeds from this offering together with our existing cash and cash equivalents as of March 31, 2019, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 18 months. We have based this estimate on assumptions that may prove to be wrong, and we could deploy our available capital resources sooner than we currently expect. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to the:

- initiation, progress, timing, costs and results of preclinical studies and clinical trials, including patient enrollment in such trials, for ANVS-401 or any other future product candidates;
- clinical development plans we establish for ANVS-401 and any other future product candidates;
- obligation to make royalty and non-royalty sublicense receipt payments to third-party licensors, if any, under our licensing agreements;
- number and characteristics of product candidates that we discover or in-license and develop;
- outcome, timing and cost of regulatory review by the FDA and comparable foreign regulatory authorities, including the potential for the FDA or comparable foreign regulatory authorities to require that we perform more studies than those that we currently expect;
- costs of filing, prosecuting, defending and enforcing any patent claims and maintaining and enforcing other intellectual property rights;
- effects of competing technological and market developments;
- costs and timing of the implementation of commercial-scale manufacturing activities; and
- costs and timing of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval.

If we are unable to expand our operations or otherwise capitalize on our business opportunities due to a lack of capital, our ability to become profitable will be compromised.

We, as well as our independent registered public accounting firm have expressed substantial doubt about our ability to continue as a going concern.

Our recurring losses from operations raise substantial doubt about our ability to continue as a going concern. As a result, our independent registered public accounting firm included an explanatory paragraph in its report on our financial statements for the year ended December 31, 2018 with respect to this uncertainty. Our ability to continue as a going concern will require us to obtain additional funding. We believe that the net proceeds from this offering and our existing cash and cash equivalents will be sufficient to fund our current operating plans through at least the next 18 months. We have based these estimates, however, on assumptions that may prove to be wrong, and we could spend our available financial resources much faster than we currently expect and need to raise additional funds sooner than we anticipate. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce or eliminate our research and development programs and commercialization efforts.

Raising additional capital may cause dilution to our stockholders, including purchasers of common stock in this offering, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial revenue, we may finance our cash needs through a combination of equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or other sources. We do not currently have any committed external source of funds. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, intellectual property, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate product candidate development or future commercialization efforts.

We have a limited operating history and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.

We were established and began operations in 2008. Our operations to date have been limited to financing and staffing our company, licensing product candidates, conducting preclinical and clinical studies of ANVS-401 for treatment of AD-DS, AD and PD and for understanding its mechanism of action and its capability of stopping the toxic cascade that leads to nerve cell death. We have further tested ANVS-401 in clinical trials for safety and proof-of-concept. We have not yet demonstrated the ability to successfully complete a large-scale, pivotal clinical trial, obtain marketing approval, manufacture a commercial scale product, arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

In addition, as a business with a limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will eventually need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition and, as a result, our business may be adversely affected.

As we continue to build our business, we expect our financial condition and operating results may fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any particular quarterly or annual period as indications of future operating performance.

Our ability to use our net operating loss carryforwards to offset future taxable income may be subject to certain limitations.

As of March 31, 2019, we had net operating loss carryforwards, or NOLs, of $3.6 million for federal income tax purposes and $3.6 million for state income tax purposes, which may be available to offset our future taxable income, if any, and begin to expire in various amounts in 2028. NOLs of $0.8 million generated after December 31, 2017 are not subject to expiration but are limited to 80% of taxable income in future years. In general, under Sections 382 and 383 of the U.S. Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to use its pre-change NOLs to offset future taxable income. Due to previous ownership changes, or if we undergo an ownership change in connection with or after this offering, our ability to use our NOLs could be limited by Section 382 of the Code. Future changes in our stock ownership, some of which are outside of our control, could result in an ownership change under Sections 382 and 383 of the Code. Furthermore, our ability to use NOLs of companies that we may acquire in the future may be subject to limitations. For these reasons, we may not be able to use a material portion of the NOLs, even if we attain profitability.

Risks Related to Development, Clinical Testing, Manufacturing and Regulatory Approval

We are heavily dependent on the success of ANVS-401, our most advanced product candidate, which is still under clinical development, and if this drug does not receive regulatory approval or is not successfully commercialized, our business may be harmed.

We do not have any products that have gained regulatory approval. Currently, our lead clinical stage product candidate is ANVS-401. As a result, our business is dependent on our ability to successfully complete clinical development of, obtain regulatory approval for, and, if approved, successfully commercialize ANVS-401 in a timely manner. We cannot commercialize ANVS-401 in the United States without first obtaining regulatory approval from the FDA; similarly, we cannot commercialize ANVS-401 outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of ANVS-401 for a target indication, we must demonstrate with substantial evidence gathered in preclinical studies and clinical trials, generally including two adequate and well-controlled clinical trials, and, with respect to approval in the United States, to the satisfaction of the FDA, that ANVS-401 is safe and effective for use for that target indication and that the manufacturing facilities, processes and controls are adequate. Even if ANVS-401 were to successfully obtain approval from the FDA and comparable foreign regulatory authorities, any approval might contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, or may be subject to burdensome post-approval study or risk management requirements. If we are unable to obtain regulatory approval for ANVS-401 in one or more jurisdictions, or any approval contains significant limitations, we may not be able to obtain sufficient funding or generate sufficient revenue to continue the development of any other product candidate that we may in-license, develop or acquire in the future. Furthermore, even if we obtain regulatory approval for ANVS-401, we will still need to develop

a commercial organization, establish commercially viable pricing and obtain approval for adequate reimbursement from third-party and government payors. If we are unable to successfully commercialize ANVS-401, we may not be able to earn sufficient revenue to continue our business

Clinical trials are expensive, time-consuming and difficult to design and implement, and involve an uncertain outcome.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Because the results of preclinical studies and early clinical trials are not necessarily predictive of future results, ANVS-401 and our other compounds may not have favorable results in later preclinical and clinical studies or receive regulatory approval. We may experience delays in initiating and completing any clinical trials that we intend to conduct, and we do not know whether planned clinical trials, including our Phase 2a trial for PD will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, or at all. Clinical trials can be delayed for a variety of reasons, including delays related to:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical studies;
- obtaining regulatory approval to commence a trial;
- reaching an agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining Institutional Review Board, or IRB, approval at each site, or Independent Ethics Committee, or IEC, approval at sites outside the United States;
- recruiting suitable patients to participate in a trial in a timely manner and in sufficient numbers;
- having patients complete a trial or return for post-treatment follow-up;
- imposition of a clinical hold by regulatory authorities, including as a result of unforeseen safety issues or side effects or failure of trial sites to adhere to regulatory requirements or follow trial protocols;
- clinical sites deviating from trial protocol or dropping out of a trial;
- addressing patient safety concerns that arise during the course of a trial;
- adding a sufficient number of clinical trial sites; or
- manufacturing sufficient quantities of product candidate for use in clinical trials.

We could also encounter delays if a clinical trial is suspended or terminated by us, the IRBs or IECs of the institutions in which such trials are being conducted, the Data Safety Monitoring Board, or DSMB, for such trial or the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Furthermore, we rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and, while we have agreements governing their committed activities, we have limited influence over their actual performance, as described in "—Risks Related to Our Dependence on Third Parties."

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for ANVS-401 or any other product candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that we will never obtain regulatory approval for ANVS-401 or any other product candidate. We are not permitted to market any of our product candidates in the United States until we receive regulatory approval of a New Drug Application (NDA) from the FDA.

- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates, or other products containing the active ingredient in our product candidates;
- negative or ambiguous results from our clinical trials or results that may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere, and we may be required to conduct additional clinical trials;
- the FDA or comparable foreign authorities may disagree regarding the formulation, labeling and/or the specifications of our product candidates;
- the FDA or comparable foreign regulatory authorities may fail to approve or find deficiencies with the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Prior to obtaining approval to commercialize a product candidate in the United States or abroad, we must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or foreign regulatory agencies, that such product candidates are safe and effective for their intended uses. Results from preclinical studies and clinical trials can be interpreted in different ways. Even if we believe the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. For diseases like AD-DS, AD and PD, the FDA has stated that one single Phase 3 trial is adequate for approval, if it demonstrates robust and unquestionable efficacy. However, the circumstances under which a single adequate and controlled study can be used as the sole basis of demonstrating efficacy of a drug are exceptional.

The FDA or any foreign regulatory bodies can delay, limit or deny approval of our product candidates or require us to conduct additional preclinical or clinical testing or abandon a program for many reasons, including:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- the FDA or comparable foreign regulatory authorities may disagree with our safety interpretation of our drug;
- the FDA or comparable foreign regulatory authorities may disagree with our efficacy interpretation of our drug;
- the FDA or comparable foreign regulatory authorities may regard our CMC package as inadequate.

Of the large number of drugs in development, only a small percentage successfully complete the regulatory approval processes and are commercialized. This lengthy approval process, as well as the unpredictability of future clinical trial results, may result in our failing to obtain regulatory approval to market ANVS-401 or another product candidate, which would significantly harm our business, results of operations and prospects.

In addition, the FDA or the applicable foreign regulatory agency also may approve a product candidate for a more limited indication or patient population than we originally requested, and the FDA or applicable foreign regulatory agency may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

We have concentrated our research and development efforts on the treatment of AD and PD, diseases that have seen limited success in drug development. Further, ANVS-401 is based on a new approach to treating AD and PD, which makes it difficult to predict the time and cost of development and subsequent obtaining of regulatory approval.

Efforts by biopharmaceutical and pharmaceutical companies in treating AD and PD have seen limited success in drug development, and there are no FDA-approved disease modifying therapeutic options available for patients with AD and PD. We cannot be certain that our approach will lead to the development of approvable or marketable products. The only drugs approved by the FDA to treat AD and PD to date address the disease's symptoms. No new treatments have been approved for AD since 2003. Since 2003, over 500 clinical studies have been completed and no compound has shown efficacy. AD drug candidates have the highest failure rate of 100%, compared to 50% to 80% for all other drug candidates. As a result, the FDA has a limited set of products to rely on in evaluating ANVS-401. This could result in a longer than expected regulatory review process, increased expected development costs or the delay or prevention of commercialization of ANVS-401 for the treatment of AD and PD.

Enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. We may encounter delays in enrolling, or be unable to enroll, a sufficient number of patients to complete any of our clinical trials, and even once enrolled, we may be unable to retain a

sufficient number of patients to complete any of our trials. Patient enrollment and retention in clinical trials depends on many factors, including:

- the patient eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the nature of the trial protocol;
- the existing body of safety and efficacy data with respect to the product candidate;
- the proximity of patients to clinical sites;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;
- competing clinical trials being conducted by other companies or institutions;
- our ability to maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

Results of preclinical studies, early clinical trials or analyses may not be indicative of results obtained in later trials.

The results of preclinical studies, early clinical trials or analyses of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. In addition, conclusions based on promising data from analyses of clinical results may be shown to be incorrect when implemented in prospective clinical trials. Even if our clinical trials for ANVS-401 are completed as planned, we cannot be certain that their results will support the safety and efficacy sufficient to obtain regulatory approval.

Interim "top-line" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim "top-line" or preliminary data from our clinical studies. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

Our product candidates may cause serious adverse events or undesirable side effects, which may delay or prevent marketing approval, or, if approved, require them to be taken off the market, require them to include safety warnings or otherwise limit their sales.

Serious adverse events or undesirable side effects caused by ANVS-401 or any other product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Results of any clinical trial we conduct could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Patients treated with ANVS-401 to date, at high doses have experienced adverse events that include nausea and vomiting.

If unacceptable side effects arise in the development of our product candidates, we, the FDA or the IRBs at the institutions in which our studies are conducted, or the DSMB, if constituted for our clinical trials, could recommend a suspension or termination of our clinical trials, or the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of a product candidate for any or all targeted indications. In addition, drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete a trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly.

Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label, such as a "black box" warning or contraindication;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof;
- we may be required to implement a Risk Evaluation and Mitigation Strategy, or REMS, or create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of a product candidate, if approved, and could significantly harm our business, results of operations and prospects.

The market opportunities for ANVS-401, if approved, may be smaller than we anticipate.

We expect to initially seek approval for ANVS-401 for AD-DS, AD and PD in the US. Our estimates of market potential have been derived from a variety of sources, including scientific literature, patient foundations and market research, and may prove to be incorrect. Even if we obtain significant market share for any product candidate, if approved, if the potential target populations are small, we may never achieve profitability without obtaining marketing approval for additional indications.

We have never obtained marketing approval for a product candidate and we may be unable to obtain, or may be delayed in obtaining, marketing approval for any of our product candidates.

We have never obtained marketing approval for a product candidate. It is possible that the FDA may refuse to accept for substantive review any NDAs that we submit for our product candidates or may conclude after review of our data that our application is insufficient to obtain marketing approval of our product candidates. If the FDA does not accept or approve our NDAs for our product candidates, it may require that we conduct additional clinical, preclinical or manufacturing validation studies and submit that data before it will reconsider our applications. Depending on the extent of these or any other FDA-required studies, approval of any NDA that we submit may be delayed or may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA to approve our NDAs.

Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing our product candidates, generating revenues and achieving and sustaining profitability. If any of these outcomes occur, we may be forced to abandon our development efforts for our product candidates, which could significantly harm our business.

Even if we obtain FDA approval for ANVS-401 or any other product candidate in the United States, we may never obtain approval for or commercialize ANVS-401 or any other product candidate in any other jurisdiction, which would limit our ability to realize their full market potential.

In order to market any products in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a country-by-country basis regarding safety and efficacy. Approval by the FDA in the United States does not ensure approval by regulatory authorities in other countries or jurisdictions. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval elsewhere. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country.

Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and increased costs for us and require additional preclinical studies or clinical trials which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved for sale in any jurisdiction, including in international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of any product we develop will be unrealized.

Even if we obtain regulatory approval for ANVS-401 or any product candidate, we will still face extensive and ongoing regulatory requirements and obligations and any product candidates, if approved, may face future development and regulatory difficulties.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, packaging, distribution, adverse event reporting, storage, recordkeeping, export, import, advertising and promotional activities for such product, among other things, will be subject to extensive and ongoing requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, establishment registration and drug listing requirements, continued compliance with current Good Manufacturing Practice, or cGMP, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements

regarding the distribution of samples to physicians and recordkeeping and Good Clinical Practice, or GCP, requirements for any clinical trials that we conduct post-approval.

Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product candidate may be marketed or to the conditions of approval, including a requirement to implement a REMS. If any of our product candidates receive marketing approval, the accompanying label may limit the approved indicated use of the product candidate, which could limit sales of the product candidate. The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use, and if we market our products for uses beyond their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act, or FDCA, relating to the promotion of prescription drugs may lead to FDA enforcement actions and investigations alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on manufacturing such products;
- restrictions on the labeling or marketing of products;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Further, the FDA's policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the current presidential administration may impact our business and industry. Namely, the current presidential administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these executive actions will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

We may seek a Breakthrough Therapy designation for ANVS-401 from the FDA at the end of the two Phase 2a studies in AD and PD, respectively. However, we might not receive such designation, and even if we do, such designation may not lead to a faster development or regulatory review or approval process.

We may seek a Breakthrough Therapy designation for ANVS-401 or one or more of our other product candidates. A Breakthrough Therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA may also be eligible for priority review if supported by clinical data at the time the NDA is submitted to the FDA.

Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such designation. Even if we receive Breakthrough Therapy designation, the receipt of such designation for a product candidate may not result in a faster development or regulatory review or approval process compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Potential product liability lawsuits against us could cause us to incur substantial liabilities and limit commercialization of any products that we may develop.

The use of ANVS-401 or any other product candidates we may develop in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation and significant negative media attention;
- withdrawal of participants from our clinical trials;
- significant costs to defend the litigation;

- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- inability to commercialize ANVS-401 or any other product candidate;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- decreased market demand for any product; and
- loss of revenue.

The product liability insurance we currently carry, and any additional product liability insurance coverage we acquire in the future, may not be sufficient to reimburse us for any expenses or losses we may suffer. In connection with our Phase 1 clinical studies, we carried insurance of $2.0 million in the aggregate for product liability claims in the United States. We intend to acquire insurance coverage to include larger clinical studies, different countries and sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. A successful product liability claim, or series of claims, brought against us could cause our share price to decline and, if judgments exceed our insurance coverage, could adversely affect the results of our operations and business, including preventing or limiting the commercialization of any product candidates we develop.

Risks Related to Commercialization

We face significant competition from other biotechnology and pharmaceutical companies and our operating results will suffer if we fail to compete effectively.

The biopharmaceutical and pharmaceutical industries are highly competitive and subject to significant and rapid technological change. Our success is highly dependent on our ability to acquire, develop, and obtain marketing approval for new products on a cost-effective basis and to market them successfully. If ANVS-401 is approved, we will face intense competition from a variety of businesses, including large, fully integrated pharmaceutical companies, specialty pharmaceutical companies and biopharmaceutical companies in the United States and other jurisdictions. These organizations may have significantly greater resources than we do and may conduct similar research; seek patent protection; and establish collaborative arrangements for research, development, manufacturing and marketing of products that may compete with us.

Our competitors may, among other things:

- have significantly greater name recognition, financial, manufacturing, marketing, drug development, technical, and human resources than we do, and future mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors;
- develop and commercialize products that are safer, more effective, less expensive, more convenient, or easier to administer, or have fewer or less severe effects;
- obtain quicker regulatory approval;
- implement more effective approaches to sales and marketing; or
- form more advantageous strategic alliances.

Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel; establishing clinical trial sites and patient registration; and in acquiring technologies complementary to, or necessary for,

our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, or are more convenient or are less expensive than ANVS-401. Our competitors may also obtain FDA or other regulatory approval for their product candidates more rapidly than we may obtain approval for ANVS-401, which could result in our competitors establishing or strengthening their market position before we are able to enter the market.

The successful commercialization of ANVS-401 and any other product candidate we develop will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels, and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

The availability and adequacy of coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford prescription medications such as ANVS-401, if approved. Our ability to achieve acceptable levels of coverage and reimbursement for products by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize our drug and any other product candidates we develop. Assuming we obtain coverage for our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States or elsewhere will be available for our product candidates or any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar, or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and offer to reimburse patients only for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing drugs may limit the amount we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates and may not be able to obtain a satisfactory financial return on our product candidates.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models in the United States for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will

be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases at short notice, and we believe that changes in these rules and regulations are likely.

We may also be subject to extensive governmental price controls and other market regulations outside of the United States, and we believe the increasing emphasis on cost-containment initiatives in other countries have and will continue to put pressure on the pricing and usage of medical products. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products but monitor and control company profits.

Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.

Even if ANVS-401 or any product candidate we develop receives marketing approval, it may fail to achieve market acceptance by physicians, patients, third-party payors or others in the medical community necessary for commercial success.

If ANVS-401 or any product candidate we develop receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If it does not achieve an adequate level of acceptance, we may not generate significant product revenues or become profitable. The degree of market acceptance of our product candidates, if approved, will depend on a number of factors, including but not limited to:

- the efficacy and potential advantages compared to alternative treatments;
- effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments, including any similar generic treatments;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our product together with other medications.

Because we expect sales of our product candidates, if approved, to generate substantially all of our revenues for the foreseeable future, the failure of our product candidates to find market acceptance would harm our business and could require us to seek additional financing.

If we are unable to establish sales, marketing and distribution capabilities either on our own or in collaboration with third parties, we may not be successful in commercializing ANVS-401, if approved.

We do not have any infrastructure for the sales, marketing or distribution of ANVS-401, and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. In order to market and successfully commercialize our drug or any product candidate we develop, if approved, we must build our sales, distribution, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. We expect to build a focused sales, distribution and marketing infrastructure to market ANVS-401, if approved, in the United States and Europe. There are significant expenses and risks involved with establishing our own sales, marketing and distribution capabilities, including our ability to hire, retain and appropriately incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities could delay any product launch, which would adversely impact the commercialization of that product. For example, if the commercial launch of ANVS-401 for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or attain adequate numbers of physicians to prescribe our products; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

We do not anticipate having the resources in the foreseeable future to allocate to the sales and marketing of our product candidates, if approved, in certain markets overseas. Therefore, our future success will depend, in part, on our ability to enter into and maintain collaborative relationships for such capabilities, the collaborator's strategic interest in a product and such collaborator's ability to successfully market and sell the product. We intend to pursue collaborative arrangements regarding the sale and marketing of ANVS-401, if approved, for certain markets overseas; however, we cannot assure you that we will be able to establish or maintain such collaborative arrangements, or if able to do so, that they will have effective sales forces. To the extent that we depend on third parties for marketing and distribution, any revenues we receive will depend upon the efforts of such third parties, and there can be no assurance that such efforts will be successful.

If we are unable to build our own sales force or negotiate a collaborative relationship for the commercialization of ANVS-401, we may be forced to delay the potential commercialization of the drug or reduce the scope of our sales or marketing activities. If we need to increase our expenditures to fund commercialization activities for ANVS-401 we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. We may also have to enter into collaborative arrangements for ANVS-401 at an earlier stage than otherwise would be ideal and we may be required to relinquish rights to it or otherwise agree to terms unfavorable to us. Any of these occurrences may have an adverse effect on our business, operating results and prospects.

If we are unable to establish adequate sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates and may never become profitable. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

A variety of risks associated with operating internationally could materially adversely affect our business.

We currently have no international operations, but our business strategy includes potentially expanding internationally if any of our product candidates receive regulatory approval. Doing business internationally involves a number of risks, including but not limited to:

- multiple, conflicting and changing laws and regulations, such as privacy regulations, tax laws, export and import restrictions, employment laws, regulatory requirements and other governmental approvals, permits and licenses;
- failure by us to obtain and maintain regulatory approvals for the use of our products in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection and enforcing our intellectual property;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors or patient self-pay systems;
- limits in our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products and exposure to foreign currency exchange rate fluctuations;
- natural disasters, political and economic instability, including wars, terrorism and political unrest, outbreak of disease, boycotts, curtailment of trade and other business restrictions;
- certain expenses including, among others, expenses for travel, translation and insurance; and
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act, its books and records provisions, or its anti-bribery provisions.

Any of these factors could significantly harm any future international expansion and operations and, consequently, our results of operations.

Risks Related to Our Dependence on Third Parties

Our employees and independent contractors, including principal investigators, CROs, consultants, vendors, and any third parties we may engage in connection with development and commercialization, may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

Our employees and independent contractors, including principal investigators, consultants, vendors and any third parties we may engage in connection with development and commercialization of our product candidates, could engage in misconduct, including intentional, reckless or negligent conduct or unauthorized activities that violate: the laws and regulations of the FDA or other similar regulatory

requirements of other authorities, including those laws that require the reporting of true, complete and accurate information to such authorities; manufacturing standards; data privacy, security, fraud and abuse and other healthcare laws and regulations; or laws that require the reporting of true, complete and accurate financial information and data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creation of fraudulent data in preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid, other U.S. federal healthcare programs or healthcare programs in other jurisdictions, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

We currently rely on third-party contract manufacturing organizations, or CMOs, for the production of clinical supply of ANVS-401 and intend to rely on CMOs for the production of commercial supply of ANVS-401, if approved. Our dependence on CMOs may impair the development and commercialization of the drug, which would adversely impact our business and financial position.

We have limited personnel with experience in manufacturing, and we do not own facilities for manufacturing. Instead, we rely on and expect to continue to rely on CMOs for the supply of cGMP grade clinical trial materials and commercial quantities of ANVS-401 and any product candidates we develop, if approved. Reliance on CMOs may expose us to more risk than if we were to manufacture our product candidates ourselves. We intend to have manufactured a sufficient clinical supply of ANVS-401 drug substance to enable us to complete our clinical trials, and we have also engaged a CMO to provide clinical and commercial supply of the drug product.

The facilities used to manufacture our product candidates must be inspected by the FDA and comparable foreign authorities. While we provide oversight of manufacturing activities, we do not and will not control the execution of manufacturing activities by, and are or will be essentially dependent on, our CMOs for compliance with cGMP requirements for the manufacture of our product candidates. As a result, we are subject to the risk that our product candidates may have manufacturing defects that we have limited ability to prevent. If a CMO cannot successfully manufacture material that conforms to our specifications and the regulatory requirements, we will not be able to secure or maintain regulatory approval for the use of our product candidates in clinical trials, or for commercial distribution of our product candidates, if approved. In addition, we have limited control over the ability of our CMOs to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or comparable foreign regulatory authority finds deficiencies with or does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval or finds deficiencies in the future, we may need to find alternative manufacturing facilities, which would delay our development program and significantly impact our ability to develop, obtain regulatory approval for or commercialize our product candidates, if approved. In addition, any failure to achieve and maintain compliance with

these laws, regulations and standards could subject us to the risk that we may have to suspend the manufacture of our product candidates or that obtained approvals could be revoked. Furthermore, CMOs may breach existing agreements they have with us because of factors beyond our control. They may also terminate or refuse to renew their agreement at a time that is costly or otherwise inconvenient for us. If we were unable to find an adequate CMO or another acceptable solution in time, our clinical trials could be delayed, or our commercial activities could be harmed.

We rely on and will continue to rely on CMOs to purchase from third-party suppliers the raw materials necessary to produce our product candidates. We do not and will not have control over the process or timing of the acquisition of these raw materials by our CMOs. Moreover, we currently do not have any agreements for the production of these raw materials. Supplies of raw material could be interrupted from time to time and we cannot be certain that alternative supplies could be obtained within a reasonable timeframe, at an acceptable cost, or at all. In addition, a disruption in the supply of raw materials could delay the commercial launch of our product candidates, if approved, or result in a shortage in supply, which would impair our ability to generate revenues from the sale of our product candidates. Growth in the costs and expenses of raw materials may also impair our ability to cost effectively manufacture our product candidates. There are a limited number of suppliers for the raw materials that we may use to manufacture our product candidates and we may need to assess alternative suppliers to prevent a possible disruption of the manufacture of our product candidates.

Finding new CMOs or third-party suppliers involves additional cost and requires our management's time and focus. In addition, there is typically a transition period when a new CMO commences work. Although we generally have not, and do not intend to, begin a clinical trial unless we believe we have on hand, or will be able to obtain, a sufficient supply of our product candidates to complete the clinical trial, any significant delay in the supply of our product candidates or the raw materials needed to produce our product candidates, could considerably delay conducting our clinical trials and potential regulatory approval of our product candidates.

As part of their manufacture of our product candidates, our CMOs and third-party suppliers are expected to comply with and respect the proprietary rights of others. If a CMO or third-party supplier fails to acquire the proper licenses or otherwise infringes the proprietary rights of others in the course of providing services to us, we may have to find alternative CMOs or third-party suppliers or defend against claims of infringement, either of which would significantly impact our ability to develop, obtain regulatory approval for or commercialize our product candidates, if approved.

We intend to rely on third parties to conduct, supervise and monitor our clinical trials. If those third parties do not successfully carry out their contractual duties, or if they perform in an unsatisfactory manner, it may harm our business.

We rely, and will continue to rely, on CROs, CRO-contracted vendors and clinical trial sites to ensure the proper and timely conduct of our clinical trials, including our two Phase 2 trials of ANVS-401. Our reliance on CROs for clinical development activities limits our control over these activities, but we remain responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards.

We and our CROs will be required to comply with the Good Laboratory Practice requirements for our preclinical studies and GCP requirements for our clinical trials, which are regulations and guidelines enforced by the FDA and are also required by comparable foreign regulatory authorities. Regulatory authorities enforce GCP requirements through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements. In addition, our clinical trials must be conducted with product produced under cGMP requirements. Accordingly, if our CROs fail to comply with these requirements, we may be required to repeat clinical trials, which would delay the regulatory approval process.

Our CROs are not our employees, and we do not control whether or not they devote sufficient time and resources to our clinical trials. Our CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other drug development activities, which could harm our competitive position. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for any other reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize any product candidate that we develop. As a result, our financial results and the commercial prospects for any product candidate that we develop would be harmed, our costs could increase, and our ability to generate revenue could be delayed.

If our relationship with any CROs terminate, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. Switching or adding additional CROs involves substantial cost and requires management's time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have an adverse impact on our business, financial condition and prospects.

- the number and type of our collaborations could adversely affect our attractiveness to future collaborators or acquirers; and

- the loss of, or a disruption in our relationship with, any one or more collaborators could harm our business.

If any collaborations do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research and development funding or milestone or royalty payments under such collaborations. If we do not receive the funding we expect under these agreements, our continued development of our product candidates could be delayed, and we may need additional resources to develop additional product candidates. All of the risks relating to product development, regulatory approval and commercialization described in this prospectus also apply to the activities of any collaborators and there can be no assurance that our collaborations will produce positive results or successful products on a timely basis or at all.

In addition, subject to its contractual obligations to us, if one of our collaborators is involved in a business combination or otherwise changes its business priorities, the collaborator might deemphasize

or terminate the development or commercialization of our product candidates. If a collaborator terminates its agreement with us, we may find it more difficult to attract new collaborators and the perception of our business and our stock price could be adversely affected.

We may in the future collaborate with additional pharmaceutical and biotechnology companies for development and potential commercialization of therapeutic products. We face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our programs, and our business may be materially and adversely affected.

Risks Related to Healthcare Laws and Other Legal Compliance Matters

Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates, if approved, and may affect the prices we may set.

In the United States and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- new requirements to report certain financial arrangements with physicians and teaching hospitals, including reporting "transfers of value" made or distributed to prescribers and other healthcare providers and reporting investment interests held by physicians and their immediate family members;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;

- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs and biologics that are inhaled, infused, instilled, implanted, or injected;
- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs thereby potentially increasing a manufacturer's Medicaid rebate liability;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- establishment of a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending;
- expansion of the entities eligible for discounts under the Public Health Service program; and
- a licensure framework for follow on biologic products.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. The current presidential administration and Congress will likely continue to seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA. This includes enactment of the Tax Cuts and Jobs Act, which, among other things, removes penalties for not complying with the ACA's individual mandate to carry health insurance. It is uncertain the extent to which any such changes may impact our business or financial condition.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, the Budget Control Act of 2011, resulted in aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2027 unless additional action is taken by Congress. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Additionally, the orphan drug tax credit was reduced as part of a broader tax reform. These new laws or any other similar laws introduced in the future may result in additional reductions in Medicare and other health care funding, which could negatively affect our customers and accordingly, our financial operations.

In addition, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been Congressional inquiries and proposed federal and state legislation designed to bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drugs. Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Individual states in the United States have also become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product

access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

In markets outside of the United States, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. We cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative action in the United States or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations, and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations, and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving, or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order, or recommendation of, any good, facility, item, or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. The U.S. federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other hand;

- the U.S. federal false claims and civil monetary penalties laws, including the civil False Claims Act, or FCA, which, among other things, impose criminal and civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. A claim includes "any request or demand" for money or property presented to the federal government. In addition, manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims;

- the U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose, among other things, specified requirements relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities subject to the rule, such as health plans, healthcare clearinghouses and healthcare providers as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;

- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;

- the U.S. federal legislation commonly referred to as the Physician Payments Sunshine Act, enacted as part of the ACA, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics, and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to the government information related to certain payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members; and

- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales, and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under such laws, it is possible that some of our business activities, including our consulting agreements and other relationships with physicians and other healthcare providers, some of whom receive stock or stock options as compensation for their services, could be subject to challenge under one or more of such laws. Ensuring that our current and future internal operations and business arrangements with third parties comply with applicable healthcare laws and regulations will involve

substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations.

If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, individual imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

Any clinical trial programs we conduct or research collaborations we enter into in the European Economic Area may subject us to the General Data Protection Regulation.

If we conduct clinical trial programs or enter into research collaborations in the European Economic Area, we may be subject to the General Data Protection regulation, or GDPR. The GDPR applies extraterritorially and implements stringent operational requirements for processors and controllers of personal data, including, for example, high standards for obtaining consent from individuals to process their personal data, robust disclosures to individuals, a comprehensive individual data rights regime, data export restrictions governing transfers of data from the European Union, or EU, to other jurisdictions, short timelines for data breach notifications, limitations on retention of information, increased requirements pertaining to health data, other special categories of personal data and coded data and additional obligations if we contract third-party processors in connection with the processing of personal data. The GDPR provides that EU member states may establish their own laws and regulations limiting the processing of personal data, including genetic, biometric or health data, which could limit our ability to use and share personal data or could cause our costs to increase. If our or our partners' or service providers' privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and/or fines of up to 20 million Euros or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, as well as compensation claims by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill.

We are subject to environmental, health and safety laws and regulations, and we may become exposed to liability and substantial expenses in connection with environmental compliance or remediation activities.

Our operations, including our development, testing and manufacturing activities, are subject to numerous environmental, health and safety laws and regulations. These laws and regulations govern, among other things, the controlled use, handling, release and disposal of and the maintenance of a registry for, hazardous materials and biological materials, such as chemical solvents, human cells, carcinogenic compounds, mutagenic compounds and compounds that have a toxic effect on reproduction, laboratory procedures and exposure to blood-borne pathogens. If we fail to comply with such laws and regulations, we could be subject to fines or other sanctions.

As with other companies engaged in activities similar to ours, we face a risk of environmental liability inherent in our current and historical activities, including liability relating to releases of or exposure to hazardous or biological materials. Environmental, health and safety laws and regulations are becoming more stringent. We may be required to incur substantial expenses in connection with future environmental compliance or remediation activities, in which case, the production efforts of our third-party manufacturers or our development efforts may be interrupted or delayed.

Recent U.S. tax legislation may materially adversely affect our financial condition, results of operations and cash flows.

Recently-enacted U.S. tax legislation has significantly changed the U.S. federal income taxation of U.S. corporations, including by reducing the U.S. corporate income tax rate, limiting interest deductions, and revising the rules governing NOLs. Many of these changes are effective immediately, without any transition periods or grandfathering for existing transactions. The legislation is unclear in many respects and could be subject to potential amendments and technical corrections, as well as interpretations and implementing regulations by the Treasury and Internal Revenue Service, or the IRS, any of which could lessen or increase certain adverse impacts of the legislation. In addition, it is unclear how these U.S. federal income tax changes will affect state and local taxation, which often uses federal taxable income as a starting point for computing state and local tax liabilities.

The reduction of the corporate tax rate under the legislation may cause a reduction in the economic benefit of our NOLs and other deferred tax assets available to us. Furthermore, under the legislation, although the treatment of tax losses generated before December 31, 2017 has generally not changed, tax losses generated in calendar year 2018 and beyond will only be able to offset 80% of taxable income. This change may require us to pay federal income taxes in future years despite generating a loss for federal income tax purposes in prior years.

While some of the changes made by the tax legislation may adversely affect us in one or more reporting periods and prospectively, other changes may be beneficial on a going-forward basis. We intend to work with our tax advisors and auditors to determine the full impact that the recent tax legislation as a whole will have on us. We urge our investors to consult with their legal and tax advisors with respect to such legislation.

Risks Related to Our Intellectual Property

If we fail to comply with our obligations under our existing intellectual property license, we risk losing the rights to the seminal composition of matter patent.

We rely upon patents and proprietary technology, currently co-owned by a subsidiary of Horizon Therapeutics, PLC and the U.S. Public Health Service (PHS) to develop ANVS-401. We have an exclusive worldwide license, subject to standard reservation of rights under federal law, to ANVS-401 for its composition of matter, its use in AD and dementia, its manufacture and its use in Down syndrome, which allows us to develop and commercialize ANVS-401. The agreement allows us to either pay license fees and royalties on sales to develop and sell ANVS-401 or to exercise an option to buy the rights out and own the compound ourselves. If we do not fulfill the terms of the license, Horizon may offer these patents to other parties and we will lose the right to develop and commercialize ANVS-401. If we do not exercise our option to buy the rights out or our right to terminate the agreement, the term of the agreement will continue until the expiration of our obligation to make royalty payments. Such royalty payments continue for each product in each country until the later of the expiration of the related patent or 10 years after the initial sale of the product in the respective country. The agreement may also be terminated for cause by either party upon the breach of the material obligations of the other party or the bankruptcy or liquidation of the other party.

If we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our drug development programs and product candidates. Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to ANVS-401 and any future product candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our development programs and product candidates. The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner.

We in-licensed issued patents that claim the structure of ANVS-401 and certain methods of its use. We have also filed patent applications covering the use of ANVS-401 at much lower doses to treat AD-DS, AD, PD and other neurodegenerative disorders based on our preclinical research. The world-wide exclusive license we have with Horizon comprises the patents co-owned by Horizon and the PHS; the patents have expiration dates between 2021 and 2022. Annovis has filed three classes of patent applications to prolong the patent life of ANVS-401. Unless these applications are approved by the U.S. and international patent offices, the patent life of ANVS-401 is limited. However, on June 25, 2019, we received a Notice of Allowance from the U.S. Patent and Trademark Office for the first of our Annovis patents covering Parkinson's disease and associated diseases. We further covered ANVS-401's use in acute as well as chronic neurodegerative conditions and the use of the mechanism of action for prevention and treatment of diseases. It is possible that we will fail to identify further patentable aspects of our research and development output before it is too late to obtain patent protection. The patent applications that we own may fail to result in issued patents with claims that provide further coverage of ANVS-401 or any other product candidate in the United States or in other foreign countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents further cover ANVS-401 or any future product candidate, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed, invalidated, or held unenforceable. Any successful opposition to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

If the patent applications we own with respect to our development programs and product candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for ANVS-401 or any future product candidate, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize future product candidates. Any such outcome could have a materially adverse effect on our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. However, in certain instances, the laws of the United States are more restrictive than those of foreign countries. For example, a recent series of Supreme Court Cases has narrowed the types of subject matter considered eligible for patenting. Accordingly, certain diagnostic methods are considered ineligible for patenting because they are directed to a "law of nature." Further, publications of discoveries in scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not

published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in patent claims being narrowed, invalidated, held unenforceable, in whole or in part, or reduced in term. Such a result could limit our ability to stop others from using or commercializing similar or identical technology and products. Moreover, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. While various extensions may be available, the life of a patent is limited. Without patent protection for our current or future product candidates, we may be open to competition from generic versions of such products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

We may become subject to third parties' claims alleging infringement of their patents and proprietary rights, or we may need to become involved in lawsuits to protect or enforce our patents, which could be costly, time consuming, delay or prevent the development and commercialization of our product candidates or put our patents and other proprietary rights at risk.

Our commercial success depends, in part, upon our ability to develop, manufacture, market and sell our product candidates without alleged or actual infringement, misappropriation or other violation of the patents and proprietary rights of third parties. Litigation relating to infringement or misappropriation of patent and other intellectual property rights in the pharmaceutical and biotechnology industries is common, including patent infringement lawsuits, interferences, oppositions and reexamination proceedings before the U.S. Patent and Trademark Office, or USPTO, and corresponding foreign patent offices. The various markets in which we plan to operate are subject to frequent and extensive litigation regarding patents and other intellectual property rights. In addition, many companies in intellectual property-dependent industries, including the biotechnology and pharmaceutical industries, have employed intellectual property litigation as a means to gain an advantage over their competitors. Numerous U.S., EU and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the intellectual property rights of third parties.

We may be subject to third-party claims including infringement, interference or derivation proceedings, post-grant review and *inter partes* review before the USPTO or similar adversarial proceedings or litigation in other jurisdictions. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed,

and the holders of any such patents may be able to block our ability to commercialize the applicable product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. These proceedings may also result in our patent claims being invalidated or narrowed in scope. Similarly, if our patents or patent applications are challenged during interference or derivation proceedings, a court may hold that a third-party is entitled to certain patent ownership rights instead of us. Further, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our compositions, formulations, methods of manufacture, or methods of treatment, prevention or use, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires or is finally determined to be invalid or unenforceable. In addition, defending such claims would cause us to incur substantial expenses and, if successful, could cause us to pay substantial damages, if we are found to be infringing a third party's patent rights. If we are found to have infringed such rights willfully, the damages may be enhanced and may include attorneys' fees. Further, if a patent infringement suit is brought against us or our third-party service providers, our development, manufacturing or sales activities relating to the product or product candidate that is the subject of the suit may be delayed or terminated. As a result of patent infringement claims, or in order to avoid potential infringement claims, we may choose to seek, or be required to seek, a license from the third party, which may require us to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if a license can be obtained on acceptable terms, the rights may be nonexclusive, which could give our competitors access to the same intellectual property rights. If we are unable to enter into a license on acceptable terms, we could be prevented from commercializing one or more of our product candidates, forced to modify such product candidates, or to cease some aspect of our business operations, which could harm our business significantly. Modifying our product candidates to design around third-party intellectual property rights may result in significant cost or delay to us and could prove to be technically infeasible. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business. In addition, if the breadth or strength of protection provided the patents and patent applications we own or in-license is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

If we were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States and in Europe, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of eligibility, lack of novelty, obviousness or non-enablement. Third parties might allege unenforceability of our patents because someone connected with prosecution of the patent withheld relevant information, or made a misleading statement, during prosecution. The outcome of proceedings involving assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity of patents, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Furthermore, our patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without infringing our patents or other intellectual property rights.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or

investors view these announcements in a negative light, the price of common stock could be adversely affected.

Finally, even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors view these announcements in a negative light, the price of our common stock could be adversely affected. Such litigation or proceedings could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have an adverse effect on our ability to compete in the marketplace.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent, which might adversely affect our ability to develop, manufacture and market our product candidates.

We cannot guarantee that any of our or our licensors' patent searches or analyses, including but not limited to the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States, Europe and elsewhere that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. For example, in the United States, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States, EU and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our future product candidates, or their manufacture or use may currently be unpublished. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates. We may incorrectly determine that our product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States, the EU or elsewhere that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our product candidates.

From time to time we may identify patents or applications in the same general area as our products and product candidates. We may determine these third-party patents are irrelevant to our business based on various factors including our interpretation of the scope of the patent claims and our interpretation of when the patent expires. If the patents are asserted against us, however, a court may disagree with our determinations. Further, while we may determine that the scope of claims that will issue from a patent application does not present a risk, it is difficult to accurately predict the scope of claims that will issue from a patent application, our determination may be incorrect, and the issuing patent may be asserted against us. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we fail in any such dispute, in addition to being forced to

pay monetary damages, we may be temporarily or permanently prohibited from commercializing our product candidates. We might, if possible, also be forced to redesign our product candidates so that we no longer infringe the third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

Changes in patent laws or patent jurisprudence could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biopharmaceutical and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical and pharmaceutical industries involve both technological complexity and legal complexity. Therefore, obtaining and enforcing biopharmaceutical and pharmaceutical patents is costly, time-consuming and inherently uncertain. In addition, the America Invents Act, or the AIA, which was passed in September 2011, resulted in significant changes to the U.S. patent system.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application, but circumstances could prevent us from promptly filing patent applications on our inventions.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent with the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action.

Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. It is not clear what, if any, impact the AIA will have on the operation of our business. However, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents.

Additionally, the U.S. Supreme Court has ruled on several patent cases in recent years either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. Similarly, the complexity and uncertainty of European patent laws has also increased in recent years. In addition, the European patent system is relatively stringent in the type of amendments that are allowed during prosecution. Complying with these laws and regulations could limit our ability to obtain new patents in the future that may be important for our business.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and European and other patent agencies over the lifetime of a patent. In addition, the USPTO and European and other patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent failure to make payment of such fees or to comply with such provisions can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which such noncompliance will result in the abandonment or lapse of the patent or patent application, and the partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents within prescribed time limits. If we or our licensors fail to maintain the patents and patent applications covering our product candidates or if we or our licensors otherwise allow our patents or patent applications to be abandoned or lapse, our competitors might be able to enter the market, which would hurt our competitive position and could impair our ability to successfully commercialize our product candidates in any indication for which they are approved.

We enjoy only limited geographical protection with respect to certain patents and we may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive. Competitors may use our and our licensors' technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we and our licensors have patent protection, but enforcement is not as strong as that in the United States or the EU. These products may compete with our product candidates, and our and our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

In addition, we may decide to abandon national and regional patent applications before grant. The grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications might in some jurisdictions be refused by the relevant patent offices, while granted by others. For example, unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. Furthermore, generic drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' patents, requiring us or our licensors to engage in complex, lengthy and costly litigation or other proceedings. Generic drug manufacturers may develop, seek approval for and launch generic versions of our products. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or rules and regulations in the United States and the EU, and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in other jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be

commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished, and we may face additional competition from others in those jurisdictions.

Some countries also have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of marketing exclusivity for our product candidates, our business may be materially harmed.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from competitive medications, including generic medications. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, we may be able to extend the term of a patent covering each product candidate under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments and similar legislation in the EU. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced, possibly materially.

Further, under certain circumstances, patent terms covering our products or product candidates may be extended for time spent during the pendency of the patent application in the USPTO (referred to as Patent Term Adjustment, or PTA). The laws and regulations underlying how the USPTO calculates the PTA is subject to change and any such PTA granted by the USPTO could be challenged by a third-party. If we do not prevail under such a challenge, the PTA may be reduced or eliminated, resulting in a shorter patent term, which may negatively impact our ability to exclude competitors.

Because PTA added to the term of patents covering pharmaceutical products has particular value, our business may be adversely affected if the PTA is successfully challenged by a third party and our ability to exclude competitors is reduced or eliminated.

Intellectual property rights do not address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make products that are similar to ANVS-401 or our future product candidates but that are not covered by the claims of the patents that we own or license from others;
- others may independently develop similar or alternative technologies or otherwise circumvent any of our technologies without infringing our intellectual property rights;
- we or any of our collaborators might not have been the first to conceive and reduce to practice the inventions covered by the patents or patent applications that we own, license or will own or license;
- we or any of our collaborators might not have been the first to file patent applications covering certain of the patents or patent applications that we or they own or have obtained a license, or will own or will have obtained a license;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights, or in countries where research and development safe harbor laws exist, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- ownership of our patents or patent applications may be challenged by third parties; and
- the patents of third parties or pending or future applications of third parties, if issued, may have an adverse effect on our business.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that our trade secrets will be misappropriated or disclosed, and confidentiality agreements with employees and third parties may not adequately prevent disclosure of trade secrets and protect other proprietary information.

We consider proprietary trade secrets or confidential know-how and unpatented know-how to be important to our business. We may rely on trade secrets or confidential know-how to protect our technology, especially where patent protection is believed by us to be of limited value. Because we expect to rely on third parties to manufacture ANVS-401 and any future product candidates, and we expect to collaborate with third parties on the development of ANVS-401 and any future product candidates, we must, at times, share trade secrets with them. We also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. However, trade secrets or confidential know-how can be difficult to maintain as confidential.

To protect this type of information against disclosure or appropriation by competitors, our policy is to require our employees, consultants, contractors and advisors to enter into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with

us prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. However, current or former employees, consultants, contractors and advisers may unintentionally or willfully disclose our confidential information to competitors, and confidentiality agreements may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. The need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have an adverse effect on our business and results of operations. Enforcing a claim that a third party obtained illegally and is using trade secrets or confidential know-how is expensive, time consuming and unpredictable. The enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential collaborators or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our unregistered trademarks or trade names. Over the long term, if we are unable to successfully register our trademarks and trade names and establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively, and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

We may need to license certain intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property, including patent rights that are important or necessary to the development or commercialization of ANVS-401 or our future product candidates. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize ANVS-401 or our product candidates, in which case we would be required to obtain a license from these third parties. Such a license may not be available on commercially reasonable terms, or at all, which could materially harm our business. At this time, we are unaware of any intellectual property that interferes with ours or is complementary and needed to commercialize ANVS-401.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of their former employers or other third parties.

We employ individuals who were previously employed at other biotechnology or pharmaceutical companies. Although we seek to protect our ownership of intellectual property rights by ensuring that our agreements with our employees, collaborators and other third parties with whom we do business include provisions requiring such parties to assign rights in inventions to us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and if we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Even if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees.

Our proprietary information may be lost, or we may suffer security breaches.

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, clinical trial data, proprietary business information, personal data and personally identifiable information of our clinical trial subjects and employees, in our data centers and on our networks. The secure processing, maintenance and transmission of this information is critical to our operations. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. Although, to our knowledge, we have not experienced any such material security breach to date, any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, significant regulatory penalties, disrupt our operations, damage our reputation and cause a loss of confidence in us and our ability to conduct clinical trials, which could adversely affect our reputation and delay our clinical development of our product candidates.

Risks Related to Our Employees, Managing Our Growth and Our Operations

Our future success depends on our ability to retain our key personnel and to attract, retain and motivate qualified personnel.

We are highly dependent on the development, regulatory, commercialization and business development expertise of Maria L. Maccecchini, PhD, as well as the other principal members of our management, scientific and clinical teams. Although we have employment agreements, offer letters or consulting agreements with our executive officers, these agreements do not prevent them from terminating their services at any time.

If we lose one or more of our executive officers or key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop product candidates, gain regulatory approval, and commercialize new products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our

research and development and commercialization strategy. Our consultants and advisors may be engaged by entities other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to develop and commercialize product candidates will be limited.

We expect to expand our development, regulatory, and sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of development, regulatory affairs and sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities or acquire new facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

We may engage in acquisitions that could disrupt our business, cause dilution to our stockholders or reduce our financial resources.

In the future, we may enter into transactions to acquire other businesses, products or technologies. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms, or at all. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and nondisruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

Our business and operations would suffer in the event of system failures.

Our computer systems, as well as those of our CROs and other contractors and consultants, are vulnerable to damage from computer viruses, unauthorized access, natural disasters (including hurricanes), terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs. For example, the loss of preclinical or clinical trial data from completed, ongoing or planned trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of personal, confidential or proprietary information, we could incur liability and the further development of ANVS-401 or any other product candidate could be delayed.

Risks Related to this Offering and Our Common Stock

No active trading market for our common stock currently exists, and an active trading market may not develop.

Prior to this offering, there has not been an active trading market for our common stock. If an active trading market for our common stock does not develop following this offering, you may not be able to sell your shares quickly or at the market price. Our ability to raise capital to continue to fund operations by selling shares of our common stock and our ability to acquire other companies or technologies by using shares of our common stock as consideration may also be impaired. The initial public offering price of our common stock will be determined by negotiations between us and the underwriters and may not be indicative of the market prices of our common stock that will prevail in the trading market.

The market price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock in this offering.

The market price of our common stock is likely to be highly volatile and may be subject to wide fluctuations in response to a variety of factors, including the following:

- any delay in the commencement, enrollment and ultimate completion of our Phase 2a trials of ANVS-401;
- if we are required to conduct more than one Phase 3 trial in any one indication;
- any delay in submitting an NDA and any adverse development or perceived adverse development with respect to the FDA's review of that NDA;
- failure to successfully develop and commercialize ANVS-401 or any future product candidate;
- inability to obtain additional funding;
- regulatory or legal developments in the United States and other countries applicable to ANVS-401 or any other product candidate;
- adverse regulatory decisions;
- changes in the structure of healthcare payment systems;
- inability to obtain adequate product supply for ANVS-401 or any other product candidate, or the inability to do so at acceptable prices;
- introduction of new products, services or technologies by our competitors;
- failure to meet or exceed financial projections we provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- changes in the market valuations of companies similar to ours;
- market conditions in the pharmaceutical and biotechnology sectors, and the issuance of new or changed securities analysts' reports or recommendations;
- announcements of significant acquisitions, strategic collaborations, joint ventures or capital commitments by us or our competitors;
- significant lawsuits, including patent or shareholder litigation, and disputes or other developments relating to our proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;

- sales of our common stock by us or our shareholders in the future;
- trading volume of our common stock;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

In addition, the stock markets have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many companies. These fluctuations have often been unrelated or disproportionate to the operating performance of those companies. Broad market and industry factors, as well as general economic, political, regulatory and market conditions, may negatively affect the market price of our common stock, regardless of our actual operating performance. The market price of our common stock may decline below the initial public offering price, and you may lose some or all of your investment.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against companies following a decline in the market price of their securities. This risk is especially relevant for us because biotechnology companies have experienced significant share price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

After this offering, our directors, executive officers and certain shareholders will continue to own a significant percentage of our common stock and, if they choose to act together, will be able to exert significant control over matters subject to shareholder approval.

Upon the closing of this offering, our directors, executive officers, and shareholders affiliated with our directors and executive officers will beneficially own approximately % of the voting power of our outstanding common stock, or approximately % if the underwriters exercise their over-allotment option from us in full. Therefore, they will have the ability to substantially influence us through their ownership position. For example, these holders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. The interests of these holders may not always coincide with our corporate interests or the interests of other shareholders, and they may act in a manner with which you may not agree or that may not be in the best interests of our other shareholders. So long as they continue to own a significant amount of our equity, these holders will be able to strongly influence or effectively control our decisions.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our common stock, our stock price and trading volume could decline.

The trading market for our common stock will depend, in part, on the research and reports that securities or industry analysts may publish about us or our business. We do not have any control over these analysts. If our financial performance fails to meet analyst estimates or one or more of the analysts who cover us downgrade our common stock or change their opinion of our common stock, our share price would likely decline. If one or more of these analysts cease coverage of us or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. As a result, capital appreciation, if any, of our common stock would be your sole source of gain on an investment in our common stock for the foreseeable future. See "Dividend Policy" for additional information.

We will have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

We will have broad discretion in the application of the net proceeds from this offering and our shareholders will not have the opportunity as part of their investment decision to assess whether the net proceeds are being used appropriately. You may not agree with our decisions, and our use of the proceeds may not yield any return on your investment. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Our failure to apply the net proceeds of this offering effectively could compromise our ability to pursue our growth strategy and we might not be able to yield a significant return, if any, on our investment of these net proceeds.

A significant portion of our total outstanding shares is restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to decline significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market after this offering, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. Of our issued and outstanding common stock, all of the shares sold in this offering will be freely transferable without restrictions or further registration under the Securities Act of 1933, as amended (the "Securities Act") except for any shares acquired by our affiliates, as defined in Rule 144 under the Securities Act. The remaining shares outstanding after this offering will be restricted as a result of securities laws, lock-up agreements or other contractual restrictions that restrict transfers for 180 days, or in the case of our directors and officers for 12 months, after the date of this prospectus. See "Shares Eligible for Future Sale—Lock-Up Agreements."

If you purchase shares of our common stock in this offering, you will incur immediate dilution in the book value of your shares.

The initial public offering price of our common stock will be substantially higher than the as adjusted net tangible book value per share of our common stock. Therefore, if you purchase our common stock in this offering, you will pay a price per share of our common stock that substantially exceeds the book value of our tangible assets after subtracting our liabilities. Based on an assumed initial public offering price of $ per share, you will experience immediate dilution of $ per share, representing the difference between our net tangible book value per share, after giving effect to this offering, and the assumed initial public offering price. Further, the future exercise of any outstanding options to purchase shares of our common stock will cause you to experience additional dilution. See "Dilution."

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we no longer qualify as an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur previously. The Sarbanes-Oxley Act of 2002, or SOX, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of Nasdaq, and other applicable securities rules and regulations impose various requirements on U.S. reporting public companies, including the establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified senior management personnel or members for our board of directors. In addition, these rules and regulations are often subject to varying interpretations, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. Pursuant to Section 404 of SOX, or Section 404, we will be required to furnish a report by our senior management on our internal control over financial reporting.

While we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To prepare for eventual compliance with Section 404, once we no longer qualify as an emerging growth company, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

We are an "emerging growth company," and the reduced reporting requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act, or JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including exemption from compliance with the auditor attestation requirements of Section 404, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the closing of this offering, (b) in which we have total annual gross revenue of at least $1.07 billion or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock held by non-affiliates exceeds $700 million as of the end of our prior second fiscal quarter, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

In addition, under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our share price may be more volatile.

Provisions in our restated certificate of incorporation and amended and restated bylaws and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our restated certificate of incorporation and our amended and restated bylaws that will become effective upon the closing of this offering may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions include those establishing:

- Advance notice bylaw provisions for proposals from stockholders for presentation at annual meetings; and
- Forum selection bylaw provisions.

Because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Furthermore, our restated certificate of incorporation that will become effective upon the closing of this offering specifies that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving actions brought against us by stockholders. We believe this provision benefits us by providing increased consistency in the application of Delaware law by chancellors particularly experienced in resolving corporate disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. However, the provision may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our restated certificate of incorporation to be inapplicable or unenforceable in such action.

Our bylaws designate the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders with respect to our company and our directors. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that the stockholder believes is favorable for disputes with us or our directors, which may discourage meritorious claims from being asserted against us and our directors. Alternatively, if a court were to find this provision of our charter inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business, financial condition or results of operations. We adopted this provision because we believe it makes it less likely that we will be forced to incur the expense of defending duplicative actions in multiple forums and less likely that plaintiffs' attorneys will be able to employ such litigation to coerce us into otherwise unjustified settlements, and we believe the risk of a court declining to enforce this provision is remote, as the General Assembly of Delaware has specifically amended the Delaware General Corporation Law to authorize the adoption of such provisions.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, timing and likelihood of success, plans and objectives of management for future operations and future results of anticipated products, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this prospectus are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions described under the sections in this prospectus titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this prospectus. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

INDUSTRY AND OTHER DATA

We obtained the industry, market and competitive position data in this prospectus from our own internal estimates and research as well as from industry and general publications and research, surveys and studies conducted by third parties. We believe that each of these studies and publications is reliable. We also believe our internal company research as to such matters is reliable and the market definitions are appropriate. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of factors including those described in the section titled "Risk Factors." These and other factors could cause results to differ materially from those expressed in the estimate made by the independent parties and by us.

TRADEMARKS, SERVICE MARKS AND TRADE NAMES

We own or have rights to use a number of registered and common law trademarks, service marks and/or trade names in connection with our business in the United States and/or in certain foreign jurisdictions.

Solely for convenience, the trademarks, service marks, logos and trade names referred to in this prospectus are without the ® and ™ symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensors to these trademarks, service marks and trade names. This prospectus contains additional trademarks, service marks and trade names of others, which are the property of their respective owners. All trademarks, service marks and trade names appearing in this prospectus are, to our knowledge, the property of their respective owners. We do not intend our use or display of other companies' trademarks, service marks, copyrights or trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

USE OF PROCEEDS

We estimate that the net proceeds from our sale of shares of our common stock in this offering will be approximately $, assuming an initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their over-allotment option in full, we estimate that our net proceeds will be approximately $, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Each $1.00 decrease in the assumed initial public offering price of $ per share, which is the midpoint of the range set forth on the cover page of this prospectus, would decrease the net proceeds to us from this offering by approximately $, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. At an assumed initial public offering price of $ per share, the net proceeds to us from this offering would increase by approximately $, assuming the number of shares offered by us, as set forth on the cover page of the prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each $1.00 increase in the initial public offering price above $ per share would increase the net proceeds to us from this offering by approximately $, assuming the number of shares offered by us, as set forth on the cover of the prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each decrease of in the number of shares we are offering would decrease the net proceeds to us from this offering, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, by approximately $, assuming the assumed initial public offering price stays the same. An increase of shares in the number of shares offered by us, as set forth on the cover page of this prospectus, to shares would increase the net proceeds to us from this offering by approximately $, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us and assuming the assumed initial public offering price stays the same. An increase in the number of shares offered by us, as set forth on the cover page of this prospectus, to shares would increase the net proceeds to us from this offering by approximately $, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us and assuming the assumed initial public offering price stays the same. Each increase of in the number of shares offered by us above would increase the net proceeds to us from this offering by approximately , after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us and assuming the initial public offering price stays the same.

We currently anticipate that we will use the net proceeds from this offering, together with our existing resources, through 2020 as follows:

- approximately $3.0 million to commence and fund the costs of the Phase 2a PD trial in the United States and, possibly, internationally, for the treatment of PD starting in the first quarter of 2020;
- approximately $0.8 million to fund the costs associated with our continuing 2a trial of ANVS-401 in the United States in AD patients. This study is presently run and paid for by the Alzheimer's Disease Cooperative Study (ADCS);
- approximately $0.2 to commence the planning of the Phase 3 study in AD-DS for the treatment of memory loss and dementia in DS;
- approximately $2.0 million to conduct the chronic toxicology studies in rats and mice;

- approximately $0.7 million for payments under our license agreement with Horizon Therapeutics, PLC;
- the rest for general and administrative expenses, research and development and to provide sufficient liquidity until we raise additional capital for the Phase 3 studies in AD-DS and PD.

We believe opportunities may exist from time to time to expand our current business through license or acquisitions of, or investments in, complementary businesses, products or technologies. While we currently have no agreements or commitments to complete any such transaction at this time, we may use a portion of the net proceeds for these purposes.

The net proceeds from this offering, together with our cash, cash equivalents and marketable securities, will not be sufficient for us to fund any of our product candidates through regulatory approval, and we will need to raise additional capital to complete the development and commercialization of our product candidates. We may satisfy our future cash needs through the sale of equity securities, debt financings, working capital lines of credit, corporate collaborations or license agreements, grant funding, interest income earned on invested cash balances or a combination of one or more of these sources. This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. We may also use a portion of the net proceeds to in-license, acquire, or invest in additional businesses, technologies, products or assets, although currently we have no specific agreements, commitments or understandings in this regard. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual expenditures and the extent of clinical development may vary significantly depending on numerous factors, including the progress of our development efforts, the clinical trials we may commence in the future, as well as any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Based on our planned use of the net proceeds from this offering and our existing cash and cash equivalents, we estimate that such funds will be sufficient to enable us to fund our operating expenses and capital expenditure requirements for at least the next 18 months. We have based this estimate on assumptions that may prove to be incorrect, and we could use our available capital resources sooner than we currently expect.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Investors should not purchase our common stock with the expectation of receiving cash dividends. Any future determination related to our dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors our board of directors deems relevant, and subject to the restrictions contained in any future financing instruments.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and our capitalization as of March 31, 2019:

- on an actual basis;
- on a pro forma basis to give effect to:
  - the automatic conversion of all outstanding shares of our preferred stock into 5,763,881 shares of our common stock upon the closing of this offering; and
  - the filing and effectiveness of our restated certificate of incorporation; and
- on a pro forma as adjusted basis, giving effect to the pro forma adjustments set forth above and to give further effect to our issuance and sale of shares of our common stock in this offering at an assumed initial public offering price of $ share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us and the issuance of shares of our common stock upon conversion of the $530,000 principal amount of our convertible promissory notes upon the closing of this offering into shares of our common stock at a 20% discount to the public offering price.

The pro forma as adjusted information below is illustrative only, and our capitalization following the completion of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read the following table together with our financial statements and the related notes appearing at the end of this prospectus and the "Selected Financial Data," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Description of Capital Stock" sections of this prospectus.

	As of March 31, 2019		
	Actual	Pro Forma	Pro Forma As Adjusted
	(in thousands, except share and per share data)		
Cash and cash equivalents	$ 336.6	$ 336.6	$
Convertible debt, net of unamortized deferred financing fees and debt discount	$ 495.9	$ 495.9	
Redeemable convertible preferred stock, $0.0001 par value: Series A—5,133,159 shares authorized, issued and outstanding, actual; no shares authorized, and no shares issued and outstanding, pro forma and pro forma as adjusted	$ 6,509.3	$ —	
Series A-1—1,111,111 shares authorized and 630,722 shares outstanding, actual; no shares authorized and no shares issued and outstanding, pro forma and pro forma as adjusted	$ 567.6	$ —	
Stockholders' equity (deficit):			
Common stock, $0.0001 par value; 10,150,000 shares authorized, and 395,653 shares issued and outstanding, actual; 200,000,000 shares authorized, pro forma and pro forma as adjusted and 6,159,534 shares issued and outstanding, pro forma and shares issued and shares outstanding, pro forma as adjusted	$ —	$ 0.6	
Additional paid-in capital	201.0	7,277.3	
Accumulated deficit	(7,976.9)	(7,976.9)	
Total stockholders' equity (deficit)	$ (7,775.9)	$ (699.0)	
Total capitalization	$ (203.1)	$ (203.1)	$

A $ decrease in the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would decrease the pro forma as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. At an assumed initial public offering price of $ per share, the pro forma as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization would increase by approximately $ million, assuming the number of shares offered by us, as set forth on the cover page of the prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. A $ increase in the initial public offering price above $ per share would increase the pro forma as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by approximately $ million, assuming the number of shares offered by us, as set forth on the cover of the prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. A decrease of shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would decrease the pro forma as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by approximately $ million, assuming no change in the assumed initial public offering price per share and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase of shares in the number of shares offered by us, as set forth on the cover page of this prospectus, to shares would increase the pro forma as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by approximately $ million, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us and assuming the assumed initial public offering price stays the same. An increase in the number of shares offered by us, as set forth on the cover page of this prospectus, to shares would increase the pro forma as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by approximately $ million, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us and assuming the assumed initial public offering price stays the same. An increase of in the number of shares offered by us above would increase the pro forma as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by approximately $ million, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us and assuming the initial public offering price stays the same.

The table above does not include:

- 495,025 shares of common stock issuable upon exercise of stock options outstanding as of , 2019, at a weighted-average exercise price of $0.13 per share; and
- 533,746 shares of our common stock that are available for future issuance under our 2018 Incentive Award Plan, or share that will become available under our 2019 Plan, which will become effective in connection with this offering.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value deficit as of March 31, 2019 was $(7.8) million, or $(19.65) per share of our common stock. Our historical net tangible book value deficit is the amount of our total tangible assets less our total liabilities and our Series A and A-1 convertible preferred stock. Historical net tangible book value deficit per share represents our historical net tangible book value deficit divided by the 395,653 shares of our common stock outstanding as of March 31, 2019.

Our pro forma net tangible book value deficit as of March 31, 2019, was $(0.7) million, or $(0.11) per share of our common stock. Pro forma net tangible book value represents the amount of our total tangible assets less our total liabilities, after giving effect to the automatic conversion of all outstanding shares of our preferred stock into 5,763,881 shares of our common stock upon the closing of this offering.

After giving further effect to our issuance and sale of shares of our common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us and after giving further effect to the issuance of shares of our common stock upon conversion of the $530,000 principal amount of our convertible promissory notes upon the closing of this offering into shares of our common stock at a 20% discount to the public offering price, our pro forma as adjusted net tangible book value as of March 31, 2019 would have been $, or $ per share. This represents an immediate increase in pro forma as adjusted net tangible book value per share of $ to our existing stockholders and immediate dilution in pro forma as adjusted net tangible book value per share of $ to new investors purchasing common stock in this offering. Dilution per share to new investors purchasing common stock in this offering is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the assumed initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Assumed initial public offering price per share		$
Historical net tangible book value deficit per share as of March 31, 2019	$ (19.65)	
Increase per share attributable to the automatic conversion of preferred stock in connection with this offering	19.54	
Pro forma net tangible book value deficit per share as of March 31, 2019	(0.11)	
Increase in pro forma net tangible book value per share attributable to this offering including the automatic conversion of convertible debt in connection with this offering		
Pro forma as adjusted net tangible book value per share after this offering		$
Dilution per share to new investors purchasing common stock in this offering		$

The dilution information discussed above is illustrative only and will change based on the actual initial public offering price and other terms of this offering determined at pricing. A $ decrease in the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would decrease our pro forma as adjusted net tangible

book value per share after this offering by $ and dilution per share to new investors purchasing common stock in this offering by $, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. A $ increase in the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus would increase our pro forma as adjusted net tangible book value per share after this offering by $ and dilution per share to new investors purchasing common stock in this offering by $, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. A decrease of shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would decrease our pro forma as adjusted net tangible book value per share after this offering by $ and increase dilution per share to new investors purchasing common stock in this offering by $, assuming no change in the assumed initial public offering price per share and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase of shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase our pro forma as adjusted net tangible book value per share after this offering by $ and decrease dilution per share to new investors purchasing common stock in this offering by $, assuming no change in the assumed initial public offering price and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters' over-allotment option is exercised in full, our pro forma as adjusted net tangible book value per share after this offering would be $ and dilution per share to new investors purchasing common stock in this offering would be $, assuming an initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The following table summarizes, as of March 31, 2019, on a pro forma as adjusted basis, the total number of shares of common stock purchased from us on an as converted to common stock basis and the total consideration paid or to be paid and the average price per share paid or to be paid by existing stockholders and by new investors in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. As the table shows, new investors purchasing our common stock in this offering will pay an average price per share substantially higher than our existing stockholders paid.

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders		%	$	%	$
New investors					
Total		%	$	%	

A $ increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the total consideration paid by new investors by $ million and, in the case of an increase, would increase the percentage of total consideration paid by new investors by percentage points and, in the case of a decrease, would decrease the percentage of total consideration paid by new investors by percentage points, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. An increase (decrease) of shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the total consideration paid by new investors by $ and, in the case of an

increase, would increase the percentage of total consideration paid by new investors by percentage points and, in the case of a decrease, would decrease the percentage of total consideration paid by new investors by percentage points, assuming no change in the assumed initial public offering price per share.

The table above assumes no exercise of the underwriters' over-allotment option. If the underwriters' over-allotment option is exercised in full, the number of shares of our common stock held by existing stockholders would be reduced to % of the total number of shares of our common stock outstanding after this offering, and the number of shares of common stock held by new investors purchasing common stock in this offering would be increased to % of the total number of shares outstanding after this offering.

The tables above do not include:

- 495,025 shares of common stock issuable upon exercise of stock options outstanding as of , 2019, at a weighted-average exercise price of $0.13 per share;

- 533,746 shares of our common stock that are available for future issuance under our 2018 Incentive Award Plan, or share that will become available under our 2019 Plan, which will become effective in connection with this offering; and

SELECTED FINANCIAL DATA

You should read the following selected financial data together with our financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus. We have derived the statement of operations data for the years ended December 31, 2018 and 2017 from our audited financial statements appearing at the end of this prospectus. We have derived the statement of operations data for the three months ended March 31, 2019 and 2018 and the balance sheet data as of March 31, 2019 from our unaudited interim financial statements appearing at the end of this prospectus. The unaudited interim financial statements have been prepared on the same basis as the audited financial statements and reflect, in the opinion of management, all adjustments of a normal, recurring nature that are necessary for a fair presentation of the unaudited interim financial statements. Our historical results are not necessarily indicative of results that should be expected in any future period, and our results for any interim period are not necessarily indicative of results that should be expected for any full year.

(in thousands, except for share and per share data)	Year Ended December 31,		Three Months Ended March 31,	
	2018	2017	2019	2018
			(Unaudited)	
Statement of Operations Data:				
Operating expenses:				
Research and development	$ 111.6	$ 273.4	$ 6.0	$ 57.8
General and administrative	602.3	409.0	180.8	132.1
Total operating expenses	713.9	682.4	186.8	189.9
Loss from operations	(713.9)	(682.4)	(186.8)	(189.9)
Other income (expense):				
Interest income (expense), net	—	—	(4.1)	—
Net loss	$ (713.9)	$ (682.4)	$ (190.9)	$ (189.9)
Net loss per common share—basic and diluted(1)	$ (1.84)	$ (1.90)	$ (0.48)	$ (0.51)
Weighted average common shares outstanding—basic and diluted(1)	388,612	358,599	395,653	375,653
Pro forma net loss per common share—basic and diluted (unaudited) (2)	$ (0.12)		$ (0.03)	
Pro forma weighted average common shares outstanding—basic and diluted (unaudited)(2)	6,152,493		6,159,534	

(1) See Note 9 to our audited financial statements and note 10 to our unaudited interim financial statements appearing at the end of this prospectus for further details on the calculation of basic and diluted net loss per common share.

(2) Reflects the automatic conversion of all outstanding shares of our preferred stock into 5,763,881 shares of our common stock upon the closing of this offering. Does not include the issuance of shares of our common stock upon conversion of the $530,000 principal amount of our

convertible promissory notes upon the closing of this offering into shares of our common stock at a 20% discount to the public offering price.

(in thousands)	As of March 31, 2019 (Unaudited)
Balance Sheet Data:	
Cash	$ 336.6
Working capital(1)	(207.6)
Total assets	431.3
Convertible debt, net of unamortized deferred financing fees and debt discount	495.9
Redeemable convertible preferred stock	7,077.0
Stockholders' equity (deficit)	(7,775.9)

(1) We define working capital as current assets less current liabilities.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion summarizes the significant factors affecting the operating results, financial condition, liquidity and cash flows of our company as of and for the periods presented below. The following discussion and analysis should be read in conjunction with "Prospectus Summary—Summary Financial Information," "Selected Financial Information" and the financial statements and the related notes thereto included elsewhere in this prospectus. The statements in this discussion regarding industry outlook, our expectations regarding our future performance, liquidity and capital resources and all other non-historical statements in this discussion are forward-looking statements and are based on the beliefs of our management, as well as assumptions made by, and information currently available to, our management. Actual results could differ materially from those discussed in or implied by forward-looking statements as a result of various factors, including those discussed below and elsewhere in this prospectus, particularly in the section entitled "Risk Factors."

Overview

Company Overview

We are a clinical stage, drug platform company focused on developing and commercializing innovative drugs for the treatment of Alzheimer's disease in Down Syndrome (AD-DS), Alzheimer's disease (AD), Parkinson's disease (PD) and other neurodegenerative diseases. Our lead compound, ANVS-401, is a small molecule administered orally that attacks neurodegeneration by entering the brain and inhibiting the translation of neurotoxic proteins thereby improving and normalizing axonal vesicle transport. By targeting and reducing the levels of three neurotoxic proteins—amyloid precursor protein APP/A β (APP), tau/phospho-tau (tau) and α -Synuclein (α SYN)—animal studies have shown that ANVS-401 normalizes axonal vesicle transport, preventing nerve cell death and neurodegeneration. Human studies have shown that ANVS-401 normalizes levels of neurotoxic proteins—APP, tau and α SYN and lowers inflammation.

AD is a substantial market affecting over 30 million people worldwide and is expected to grow to over 100 million by 2050. While the market for neurodegeneration is over $100 billion, to date there are no disease modifying drugs (DMD) for any neurodegenerative disease. Enormous efforts have gone into developing better drugs to treat neurodegeneration and the outcomes have been sobering. The results of clinical trials in AD, the two AD orphan indications AD-DS and early onset familial AD (EOFAD) or in PD have not supported the development of successful disease modifying therapies.

ANVS-401 is a small lipophilic molecule that is orally available and readily enters the brain, as demonstrated by pharmacokinetics analyses showing brain concentrations approximately 6 to 8 times higher than plasma concentrations. ANVS-401 has a mechanism of action that we believe to be unique, in that it inhibits the translation and, therefore, the levels of several neurotoxic aggregating proteins both in vitro and in vivo including APP, tau and α SYN. ANVS-401's safety has been established in three Phase 1 clinical studies by Maccecchini et al. They show that ANVS-401 has no side effects up to a single dose of 160 mg. The third study also shows that ANVS-401 normalized levels of APP, tau and α SYN in the cerebrospinal fluid (CSF) of mildly cognitively impaired (MCI) patients. Additionally, we now have preclinical data proving ANVS-401's efficacy in restoring memory and learning in an APP/PS1 transgenic (tg) as well as in a DS trisomic mouse model of AD, in restoring colonic motility in a human SNCAA53T tg mouse model of PD and preserving memory and learning in traumatic brain injury rats.

By targeting multiple neurotoxic proteins, ANVS-401 resembles a combination therapy approach, with the added convenience of being a single drug with a single drug target. Therefore, we have worked to understand how ANVS-401 is able to inhibit the translation of more than one neurotoxic protein.

We are presently conducting a Phase 2a study in AD patients in collaboration with the Alzheimer Disease Cooperative Study (ADCS) group and plan to initiate a second Phase 2a proof-of-concept study of ANVS-401 in the first quarter of 2020 with 50 PD patients. We have designed the study with Parexel by applying our understanding of the underlying disease states in neurodegeneration and by measuring not just target, but also pathway validation in the spinal fluid of these patients. Successful completion of the AD and PD study will validate the target, the pathway and de-risk ANVS-401 for use in neurodegerative diseases.

We have never been profitable and have incurred net losses since inception. Our net losses were $713,871 and $682,349 for the years ended December 31, 2018 and 2017, respectively. Our net losses for the three months ended March 31, 2019 and 2018 were $190,903 and $189,940, respectively, and our accumulated deficit at March 31, 2019 was $7,976,951. We expect to incur losses for the foreseeable future, and we expect these losses to increase as we continue our development of, and seek regulatory approvals for, our product candidate. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when, or if, we will be able to achieve or maintain profitability.

Financial Operations Overview

The following discussion sets forth certain components of our statements of operations as well as factors that impact those items.

Research and Development Expenses

Our research and development expenses consist of expenses incurred in development and clinical studies relating to our product candidate, including:

- expenses associated with clinical development;
- personnel-related expenses, such as salaries, benefits, travel and other related expenses, including stock-based compensation;
- payments to third-party contract research organizations, or CROs, contractor laboratories and independent contractors; and
- depreciation, maintenance and other facility-related expenses.

We expense all research and development costs as incurred. Clinical development expenses for our product candidate is a significant component of our current research and development expenses. Product candidates in later stage clinical development generally have higher research and development expenses than those in earlier stages of development, primarily due to increased size and duration of the clinical trials. We track and record information regarding external research and development expenses for each study or trial that we conduct. From time to time, we use third-party CROs, contractor laboratories and independent contractors in clinical studies. We recognize the expenses associated with third parties performing these services for us in our clinical studies based on the percentage of each study completed at the end of each reporting period.

We expect that our research and development expenses in 2019 and for the next several years will be higher than in 2018 as a result of increased expenditures for our Phase 2a study in AD and the work needed for our expected initiation of our Phase 2a study in PD during the first quarter of 2020. These expenditures are subject to numerous uncertainties regarding timing and cost to completion. Completion of our clinical development and clinical trials may take several years or more and the length of time generally varies according to the type, complexity, novelty and intended use of our

product candidate. The cost of clinical trials may vary significantly over the life of a project as a result of differences arising during clinical development, including, among others:

- the number of sites included in the clinical trials;
- the length of time required to enroll suitable patients;
- the size of patient populations participating in the clinical trials;
- the duration of patient follow-ups;
- the development stage of the product candidates; and
- the efficacy and safety profile of the product candidates.

Due to the early stage of our research and development, we are unable to determine the duration or completion costs of our development of ANVS-401. As a result of the difficulties of forecasting research and development costs of ANVS-401 as well as the other uncertainties discussed above, we are unable to determine when and to what extent we will generate revenues from the commercialization and sale of an approved product candidate.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, benefits and other related costs, including stock-based compensation, for personnel serving in our executive, finance, accounting, legal and human resource functions. Our general and administrative expenses also include facility and related costs not included in research and development expenses, professional fees for legal services, including patent-related expenses, consulting, tax and accounting services, insurance and general corporate expenses. We expect that our general and administrative expenses will increase with the continued development and potential commercialization of our product candidate.

We expect that our general and administrative expenses in 2019 and for the next several years will be higher than in 2018 as we increase our headcount. We also anticipate increased expenses relating to our operations as a public company, including increased costs for the hiring of additional personnel, and for payment to outside consultants, including lawyers and accountants, to comply with additional regulations, corporate governance, internal control and similar requirements applicable to public companies, as well as increased costs for insurance.

Interest Income (Expense), net

Interest income (expense) consists primarily of interest earned on our money market bank account and interest expense on our convertible debt, including amortization of deferred financing fees and debt discount.

Income Taxes

As of December 31, 2018, the Company had U.S. federal net operating loss carryforwards of $3,394,475, which may be available to offset future income tax liabilities. Federal net operating loss carryforwards generated in 2017 and prior of $2,764,240 will expire beginning 2028. The remaining $630,235 of federal net operating loss carryforwards generated in 2018, do not expire but are limited 80% of taxable income in future years. These operating loss and research tax credit carryforwards will begin to expire in 2027 and 2034, respectively.

On December 22, 2017, the President of the United States signed into law the Tax Cuts and Jobs Act tax reform legislation ("TCJA"). This legislation makes significant changes in U.S. tax law including a reduction in the corporate tax rates, changes to net operating loss "NOL" carryforwards and carrybacks, and a repeal of the corporate alternative minimum tax. The legislation reduced the U.S.

corporate tax rate from the current rate of 34% to 21%. As a result of the enacted law, the Company was required to revalue deferred tax assets and liabilities at the enacted rate. This revaluation resulted in a decrease in net deferred tax asset of $335,717 million and a corresponding reduction in the valuation allowance against these assets. There is no impact to income tax expense. The other provisions of the TCJA did not have a material impact on the 2018 or 2017 financial statements.

Our preliminary estimate of the TCJA and the re-measurement of its deferred tax assets and liabilities is subject to the finalization of management's analysis related to certain matters, such as developing interpretations of the provisions of the TCJA, changes to certain estimates and the filing of our tax returns. U.S. Treasury regulations, administrative interpretations or court decisions interpreting the TCJA may require further adjustments and changes in our estimates. We completed the analysis of the 2017 Tax Act during the fourth quarter of 2018 and had no material changes to the original analysis.

Net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service (the "IRS") and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50% as defined under Sections 382 and 383 in the Internal Revenue Code. This could substantially limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on our value immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years.

Critical Accounting Policies and Use of Estimates

We have based our management's discussion and analysis of financial condition and results of operations on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements as well as the reported revenues and expenses during the reporting periods. On an ongoing basis, we evaluate our estimates and judgments, including those related to clinical development expenses and stock-based compensation. We base our estimates on historical experience and on various other factors that we believe to be appropriate under the circumstances. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully discussed in note 2 to our audited financial statements appearing at the end of this prospectus, we believe that the following accounting policies are critical to the process of making significant judgments and estimates in the preparation of our financial statements.

Research and Development Expenses

We rely on third parties to conduct our preclinical studies and to provide services, including data management, statistical analysis and electronic compilation. Once our clinical trials begin, at the end of each reporting period, we will compare the payments made to each service provider to the estimated progress towards completion of the related project. Factors that we will consider in preparing these estimates include the number of patients enrolled in studies, milestones achieved and other criteria related to the efforts of our vendors. These estimates will be subject to change as additional information becomes available. Depending on the timing of payments to vendors and estimated services provided, we will record net prepaid or accrued expenses related to these costs.

Fair Value of Common Stock and Stock-Based Compensation

We account for grants of stock options to employees and non-employees based on their grant date fair value and recognize compensation expense over the vesting periods. We estimate the fair value of stock options as of the date of grant using the Black-Scholes option pricing model. Estimates in our share-based compensation valuations are highly complex and subjective.

In the absence of a public trading market for our common stock, on each grant date, we develop an estimate of the fair value of our common stock underlying the option grants. Once our common stock is publicly traded, we will no longer have to estimate the fair value of the common stock, rather we will determine the value based on quoted market prices. We determined the fair value of our common stock using methodologies, approaches and assumptions consistent with the AICPA Practice Guide, Valuation of Privately Held Company Equity Securities Issued as Compensation, and based in part on input from an independent third-party valuation firm.

During the two-year period ended December 31, 2016, we issued an aggregate of 176,000 options with exercise prices of $0.10 per share. During the year ended December 31, 2017, we issued an additional 216,666 options with exercise prices of $0.10 per share. For purposes of recognizing compensation expense in our financial statements, we retrospectively estimated the value of the common stock underlying these grants to be $0.26 per share. We used the Option Pricing Model (OPM) Backsolve method utilizing the Series A preferred stock price of $0.50 per share. The OPM requires the use of assumptions such as the volatility of our stock and the time period until a potential liquidity event. We also estimated and applied a discount for the lack of marketability of our stock. We determined the value per common share had remained constant during this period because we issued Series A preferred stock at $0.50 per share at various dates from December 2014 through October 2016. Further, our research and development efforts, our clinical programs and our stage of development had not progressed significantly over this period.

In April 2018, we issued 173,332 options with exercise prices of $0.18 per share. For purposes of recognizing compensation expense in our financial statements, we retrospectively estimated the value of the common stock underlying these grants to be $0.61 per share using the Probability Expected Return Method (PWERM). The PWERM requires us to make assumptions regarding the likelihood of potential outcomes such as a sale of Annovis, an initial public offering, or dissolution, as well as the timing and estimated proceeds to be received in each scenario. We estimated the proceeds to be received based on a market approach utilizing values for the acquisition or initial public offering of comparable public companies. We also estimated and applied a discount for the lack of marketability of our stock. The increase in the fair value per share of common stock compared to prior grant dates reflected our expectations of progress to be made in our clinical trials in 2018. In addition, the increase was consistent with the increase in the price per share of our preferred stock as we issued shares of our Series A-1 preferred stock in December 2017 and March 2018 at a price per share of $0.90.

Results of Operations

Operating expenses were comprised of the following:

	Year Ended December 31,		Three Months Ended March 31,	
	2018	2017	2019	2018
			(Unaudited)	
Research and development	$ 111,608	$ 273,370	$ 6,021	$ 57,815
General and administrative	602,329	409,063	180,769	132,151
	$ 713,937	$ 682,433	$ 186,790	$ 189,966

Years Ended December 31, 2018 and December 31, 2017

Research and Development Expenses

Research and development expenses decreased by $161,762, or 59%, to $111,608 for the year ended December 31, 2018 from $273,370 for the year ended December 31, 2017. The decrease was primarily the result of a $162,000 decrease in contract research costs.

General and Administrative Expenses

General and administrative expenses increased by $193,267 to $602,329 for the year ended December 31, 2018 from $409,063 for the year ended December 31, 2017. The increase was primarily the result of a $128,000 increase for intellectual property legal costs, an increase in consulting costs for legal and business development and an increase in stock-based compensation expense.

Three Months Ended March 31, 2019 and March 31, 2018

Research and Development Expenses

Research and development expenses decreased by $51,794, or 90%, to $6,021 for the three months ended March 31, 2019 from $57,815 for the three months ended March 31, 2018. The decrease was primarily the result of the completion of a number of studies in 2018.

General and Administrative Expenses

General and administrative expenses increased by $48,618, or 37%, to $180,769 for the three months ended March 31, 2019 from $132,151 for the three months ended March 31, 2018. The increase was primarily the result of an increase in accounting, legal and consulting costs.

Liquidity and Capital Resources

Since our inception in 2008, we have devoted most of our cash resources to research and development and general and administrative activities. We have financed our operations primarily with the proceeds from the sale of common stock, convertible preferred stock and convertible promissory notes. To date, we have not generated any revenues from the sale of products, and we do not anticipate generating any revenues from the sales of products for the foreseeable future. We have incurred losses and generated negative cash flows from operations since inception. As of March 31, 2019, our principal source of liquidity was our cash, which totaled $336,573. In March 2019, we issued unsecured convertible promissory notes to various investors in the aggregate principal amount of $530,000.

Equity Financings

For the years ended December 31, 2018 and 2017, we received net proceeds of $246,449 and $332,495, respectively, from the sale of common and redeemable convertible preferred stock. For the three months ended March 31, 2019 and 2018, we received proceeds of $0 and $243,649, respectively, from the sale of common and redeemable convertible preferred stock.

Debt

We had no debt outstanding during the years ended December 31, 2018 and 2017. In March 2019, we issued an aggregate of $530,000 principal amount of convertible promissory notes, which will convert upon the closing of this offering into shares of our common stock at a 20% discount to the public offering price.

Future Capital Requirements

We expect that the net proceeds from this offering and our existing cash and cash equivalents will be sufficient to fund our operations and capital requirements for at least the next 18 months. We believe that these available funds will be sufficient to complete our Phase 2a clinical trial for ANVS-401 and commence the planning of our Phase 3 study in AD-DS for this product candidate. However, it is difficult to predict our spending for our product candidates prior to obtaining FDA approval. Moreover, changing circumstances may cause us to expend cash significantly faster than we

currently anticipate, and we may need to spend more cash than currently expected because of circumstances beyond our control.

Our expectations regarding future cash requirements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we make in the future. We have no current understandings, agreements or commitments for any material acquisitions or licenses of any products, businesses or technologies. We may need to raise substantial additional capital in order to engage in any of these types of transactions.

We expect to continue to incur substantial additional operating losses for at least the next several years as we continue to develop our product candidate and seek marketing approval and, subject to obtaining such approval, the eventual commercialization of our product candidate. If we obtain marketing approval for our product candidate, we will incur significant sales, marketing and outsourced manufacturing expenses. In addition, we expect to incur additional expenses to add operational, financial and information systems and personnel, including personnel to support our planned product commercialization efforts. We also expect to incur significant costs to comply with corporate governance, internal controls and similar requirements applicable to us as a public company following the closing of this offering.

Our future use of operating cash and capital requirements will depend on many forward-looking factors, including the following:

- the initiation, progress, timing, costs and results of clinical trials for our product candidate;
- the clinical development plans we establish for this product candidate;
- the number and characteristics of product candidates that we develop or may in-license;
- the terms of any collaboration agreements we may choose to execute;
- the outcome, timing and cost of meeting regulatory requirements established by the DEA, the FDA, the EMA or other comparable foreign regulatory authorities;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending intellectual property disputes, including patent infringement actions brought by third parties against us;
- costs and timing of the implementation of commercial scale manufacturing activities; and
- the cost of establishing, or outsourcing, sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval in regions where we choose to commercialize our products on our own.

To the extent that our capital resources are insufficient to meet our future operating and capital requirements, we will need to finance our cash needs through public or private equity offerings, debt financings, collaboration and licensing arrangements or other financing alternatives. We have no committed external sources of funds. Additional equity or debt financing or collaboration and licensing arrangements may not be available on acceptable terms, if at all.

If we raise additional funds by issuing equity securities, our stockholders will experience dilution. Debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Any debt financing or additional equity that we raise may contain terms, such as liquidation and other preferences that are not favorable to us or our stockholders. If we raise additional funds through collaboration and licensing arrangements with third parties, it may be necessary to relinquish valuable rights to our technologies,

future revenue streams or product candidates or to grant licenses on terms that may not be favorable to us.

Cash Flows

The following table summarizes our cash flows from operating, investing and financing activities.

	Years Ended December 31,		Three Months Ended March 31,	
	2018	2017	2019	2018
			(Unaudited)	
Statement of Cash Flows Data:				
Total net cash provided by (used in):				
Operating activities	$ (558,609)	$ (537,481)	$ (228,739)	$ (156,949)
Financing activities	246,449	332,495	530,000	243,649
Increase (decrease) in cash and cash equivalents	$ (312,160)	$ (204,986)	$ 301,261	$ 86,700

Years ended December 31, 2018 and 2017

Operating Activities

For the year ended December 31, 2018, cash used in operations was $558,609 compared to $537,481 for the year ended December 31, 2017. The increase in cash used in operations was primarily the result of the increase in net loss and a reduction in accounts payable and accrued expense balances from 2017.

We expect cash used in operating activities to continue to increase in 2019 as compared to 2018 due to an expected increase in our operating losses associated with ongoing development of our product candidate.

Financing Activities

Cash provided by financing activities was $246,449 during the year ended December 31, 2018, attributable to $243,649 from the sale of 270,722 shares of our Series A-1 Preferred Stock and $2,800 from the sale of 20,000 shares of our common stock. Cash provided by financing activities was $332,495 during the year ended December 31, 2017, attributable to $324,000 from the sale of 360,000 shares of our Series A-1 Preferred Stock and $8,495 from the sale of 70,179 shares of our common stock.

Three Months Ended March 31, 2019 and 2018

Operating Activities

For the three months ended March 31, 2019, cash used in operations was $228,739 compared to $156,949 for the three months ended March 31, 2018. The increase in cash used in operations was primarily the result of an increase in prepaid expense balances.

Financing Activities

Cash provided by financing activities was $530,000 for the three months ended March 31, 2019, attributable to the proceeds from the sale of convertible promissory notes. Cash provided by financing activities was $243,649 for the three months ended March 31, 2018, attributable to the sale of 270,722 shares of our Series A-1 Preferred Stock.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements, except for operating leases, or relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities.

Recent Accounting Pronouncements

In February 2016, the FASB issued its final standard on lease accounting, ASU No. 2016-02, "Leases (Topic 842)," which superseded Topic 840, "Leases," which was further modified in ASU No. 2018-10, "Codification Improvements to Topic 842, Leases," ASU No. 2018-11, "Leases (Topic 842) Targeted Improvements" and ASU No. 2019-01 "Leases (Topic 842) Codification Improvements" to clarify the implementation guidance. The new pronouncement requires the recognition on the balance sheet of right-of-use assets and lease liabilities for all long-term leases, including operating leases, on the balance sheet. The pronouncement requires that lease arrangements longer than 12 months result in an entity classifying leases as a finance or operating leases. However, unlike current U.S. GAAP, which requires only capital leases to be recognized on the balance sheet, ASU 2016-02 will require both types of leases to be recognized on the balance sheet. ASU 2016-02 also requires disclosures about the amount, timing, and uncertainty of cash flows arising from leases. These disclosures include qualitative and quantitative requirements, providing additional information about the amounts recorded in the financial statements.

The pronouncement is effective for all public business entities for interim and annual periods beginning after December 15, 2018 and for non-public business entities with annual periods beginning after December 15, 2019 with early adoption permitted. In July 2018, the FASB issued ASU No. 2018-11, which provides targeted improvements to the new lease standard, including an option to apply the transition provisions at its adoption date instead of at the earliest comparative period presented in its financial statements. We adopted the new leasing standards using a modified retrospective transition approach to be applied to leases existing as of or entered into after January 1, 2019. The adoption of this guidance did not have a material impact on our financial statements.

In May 2014, the FASB issued ASU 2014-09, Revenue from Contracts with Customers (Topic 606), requiring an entity to recognize the amount of revenue to which it expects to be entitled for the transfer of promised goods or services to customers. ASU 2014-09 supersedes nearly all existing revenue recognition guidance under U.S. GAAP and requires revenue to be recognized when promised goods or services are transferred to customers in an amount that reflects the consideration that is expected to be received for those goods or services. Additionally, qualitative and quantitative disclosures are required about customer contracts, significant judgments and changes in judgments, and assets recognized from the costs to obtain or fulfill a contract.

The FASB also issued the following amendments to ASU No. 2014-09 to provide clarification on the guidance:

- ASU No. 2015-14, Revenue from Contracts with Customers (Topic 606)—Deferral of the Effective Date
- ASU No. 2016-08, Revenue from Contracts with Customers (Topic 606)—Principal versus Agent (Reporting Revenue Gross vs. Net)
- ASU No. 2016-10, Revenue from Contracts with Customers (Topic 606)—Identifying Performance Obligations and Licensing
- ASU No. 2016-12, Revenue from Contracts with Customers (Topic 606)—Narrow-Scope Improvements and Practical Expedients

We have elected to early adopt ASU 2014-09 effective January 1, 2017. The standard did not have an impact on our financial statements

In August 2016, the FASB issued ASU 2016-15, Classification of Certain Cash Receipts and Cash Payments, which provides specific guidance related to eight cash flow classification issues. The pronouncement is effective for interim and annual periods beginning after December 15, 2018, and interim periods within fiscal years beginning after December 15, 2019. We elected to early adopt the new pronouncement in the first quarter of 2019. Such early adoption of ASU 2016-15 in the first quarter of 2019 will not have an impact on our financial statements.

In November 2016, the FASB issued ASU 2016-18, Restricted Cash, which requires changes in restricted cash and restricted cash equivalents to be explained on the statement of cash flows by including restricted cash and restricted cash equivalents in the beginning-of-period and end-of-period total cash and cash equivalents shown on the statement of cash flows. The pronouncement is effective for interim and annual periods beginning after December 15, 2018, and interim periods within fiscal years beginning after December 15, 2019. Early adoption is permitted, including adoption in an interim period. If an entity early adopts the amendments in an interim period, any adjustments should be reflected as of the beginning of the fiscal year that includes that interim period. We elected to early adopt ASU 2016-18. The early adoption of ASU 2016-18 in the first quarter of 2019 will not have an impact on our Company's financial statements.

In March 2018, the FASB issued ASU 2018-5—Income Taxes (Topic 740): Amendments to SEC Paragraphs pursuant to SEC Staff Accounting Bulletin No. 118. This ASU provided guidance related to Securities and Exchange Commission ("SEC") Staff Accounting Bulletin No. 118 ("SAB 118"), which addresses the accounting implications of the Tax Act. SAB 118 allows a company to record provisional amounts during a measurement period not to extend beyond one year of the enactment date and was effective upon issuance. We have analyzed the Tax Act, and in certain areas, has made reasonable estimates of the effects on its financial statements and tax disclosures.

In June 2018, the FASB issued ASU 2018-07, Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting. The new guidance expands the scope of Topic 718 to include share-based payments granted to nonemployees in exchange for goods or services used or consumed in an entity's own operations, and supersedes the guidance in ASC 505-50, Equity-Based Payments to Non-Employees. The most significant change resulting from this update is that stock-based awards granted to non-employees will no longer need to be re-measured at fair value at each financial reporting date until performance is complete, as these awards will be measured at fair value at the grant date. The guidance is effective January 1, 2019 with early adoption permitted, including in an interim period for which financial statements have not been issued. We have elected to apply the provisions of this ASU in the Company's financial statements effective January 1, 2017.

In August 2018, the FASB issued ASU No. 2018-13, Fair Value Measurement (Topic 820)—Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement. The new guidance improves and clarifies the fair value measurement disclosure requirement of ASC 820. The new disclosure requirements include the changes in unrealized gains or losses included in other comprehensive income for recurring Level 3 fair value measurement held at the end of reporting period and the explicit requirement to disclose the range and weighted average used to develop significant unobservable inputs for Level 3 fair value measurements. The other provisions of ASU 2018-13 also include eliminated and modified disclosure requirements. The guidance is effective for fiscal years beginning after December 15, 2019 with early adoption permitted, including in an interim period for which financial statements have not been issued or made available for issuance. We have evaluated the impact of adoption of this ASU and determined that it will not have a significant impact on our financial statements.

Quantitative and Qualitative Disclosures about Market Risk

We are exposed to various market risks, which may result in potential losses arising from adverse changes in market rates, such as interest rates and foreign exchange rates. We do not enter into derivatives or other financial instruments for trading or speculative purposes and do not believe we are exposed to material market risk with respect to our cash and cash equivalents.

We currently have no operations outside the United States, but we have contracted with third parties to manufacture our product candidates and conduct clinical trials outside of the United States. At this time, such manufacturing and research costs are paid for in U.S. dollars and, therefore, are not subject to fluctuations in exchange rates. If we conduct additional clinical trials outside of the United States in the future, we may be required or may choose to pay for those clinical trials in a local foreign currency and could incur foreign currency exchange rate risk.

We do not engage in any hedging activities against changes in interest rates or foreign currency exchange rates. Because of the short-term maturities of our cash and cash equivalents, we do not believe that an immediate 10% increase in interest rates would have any significant impact on the realized value of our investments.

JOBS Act

On April 5, 2012, the Jumpstart Our Business Startups Act of 2012, or JOBS Act, was signed into law. The JOBS Act contains provisions that, among other things, reduce certain reporting requirements for an "emerging growth company." As an "emerging growth company," we are electing not to take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards, and as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies. Section 107 of the JOBS Act provides that our decision not to take advantage of the extended transition period is irrevocable.

Subject to certain conditions set forth in the JOBS Act, as an "emerging growth company," we are not required to, among other things, (i) provide an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404, (ii) provide all of the compensation disclosure that may be required of non-emerging growth public companies under the Dodd-Frank Wall Street Reform and Consumer Protection Act, (iii) comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements (auditor discussion and analysis), and (iv) disclose certain executive compensation-related items such as the correlation between executive compensation and performance and comparisons of the chief executive officer's compensation to median employee compensation. These exemptions will apply until the fifth anniversary of the completion of our initial public offering or until we no longer meet the requirements for being an "emerging growth company," whichever occurs first.

FOUNDERS' VISION

WE STRIVE TO PROTECT NERVE CELLS FROM DYING

Neurodegenerative diseases impact millions of people including our own families and friends, and eventually many of us may be afflicted by one of them. Research has come a long way in providing better insights into the brain, its workings and its shortfalls, and our goal is to defeat these diseases by protecting nerve cells from dying and by restoring homeostasis in the brain.

This is a great challenge and an even greater opportunity: defeating neurodegeneration by preserving nerve cells and their function allows people to age with dignity, allows loved ones to enjoy their parents and family members into old age and may help healthcare systems from becoming overwhelmed.

Recent insights into the functioning of the brain and the interaction between nerve cells have given us the tools to look at the toxic cascades, at their path of destruction and at how to stop the course. We are working hard to engineer medicines that are orally available, cross the blood brain barrier and normalize brain homeostasis. While we are in clinical stage, we have not yet established the safety and efficacy of our drug candidates. We will need to obtain regulatory approval after further clinical trials, which we cannot assure will be successful. However, we have been able to show in preclinical and early clinical studies that these drugs can interfere with the toxic cascade at the very beginning and by doing so, may slow down or stop the destruction of nerve cells.

We have assembled what we believe to be an outstanding team and a network of collaborators who are passionate about solving the diseases all leading to neurodegeneration, such as Alzheimer's disease in Down syndrome, Alzheimer's disease and Parkinson's disease.

Our main goal is to provide a solution to the problems that patients of neurodegenerative diseases face. We are also mindful, however, of the risks that we will face in this process. Please, join us in our journey as we seek to develop drugs to mitigate the effects of neurodegeneration.

Maria Maccecchini, Ph.D.
CEO and Founder

Jeffrey Cummings, MD
CMO

BUSINESS

Our Company

Annovis is a clinical stage, drug platform company addressing neurodegeneration, such as Alzheimer's disease in Down syndrome (AD-DS), Alzheimer's disease (AD) and Parkinson's disease (PD). We have an ongoing Phase 2a proof-of-concept study in AD patients and have planned to commence a second Phase 2a study in PD patients. We are developing our lead compound, ANVS-401, for chronic neurodegenerative diseases, such as AD-DS, AD and PD. In a number of studies, ANVS-401 inhibited the synthesis of neurotoxic proteins—APP/A β (APP), tau/phospho-tau (tau) and α -Synuclein (α -SYN)—that are the main cause of neurodegeneration. High levels of neurotoxic proteins lead to impaired axonal transport, which is responsible for the communication between and within nerve cells. When that communication is impaired, the immune system is activated and attacks the nerve cells, eventually killing them. Through our patented product platform, in clinical studies in mildly cognitive impaired (MCI) patients, ANVS-401 normalized levels of neurotoxic proteins and inflammatory factors. In preclinical studies, the lowering of neurotoxic proteins also led to the restoration of axonal transport, lowering of inflammation and prevention of nerve cell death.

The industry has encountered challenges in targeting specifically one or the other neurotoxic protein, be it APP, tau or α SYN, indicating that targeting one neurotoxic protein alone does not change the course of neurodegeneration. Our goal is to develop a disease modifying drug (DMD) for patients with neurodegeneration by leveraging our clinical and animal evidence in inhibiting at least the three most relevant neurotoxic proteins.

We believe that we are the only company developing a clinical stage proof-of-concept drug for AD-DS, AD and PD that inhibits more than one neurotoxic protein and has a mechanism of action designed to restore nerve cell axonal and synaptic activity. By restoring axonal transport and homeostasis in the brain we expect to treat memory loss and dementia associated with AD-DS and AD as well as body and brain function in PD.

We believe that ANVS-401 has the potential to be the first drug to interfere with the underlying mechanism of neurodegeneration. ANVS-401 is a small, once a day, orally administered, brain penetrant inhibitor of neurotoxic proteins. The biological activity of ANVS-401 has been evaluated in 19 animal studies conducted in leading institutions such as the Karolinska Institute, Columbia University and Harvard University. We also conducted three clinical trials with 125 humans including two safety studies in 120 healthy volunteers and a proof-of-concept study in five MCI patients with Parexel, an international clinical research organization. In these studies, we showed that ANVS-401 was well tolerated and we saw promising clinical signals: ANVS-401 reduced and normalized the levels of APP, tau and α SYN back to the levels seen in healthy volunteers and statistically lowered inflammation.

We are presently conducting a Phase 2a study in AD patients in collaboration with the Alzheimer Disease Cooperative Study (ADCS) group and plan to initiate a second Phase 2a proof-of-concept study of ANVS-401 in the first quarter of 2020 with 50 PD patients. The study being conducted by ADCS is expected to enroll a total of 24 persons at three dose levels plus placebo in a double-blind, placebo controlled fashion. To date, the study has enrolled and treated six early to moderate AD patients and has enrolled two additional patients. Under an agreement with UC San Diego, where ADCS is located, we have agreed to provide study supplies at our cost. The agreement also contains standard indemnification and confidentiality provisions and may be terminated by either party upon 30 days' written notice. We have designed the two Phase 2a studies with Parexel by applying our understanding of the underlying disease states in neurodegeneration and by measuring not just target, but also pathway validation in the spinal fluid of these patients. By showing both target and pathway validation in two patient populations, we believe that our opportunity for successful Phase 3 studies is better than if we merely demonstrated target validation in one patient population.

We believe AD and PD are two of the largest medical needs of the aging U.S. population, and two potentially large markets, once a DMD has been developed and approved. Therefore, we desire to demonstrate ANVS-401's efficacy in both indications. However, since AD studies are very large and time and capital consuming, we plan to focus on an orphan population that is substantially similar to AD, but in a very controlled and limited setting. We intend to focus on AD in the DS population; in DS the APP gene is triplicated, leading to early onset AD with similar pathology as sporadic AD. In accordance with our animal studies in DS mice, lowering their high levels of APP is expected to restore axonal transport and homeostasis in the brain of DS patients and normalize their memory loss and dementia. This will allow us to obtain human data for AD in an orphan subpopulation much faster than in the regular AD population. Concomitantly, our goal is to also conduct a Phase 3 pivotal study in early PD patients. By the end of 2024, we expect to have conducted two pivotal studies for ANVS-401, one in AD-DS and one in PD, and to have filed a new drug application (NDA) with the U.S. Food and Drug Administration (FDA).

Landscape of Drug Development for Alzheimer's Drugs

Drug development for AD has proven to be very difficult. Five drugs are approved for the treatment of AD including four cholinesterase inhibitors (tacrine, donepezil, rivastigmine, galantamine) and an N-methyl-D-aspartate (NMDA) receptor antagonist (memantine). No new treatments have been approved for AD since 2003. While these drugs ameliorate the symptoms, the ultimate aim is the development of disease modifying therapies (DMT) that stop or slow the progression of AD.

Since 2003, over 500 clinical studies have been completed and no compound has shown efficacy. AD drug candidates have the highest failure rate of 100%, compared to 50% to 80% for other indications. Among the DMTs the most common pathway has been to target amyloid beta as dictated by the amyloid hypothesis. All studies attacking A β to date have failed, but since A β accumulates years before the symptoms of AD are visible, there is a movement in the industry toward treating patients with milder forms of AD including cognitively normal individuals with evidence of amyloid pathology in spinal fluid or by amyloid positron emission tomography (PET) or who have genetic profiles that place them at high risk for developing AD. These approaches have missed their endpoints as shown by the very recent discontinuations of the Roche/ACImmune and the Biogen/Eisai studies. To date, over $40 billion have been spent on dead-end approaches.

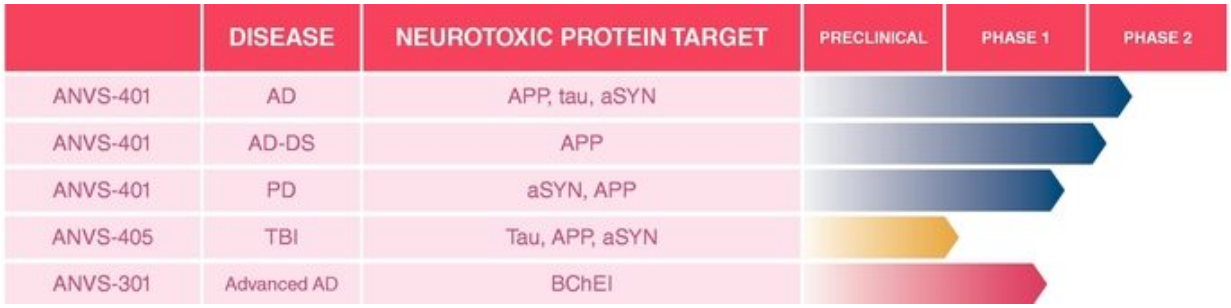
Why have all DMD approaches failed to date? In 1906 Alois Alzheimer opened the brain of a woman that had died with severe dementia and he found plaques, tangles and brain shrinkage. He called the condition Alzheimer's disease. Today we are still calling this condition AD. However, what Alois Alzheimer found was the end stage. Removing plaques and tangles does not restore the brains vigor, communication system and homeostasis.

What is the beginning of neurodegeneration? It starts out with high levels of neurotoxic proteins that cause impairments in axonal transport.

Innovation

Pipeline

Our Pipeline is focused primarily on drugs for chronic neurodegeneration—AD, its orphan indication AD-DS and PD. Additionally, we have a compound to treat acute neurodegeneration—traumatic brain injury (TBI) and stroke—and a third compound for advanced AD.



ANVS-401

Anvs-401 is being developed for AD-DS, AD and PD, because in preclinical studies it normalized axonal transport in these diseases by inhibiting neurotoxic proteins that kill nerve cells. The compound was tested in three Phase 1 clinical studies that showed it to be well tolerated. This safety data is applicable to the clinical development of ANVS-401 for AD-DS, AD, PD and other chronic neurodegenerative disorders.

ANVS-405

For acute indications, we are developing ANVS-405, focused on protecting the brain after TBI and/or stroke. In a preclinical study, TBI rats that were treated with ANVS-405 after the insult exhibited normal memory and learning, normalized inflammation and re-established homeostasis in the brain.

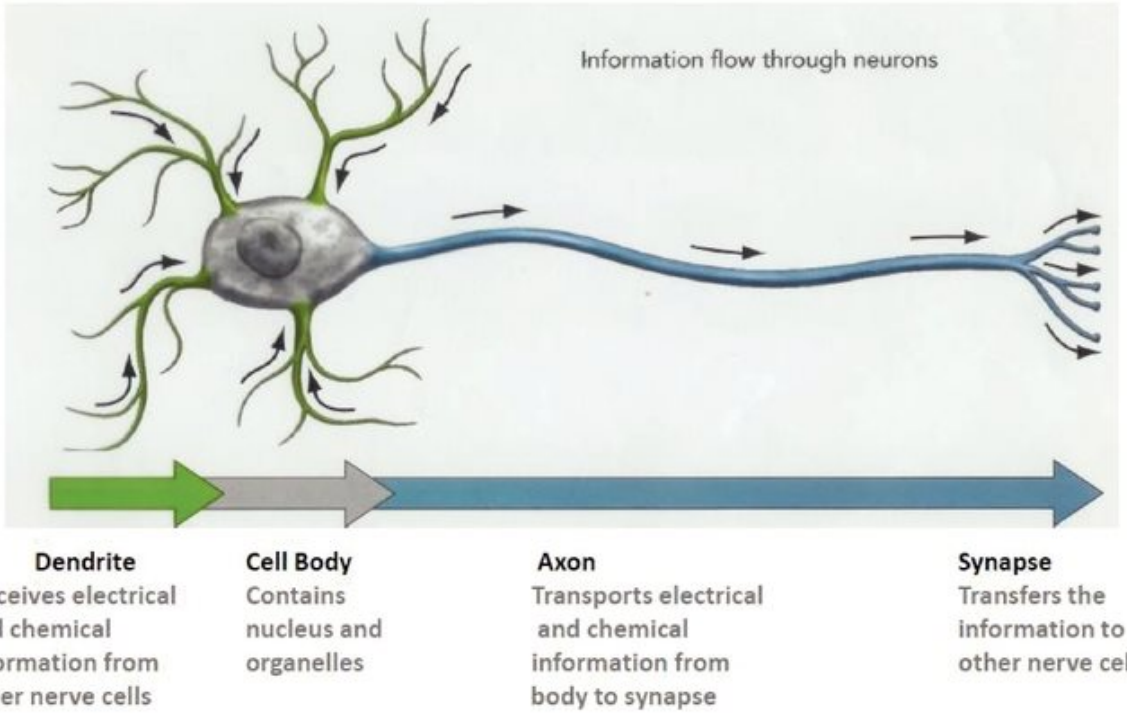
ANVS-301

Our compound ANVS-301 is expected to increase cognitive capability in later stages of AD and dementia. In preclinical studies, ANVS-301 fully restored memory and learning in very old rats and made the old rats cognitively equivalent to young rats. ANVS-301 is in a Phase 1 clinical trial that is being conducted and financed by the National Institutes of Health (NIH).

Background—What is Neurodegeneration?

A normal nerve cell receives signals, processes them in the cell body and transports them through the axon, a long-arm nerve fiber that extends out from the cell body and connects to the synapses, or fingers. These fingers then touch the successive nerve cell(s), where the signals are relayed further.

Nerve Cell with Axon and Synapse



When brain cells become injured or stressed their first response is reduction and impairment of axonal transport. If the insult persists, axonal vesicle transport remains impaired resulting in decreased levels of neurotransmitters and leading to depression (serotonin), anxiety and insomnia (GABA), AD (acetylcholine) and PD (dopamine). It also results in lower levels of neurotrophic factors and in nerve cells getting sick. When the immune system sees a sick cell, it attempts to remove it, which leads to inflammation in the brain. Eventually, the sick cell is then killed by the immune system.

ANVS-401—Our Solution to Reverse Neurodegeneration

ANVS-401 is a small lipophilic molecule that is orally available and readily enters the brain, as demonstrated by pharmacokinetics analyses showing brain concentrations approximately 6 to 8 times higher than plasma concentrations. In different studies we found slightly different ratios because of the time of measurement after administration and the average is approximately 6 to 8 times higher than plasma concentrations. In preclinical studies, ANVS-401 showed a mechanism of action we believe to be unique, in that it inhibited the translation and, therefore, the levels of several key neurotoxic aggregating proteins both *in vitro* and *in vivo* including APP, tau and α SYN. Three Phase 1 clinical studies demonstrated that ANVS-401 was well tolerated. The third proof-of-concept study showed that it normalized levels of APP, tau and α SYN (α SYN is an unpublished observation) in the cerebrospinal fluid (CSF) of MCI patients. Additionally, we now have preclinical data that showed that ANVS-401 restored memory and learning in AD transgenic (tg) and DS trisomic mice models. ANVS-401 also restored colonic motility in a PD tg mouse model of PD.

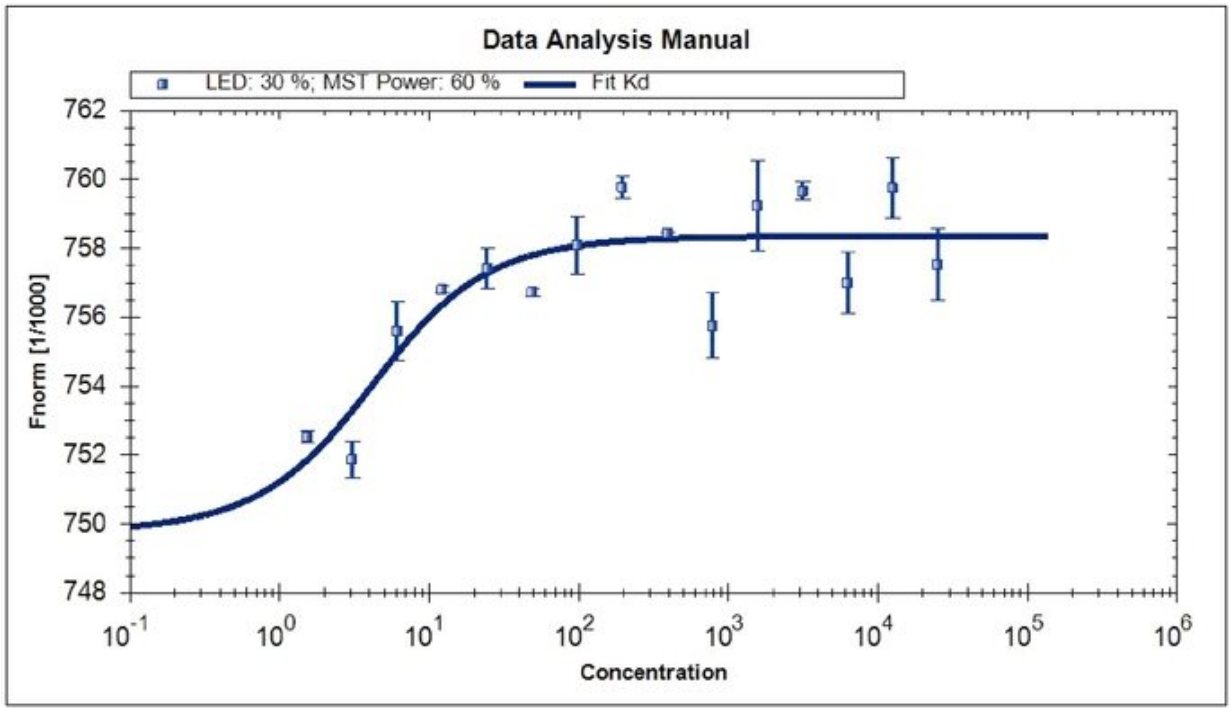
By targeting multiple neurotoxic aggregating proteins, ANVS-401 resembles a combination therapy approach, with the added convenience of being a single drug with a single drug target. Therefore, we have worked to understand how ANVS-401 is able to inhibit the translation of more than one neurotoxic protein.

Novel Mechanism of Action and Target Engagement

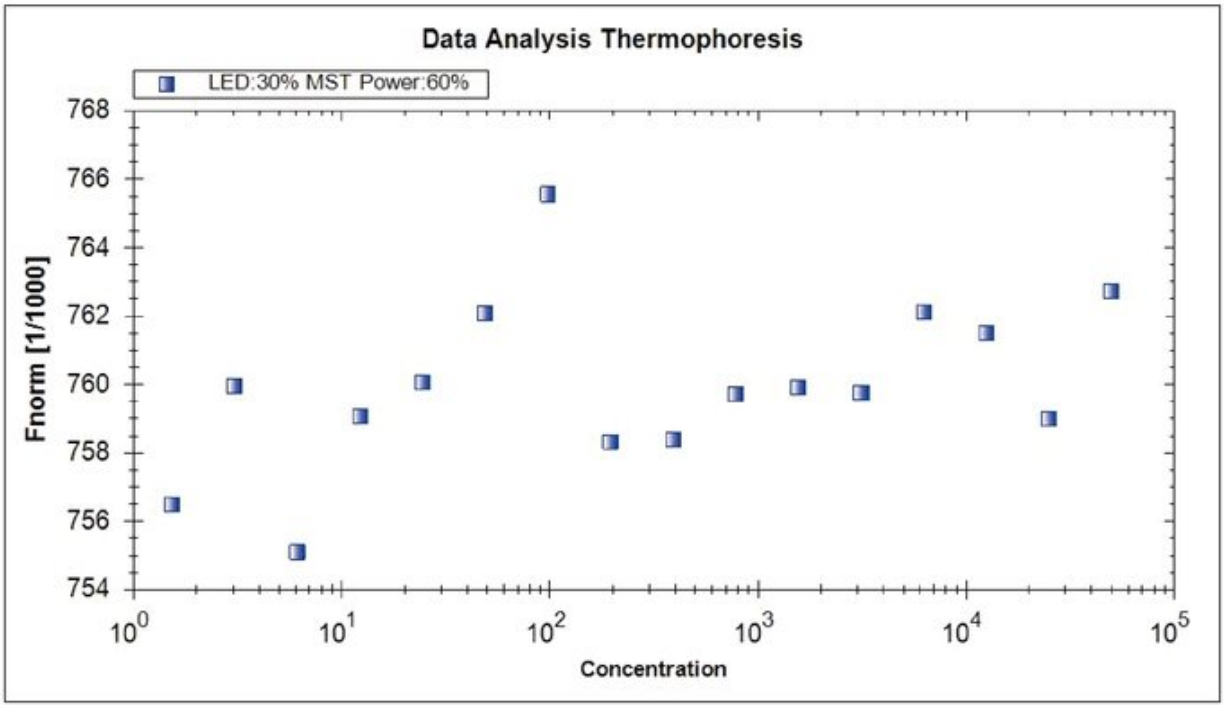
We undertook an extensive exploration of the mechanism of action of ANVS-401 on APP and α SYN synthesis and determined that ANVS-401 specifically inhibits translation of mRNAs coding for neurotoxic proteins only. Using 5 different methods we produced overlapping results *in vitro* . mRNAs of neurotoxic proteins have a conserved stem loop in the 5' untranslated region (5'UTR) called an iron-response element (IRE) type II stem loop. These IREs bind to an RNA binding protein, specifically to iron regulatory protein 1 (IRP1). When the mRNAs are bound, they are not translated, when the iron levels in the cytoplasm go up, IRP1 releases its mRNAs and they are translated.

Target Engagement

In preclinical studies, ANVS-401 specifically became bound to the IRE/IRP1 complex of mRNAs coding for neurotoxic proteins and stops the release of the mRNAs under high iron conditions. It did not bind to IRE/IRP1 complexes of mRNAs coding for iron carrying or shuttling proteins, such as ferritin transferring or ferriportin.



APP/IRE/IRP1/ ANVS-401 Kd 3.2 nM

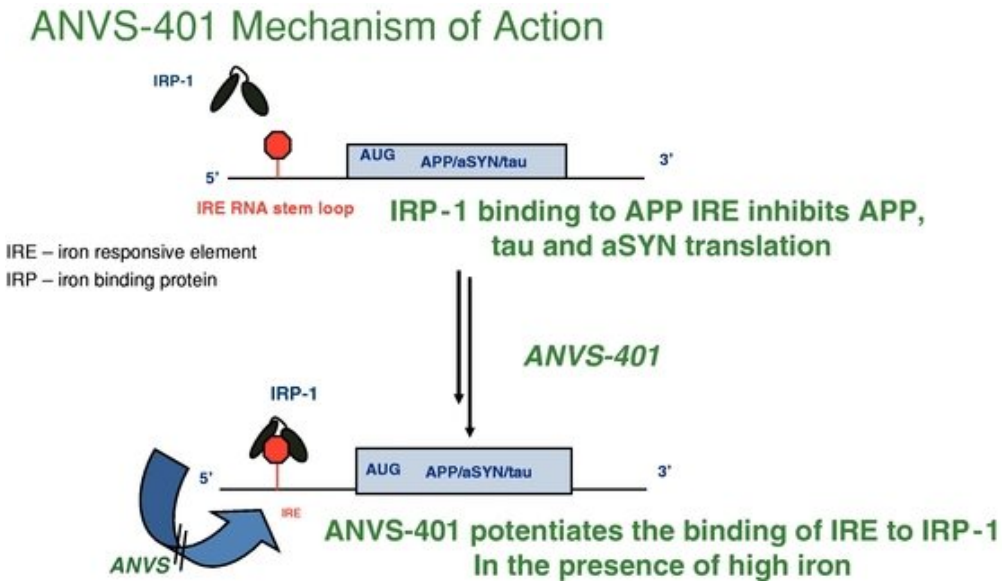


Ferritin IRE/IRP1/ANVS-401 no Kd

ANVS-401 binds to the APP IRE/IRP1 complex but not the Ferritin IRE/IRP1 complex

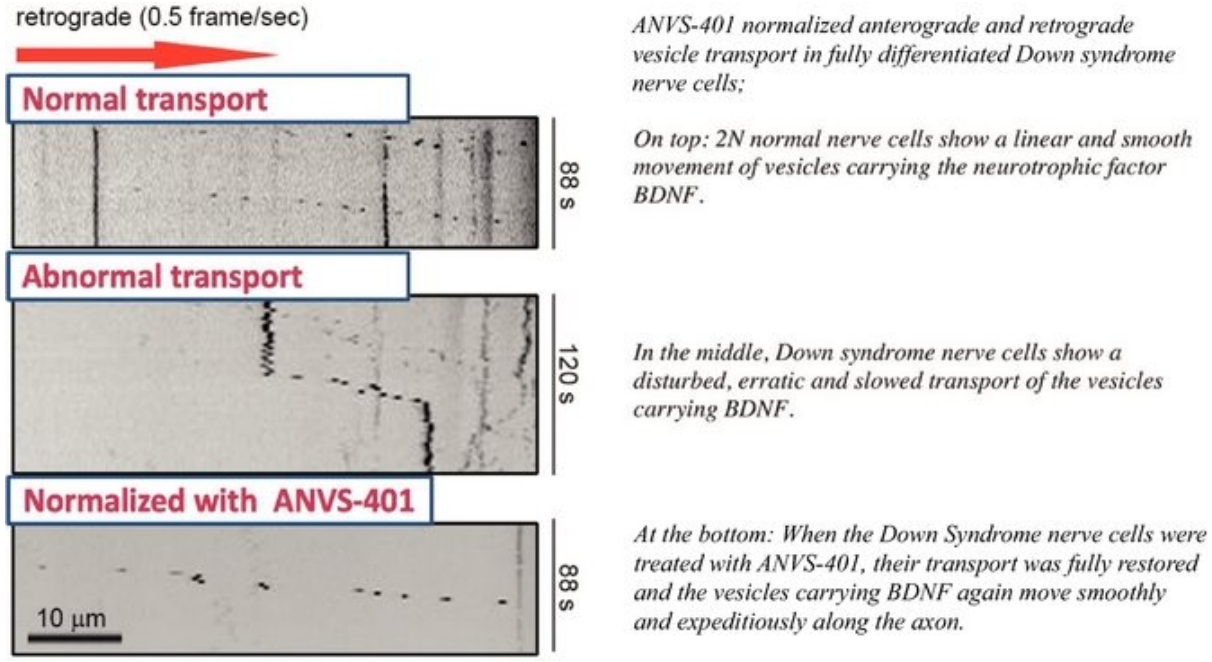
Since the 5' UTR IRE is highly conserved among the mRNAs of neurotoxic proteins, we believe ANVS-401 can inhibit the translation of several neurotoxic aggregating proteins by having just one binding site and by increasing the binding of that conserved IRE to IRP1 under high iron conditions (see graph below). This has been shown for APP and α SYN. We now know that homologous IRE type II loops are also present in the 5'UTR of mRNAs that code for other neurotoxic aggregating proteins: tau, Prion protein (PrP), huntingtin (htt), and superoxide dismutase 1 (SOD1). Furthermore, we have binding data confirming the interaction of IRP1 with the IREs from human APP, α SYN, tau, PrP, htt, and SOD1 (not shown). Finally, we now understand that ANVS-401 only increases the binding of IREs of neurotoxic aggregating proteins to IRP1 under stress conditions, so it does not affect healthy tissue and does not affect other proteins whose mRNAs form a different kind of IRE stem loop (e.g. ferritin).

In preclinical studies, ANVS-401 inhibited over-expression of neurotoxic proteins by binding to the IRE-IRP1 complex and preventing the opening of IRP1 and concomitant release of the mRNA under high iron conditions.



Axonal Transport and Pathway Engagement

APP, tau, and α SYN impair axonal transport and synaptic transmission, causing inflammation, forming aggregates, and, finally, leading to nerve cell death. Through several studies, we have found that, by reducing APP, tau and α SYN levels, ANVS-401 treatment restored normal axonal transport and prevented or restored all those events.



ANVS-401 normalized anterograde and retrograde vesicle transport in fully differentiated Down syndrome nerve cells;

On top: 2N normal nerve cells show a linear and smooth movement of vesicles carrying the neurotrophic factor BDNF.

In the middle, Down syndrome nerve cells show a disturbed, erratic and slowed transport of the vesicles carrying BDNF.

At the bottom: When the Down Syndrome nerve cells were treated with ANVS-401, their transport was fully restored and the vesicles carrying BDNF again move smoothly and expeditiously along the axon.

In preclinical trials, by normalizing axonal transport, ANVS-401 and/or ANVS-405 normalized all the functions that are negatively affected by disturbances of the transport.

Pathway Engagement:

- Studies showed that ANVS-401 lowered and normalized levels of neurotoxic proteins:
  - AD tg mice—restored normal levels of APP and its fragments with full recovery of memory, learning and brain function. The AD tg mice on placebo never learned to find their way in the 7-arm water maze with less than 3 to 4 mistakes, whereas the ANVS-401 treated mice found their way with one mistake, just like the normal wild-type mice.
  - DS trisomic mice—restored normal levels of APP and fully recovered memory and learning. The trisomic mice moved 38% less and made 68% more mistakes in the maze, whereas the ANVS-401 treated mice performed like normal wild-type mice.
  - PD tg mice—restored normal levels of α SYN in brain and gut with full recovery of gut motility. The PD tg mice at 4 months had 4 times slower and at 7 months 7 times slower gut motility than normal wild-type mice. ANVS-401 restored colonic motility.
  - MCI patients—restored normal levels of APP, tau and α SYN.
- Studies showed that ANVS-401 normalized retrograde and anterograde transport:
  - DS trisomic mice nerve cells—in studies conducted at UCSD, inhibition and normalization of APP levels led to restoration of anterograde and retrograde vesicle transport. ANVS-401 treatment of the DS nerve cells resulted in an increase in velocity of 70%, a value comparable to the velocity seen in normal neurons. ANVS-401 also decreased the pause time by 29%, again bringing it to the same pause time as in healthy normal cells. This was measured *in vitro* in isolated fully differentiated nerve cells.
- Studies showed that ANVS-401 normalized impaired synaptic transmission in:
  - AD tg mice—A Columbia University study showed that the AD tg mice treated with ANVS-401 had normal long-term potentiation, whereas long-term potentiation of the placebo treated AD tg mice was reduced by 66%.
- Studies showed that ANVS-405 increased neurotransmitter release in:
  - Rat striatum after TBI—A UCLA study showed that after TBI animals treated with placebo had 31% less dopamine than animals treated with ANVS-405.
- Studies showed that ANVS-401 increased levels of neurogenesis and brain derived neurotrophic factor (BDNF) in:
  - DS trisomic mice. A UCSD study, *in vivo* , was able to show a 60% increase in BDNF in DS trisomic animals treated with ANVS-401 compared to placebo.
  - AD tg mice brains—The Karolinska Institute measured BDNF and found that after ANVS-401 treatment, old AD tg mice showed increased levels of BDNF.
- Studies showed that ANVS-401 and/or ANVS-405 lowered inflammation in:
  - MCI patients—In a proof of concept clinical trial, 5 MCI patients treated with ANVS-401 had inflammatory factors that were statistically reduced.
  - TBI rats—rats with traumatic brain injury had much larger microglia than normal rats. Enlarged microglia means that the microglia is activated and shows inflammation. After treatment with ANVS-405, the size of the microglia shrank back to the size seen in healthy normal rat brain.
- Studies showed that ANVS-405 protected nerve cells in:
  - TBI rats—A UCLA study stained the rat substantia nigra for dead cells and found after TBI that 15% of the cells had died in placebo treated TBI rats. In ANVS-405 treated rats the nerve cells did not die.

- Retina rats—In a Hershey Medical Center unpublished study in which saline was injected into one eye to increase the pressure, which kills retinal cells, ANVS-405 protected 67% of the retina.

By normalizing levels of neurotoxic proteins, ANVS-401 normalized the affected functions in all diseases we tested. Rat TBI and glaucoma are acute indications. These studies were done with ANVS-405. These functions are: memory, learning, fear conditioning and long-term potentiation in AD mice; gut and gait function in PD mice; memory and learning in TBI rats; and sight in acute glaucoma rats.

Collectively, we believe these effects make ANVS-401 a very promising drug for the treatment of memory loss and dementia in AD-DS and AD and bodily and brain functions in PD.

Impact: Our goal, in our Phase 2a studies in AD and PD patients, is to demonstrate that ANVS-401 is well tolerated and is able to normalize the CSF levels of neurotoxic proteins (at least APP, tau, and α SYN) and inflammatory markers, as previously seen in preclinical studies. In these studies, we are also planning to analyze the CSF levels for additional neurotoxic aggregating proteins, control proteins lacking the conserved mRNA sequence of neurotoxic aggregating proteins, as well as neurotransmitters, neurotrophic factors, degeneration markers, and cognitive outcomes. Thus, we expect that we will be able to identify biomarkers for use in later studies.

ANVS-401—How was it discovered?

ANVS-401 is a small orally available molecule that readily passes the blood brain barrier and reaches high brain levels. It is the only molecule discovered to date that inhibits more than one neurotoxic protein and restores axonal transport, synaptic function and nerve cell health.

It was synthesized and invented by Dr. Nigel Greig at the National Institute on Aging (NIA) of the National Institutes of Health (NIH), which is a part of the U.S. Public Health Service (PHS). Originally Dr. Greig set out to make a better acetylcholinesterase inhibitor (AChEI), similar to Aricept but better. He discovered over 500 analogs of physostigmine and chose phenserine as the best AChEI. Phenserine had an affinity for AChE of 22 nM and was an improvement over Aricept with 900 nM. Axonyx, Inc. licensed phenserine and developed it as an AChEI through three Phase 3 studies that all failed. Even though a potent AChEI, phenserine had caused severe vomiting.

When Dr. Greig made the 500 analogs, he had a group that had no acetylcholinesterase activity. Therefore, at that time they were of no importance to him. Ten years later a friend of his, Debomoy Lahiri, told him that he had developed a phenotypic screen for APP inhibition and Dr. Greig gave him all his compounds. It turned out that the group that had no AChEI activity did inhibit APP in the screen. As it looked like the analogs had similar affinity for APP inhibition, Dr. Greig chose ANVS-401, the positive enantiomer of phenserine, as the lead compound.

Dr. Greig patented the new group of compounds and also licensed them to Axonyx. He published extensively and patented his inventions.

Axonyx Inc. conducted the preclinical toxicology in three animal species (mice, rats and dogs), conducted pharmacokinetic studies and pharmacodynamic studies in several animal species, manufactured adequate amounts of GMP material, and filed an investigational new drug application with the FDA. In October 2006 phenserine failed and Axonyx Inc. merged with TorreyPines Therapeutics, Inc., which later in 2009 merged with Raptor Pharmaceuticals, Inc. Raptor Pharmaceuticals was acquired by Horizon Therapeutics PLC in 2016. Currently, the technology is co-owned by a subsidiary of Horizon and the PHS and Annovis has exclusive worldwide rights to the technology.

In summary the (–) enantiomers including phenserine are symptomatic AChEIs, whereas the (+) enantiomers including ANVS-401 have no AChEI activity and inhibit the translation of neurotoxic proteins, such as APP/A β , tau/p-tau and α SYN and protect nerve cells from dying. They are DMDs and promise to stop or slow the course of neurodegeneration

Clinical Human Data

Three clinical studies have been conducted with ANVS-401. Clinical studies with single and repeated daily oral administration of ANVS-401 tartrate showed ANVS-401 to be well tolerated up to single doses of 80 mg or QID (four times a day) doses of 60 mg. A single dose of 160 mg was associated with an increased incidence of nausea and vomiting so higher doses were not tested. ANVS-401 is not an AChE inhibitor, but its N^1 dimethyl metabolite (10-20%) has some AChE inhibitor activity and may be responsible for these observations. The only consistent adverse events (AEs) seen were dizziness/fainting and headaches. These effects were seen to varying degrees at all doses of ANVS-401 and also in the placebo group. There were no serious AEs in any of the clinical studies.

The key findings from the three clinical studies are highlighted below.

- **Single ascending dose (SAD) in 60 healthy volunteers**

  Drug determined to be well-tolerated, with an no adverse events (AE) at 80 mg and a maximum tolerated dose maximum tolerated dose (MTD) of 160 mg

  Dose limiting toxicity was nausea

- **Multiple ascending doses (MAD) in 48 healthy volunteers vs. placebo control**

  Drug determined to be well-tolerated with no AEs at 240 mg/day (60 mg QID)

  PK: Drug absorbed rapidly; C_{max} = 1.5 hrs, $T_{1/2}$ = 5 hrs in plasma

  At doses up to 60 mg QID, ANVS-401 showed no symptoms indicative of inhibition of either acetyl- or butyrylcholinesterase

- **Proof of Concept (POC) in five Mild Cognitive Impairment (MCI) patients**

  Concentrations of ANVS-401 in the brain, extrapolated from blood and CSF, were 8x higher than in plasma

  The half-life of ANVS-401 in the CSF/brain was twelve hours vs. five in plasma

  Ten days of treatment with ANVS-401 normalized CSF levels of sAPP, and Tau, and reduced α SYN and a series of inflammatory markers

  The concentration and persistence of ANVS-401 in the brain suggest that much lower doses of drug administered once daily could achieve the desired pharmacodynamic effect

  These data are reported to the FDA in SN 0016 and SN 0018 and published.

Summary of Pharmacokinetics (PK) in Humans

ANVS-401 is stable, orally available, has a half-life of >12 hours, and is well qualified as an oral development candidate. The systemic oral availability of ANVS-401 increased disproportionately with increasing dose over the range 10–160 mg

T_{max} was 1.3–1.6 hours post dose, independent of dose and comparable for both sexes

AUC and C_{max} for ANVS-401 increase faster than linearly with increasing dose in this range

At doses 40-160 mg, ANVS-401 exhibited a dose-independent $T_{1/2}$ of approximately 5 hours in plasma of both males and females

Differences in AUC values and C_{max} for the fixed doses of ANVS-401 used in this unreported study are well-explained by body weight

PK after 7 and 9 days of QID ANVS-401 was similar to Day 1, with no significant accumulation of drug in plasma.

Summary of Safety in Humans

ANVS-401's pattern of AEs was similar to that seen in typical studies in healthy normal volunteers, with an overall incidence of 33.3% among placebo-treated subjects and 35% for all ANVS-401 treatment groups combined. In the single ascending dose study, the group given the highest dose of 160 mg/day showed 31.7% AEs that were treatment-related. In the multiple ascending dose and in the POC study there was no dose response to the adverse events. Most AEs were of short duration, mild or moderate in severity, resolved without medical intervention, and occurred in one or a few subjects. Only two subjects experienced severe AEs, including symptoms associated with orthostatic hypotension (1 placebo and 1 ANVS-401 20-mg subject).

Adverse events seen in the first human SAD study conducted with ANVS-401

Single Ascending Dose in 72 Healthy Volunteers # of Events (% of Group)	**10 mg n=10**	**20 mg n=20**	**40 mg n=10**	**80 mg n=10**	**160 mg n=10**	**All ANVS-401 n=60**	**Placebo n=12**
Adverse Events							
AEs, mild	2 (20)	4 (20)	1 (10)	3 (30)	3 (30)	13 (21.7)	2 (16.7)
AEs, moderate	1 (10)	2 (10)	0 (0)	0 (0)	4 (40)	7 (11.7)	1 (8.3)
AEs, serious	0 (0)	1 (5.0)	0 (0)	0 (0)	0 (0)	1 (1.7)	1 (8.3)
Gastrointestinal Disorders							
Nausea	0 (0)	2 (10)	0 (0)	0 (0)	4 (40)	6 (10)	0 (0)
Vomiting	0 (0)	0 (0)	0 (0)	0 (0)	3 (30)	3 (5.0)	0 (0)
Nervous System Disorders							
Dizziness	1 (10)	4 (20)	1 (10)	3 (30)	4 (40)	13 (21.7)	3 (25)
Fainting	1 (10)	1 (5.0)	0 (0)	0 (0)	0 (0)	2 (3.3)	1 (8.3)
Others	2 (20)	4 (20)	0 (0)	0 (0)	0 (0)	6 (10)	3 (25)

Adverse events seen in the second and third human MAD and POC studies conducted with ANVS-401

Multiple Ascending Dose in 48 Healthy and 5 MCI Volunteers # of Events (% of Group)	4 x 20 mg n=12	4 x 40 mg n=12	4 x 60 mg n=12	All ANVS-401 n=36	Placebo n=12	MCI 4 x 60 mg n=5
Adverse Events						
AEs, mild	6 (50)	3 (25)	3 (25)	12 (33.3)	4 (33.3)	3 (60)
AEs, moderate	2 (16.7)	0 (0)	1 (8.3)	3 (8.3)	2 (16.7)	0 (0)
AEs, serious	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Gastrointestinal Disorders						
Nausea	1 (8.3)	0 (0)	2 (16.7)	3 (8.3)	1 (8.3)	1 (20)
Vomiting	0 (0)	0 (0)	3 (25.0)	3 (8.3)	0 (0)	0 (0)
Nervous System Disorders						
Dizziness	2 (16.7)	2 (16.7)	3 (25.0)	7 (19.4)	1 (8.3)	1 (20)
Fainting	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Others	8 (6.6)	4 (33.3)	2(16.6)	14 (38.8)	8(22.2)	7 (140)

POC in Humans

In the human POC study, five patients with MCI were treated for 10 days with ANVS-401 with a dose of 4x60 mg, (240 mg/day), which we knew from our MAD study to be a safe level. CSF and plasma were drawn over 12 hours on day 0 and day 11. Levels of ANVS-401 and metabolites were measured in plasma and CSF over the 12 hours. ANVS-401 PK in plasma corresponded to what the Company had seen in the previous clinical safety studies: $T_{1/2}$ = 5 hrs. In CSF, however, ANVS-401 showed a much longer half-life of $T_{1/2}$ > 12 hours. Annovis conducted an identical experiment in rats, where it is possible to measure the PK of ANVS-401 in plasma, CSF and brain. By taking the human plasma/CSF and rat plasma/CSF/brain levels, Annovis was able to extrapolate to the human brain levels and calculate them to be eight times higher than plasma levels. This is consistent with the data the Company has in mice, where in a number of studies, ANVS-401 levels were found to be 8-9 times higher in brain than in plasma.

ANVS-401's extended presence in the brain is matched by an extended effect, reducing levels of APP, tau and α SYN for the whole period tested (over 12 hours). The extended effect of ANVS-401 in humans was consistent with the preclinical data in rodent brains.

The persistence of ANVS-401 in the CSF and brain and the extended pharmacodynamic effect observed make ANVS-401 a good candidate for once a day dosing. Extrapolated brain levels of ANVS-401 at 60 mg QID were far in excess of levels required to down-regulate APP and α SYN. The doses of ANVS-401 needed to lower the levels of neurotoxic proteins are similar for the toxic aggregating proteins, suggesting similar dosing in AD, AD-DS, PD as well as Frontotemporal Dementia (FTD) and Huntington's disease (HD). Annovis further compared ANVS-401 brain levels of mice that showed full reversal of their AD or PD and calculated that the optimum brain levels to achieve full efficacy are between 150 and 500 nM. Using three different extrapolation/comparison calculations the Company deduced that a daily dose of 20-60 mg should achieve desired brain levels and efficacy.

CSF BIOMARKERS SIGNIFICANTLY DECREASE AFTER 10 DAYS OF ORAL ANVS-401 IN MCI PATIENTS

Human Biomarker	CSF % of Baseline	p-Value
sAPP α	–59.9%	0.0006
sAPP β	–57.7%	0.0001
A β 42	–51.4%	0.053
Tau	–46.2%	0.002
p-Tau	–61.0%	0.0005
α SYN	–41.2%	0.091*

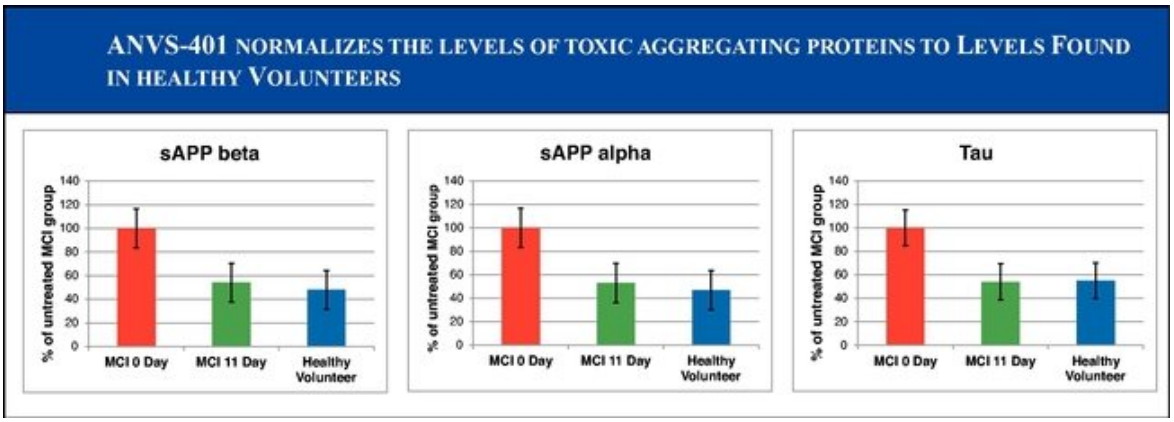
* Represents unpublished results.

MCI patients were treated for 10 days and CSF was extracted for 12 hours before and after the last administration of ANVS-401. Data show about 50% lower levels of aggregating toxic proteins; the levels measured have dropped to levels found in healthy normal volunteers.

TABLE: INFLAMMATORY MARKERS AFTER 10 DAYS ON ANVS-401

Human Inflammatory Protein	CSF % of Baseline	p-Value
Complement C3	–86.9%	0.0007
MCP-1	–87.5%	0.0007
YKL40	–72.7%	0.0113
sCD14	–26.1%	0.1159
Factor FH	23.7%	0.4988

MCI patients also show high levels of inflammatory factors and microglia activation factors in their CSF. ANVS-401 significantly lowered the levels of a number of inflammation factors in their CSF. As expected, Complement factor H (a regulator) was not altered).



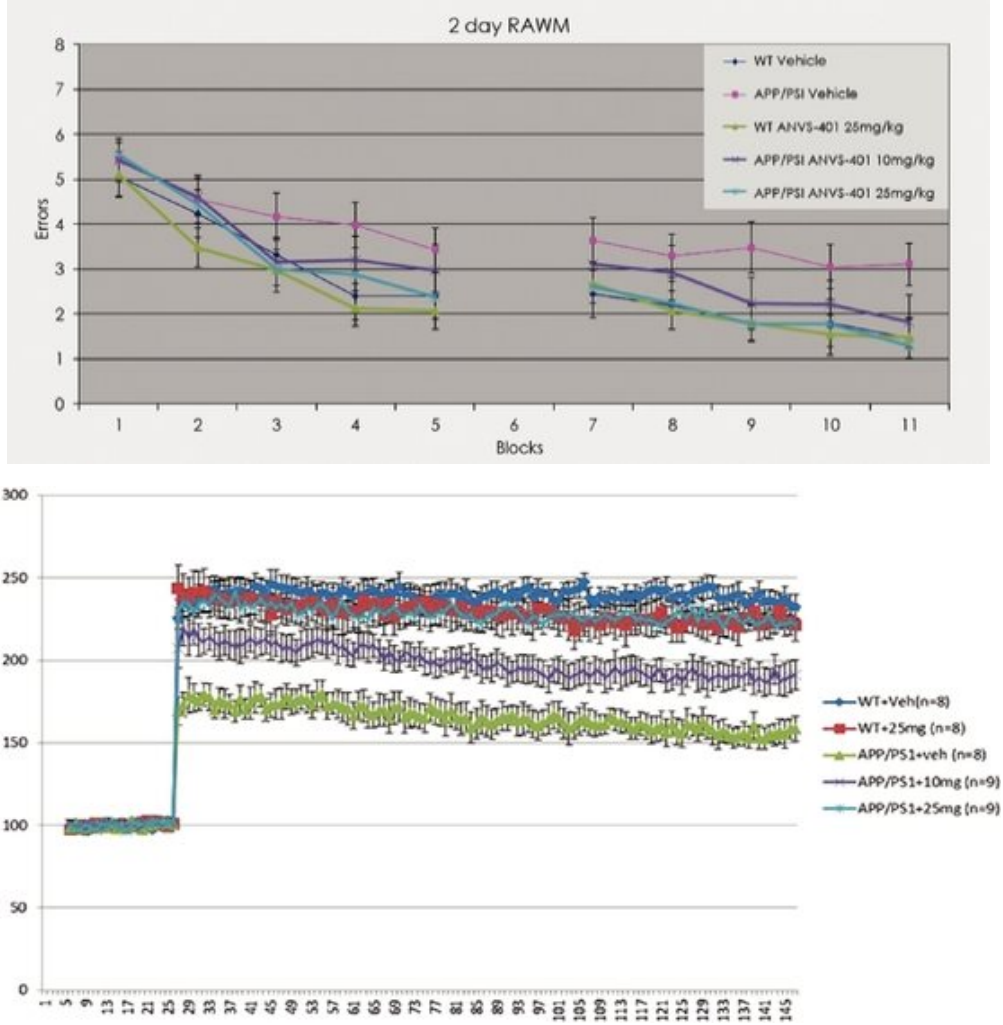
Aggregating proteins measured in the CSF of MCI patients in the POC study described above. ANVS-401 given for 10 days normalizes APP and Tau.

Preclinical Animal Studies

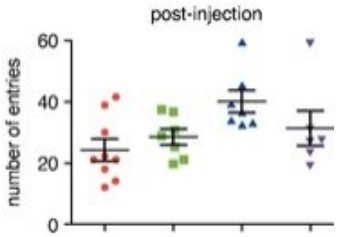
By normalizing the expression of neurotoxic aggregating proteins, ANVS-401 restores or prevents the symptoms associated with chronic as well as acute neurodegeneration in a number of animal models. The data most relevant to the present application are shown.

APP/PS1 tg Mouse Model of AD

ANVS-401 fully rescued spatial-working memory defects in a 2-day radial arm water maze test in this mouse AD model at a 25 mg/kg oral dose (*P* =0.03, figure below-left). It also rescued the impairment in contextual fear learning at both doses tested, in comparison to vehicle (10mg/kg - *P* =0.005, 25mg/kg - *P* =0.019, not shown). In the same study ANVS-401 fully rescues synaptic function and long-term potentiation in hippocampal slices at both doses (10mg/kg - *P* =0.005, 25mg/kg - *P* <0.0001, figure below-bottom). ANVS-401 treatment did not affect wild-type (WT) mice.



APP/PS1 AD tg mice were treated for 1 month with ANVS-401, before the behavioral evaluation. 2-day radial arm water maze test results are shown on the top, and electrophysiology (extracellularly recorded field excitatory postsynaptic potentials – fEPSP) between Shaffer collateral and pyramidal neurons from CA1 stratum radiatum is shown on the bottom.



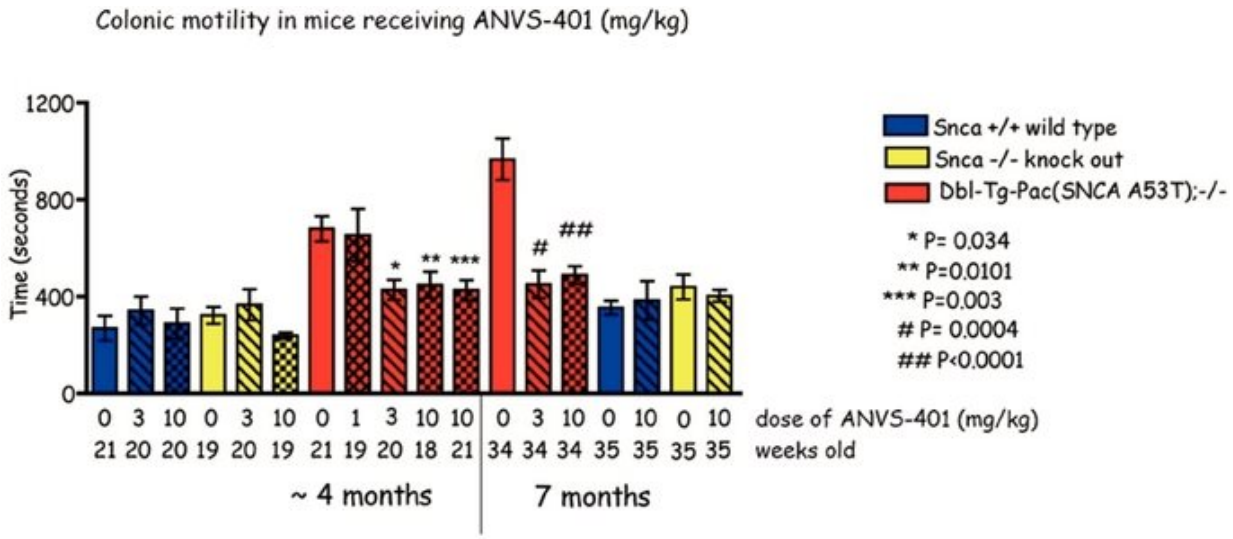
Trisomic Mouse Model of AD-DS

DS mice are used as a model for AD, because they have impaired memory and learning. DS trisomic mice were tested for correct entries into a radial arm water maze and it took them 20 tries to find the correct entry than healthy mice. After treatment with ANVS-401 they find the correct arm as well as healthy mice

ANVS-401 fully rescued spatial-working memory defects in a radial arm water maze test in this AD-DS mouse model at a 50 mg/kg dose (P =0.04). In the same study ANVS-401 normalized levels of APP: fully rescues axonal vesicle transport and synaptic function; increased levels of BDNF; while ANVS-401 treatment did not affect wild-type (WT) mice.This work is being conducted by Xu Chen in William Mobley's laboratory at UCSD, manuscript in preparation

SNCA ^{A53T} and SNCA ^{A30P} Mouse Models of PD

We used these tg PD mice as models of early gastrointestinal dysfunction, which is common in PD patients and proceeds the onset of motor symptoms by many years to decades. Untreated transgenic PD mice resemble pre-Parkinson's patients, showing symptoms of constipation by five to six months of age. Here we assessed the colonic motility by measuring the time required to expel a glass bead inserted into the colon at a distance of 2 cm above the anus at 4 and 7 months of age. ANVS-401 statistically significantly decreased the bead expulsion time; thus, it reversed the constipation of tg PD mice (figure below). Furthermore, even after we stopped treatment for 9 weeks, the constipation was still reduced (data not shown). ANVS-401 does not act as a laxative, since, when given to two different control mice breeds that do not develop constipation (*Snca* $^{+/+}$ and *Snca* $^{[ib]-/[ib]-}$), it does not affect their gut motility.



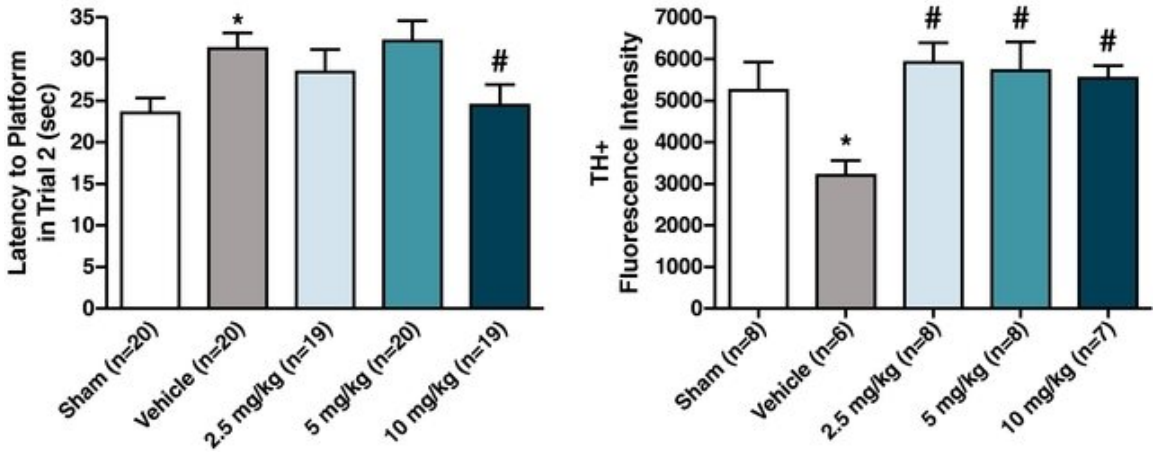
SNCA ^{A53T} and SNCA ^{A30P} mice (producing human mutant α SYN associated with familial PD) were treated intraperitoneally with vehicle or ANVS-401 beginning at six weeks up to seven months of age. ANVS-401 prevented the impaired gut motility of the SNCA ^{A53T} and SNCA ^{A30P} mice at 3 or 10 mg/kg. Older mice demonstrate a more severe phenotype that nonetheless responds to ANVS-401.

TBI in Rats

TBI causes severe cognitive and neurological impairment, which can incapacitate the patient, reduce quality of life, and increase the risk of morbidity and mortality. TBI is known to increase the risk for neurodegenerative disorders such as AD and PD. A number of studies have analyzed changes in the brain after TBI and identified up-regulation of neurotoxic aggregating proteins, such as Amyloid β (A β), tau, and α SYN.

Annovis received $ 1.5 million from the US Army to study the effect of ANVS-405 in blunting the damage caused by TBI in rats. Our partnering PI, Dr. Marie-Francoise Chesselet and her collaborator, Dr. David Hovda at UCLA have used different rat models to study the behavioral, biochemical, and neuropathological consequences of TBI as well as to identify potential drug treatments.

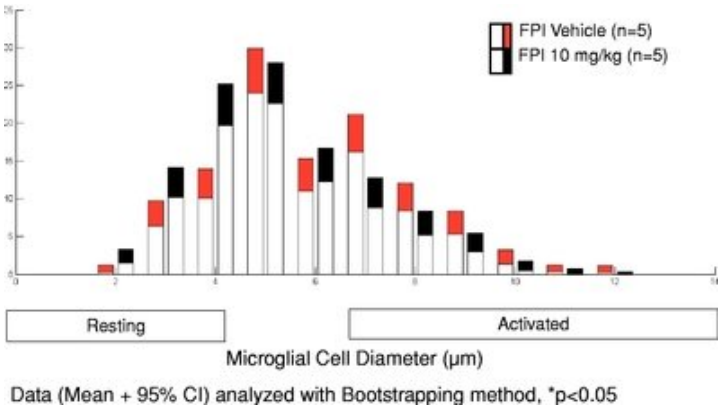
In our study (manuscript in preparation), rats were subjected to fluid percussion injury (FPI) or sham operation to one side of the brain. Three different ANVS-405 doses or saline were given intraperitoneally to rats subjected to FPI for 4 weeks, with the first dose administered one-hour post-injury. At the termination of the treatment, all the rats were first tested for their performance in the water maze, and then they were sacrificed for brain staining and determination of microglia activation. As shown, 10 mg/kg ANVS-405 rescued memory and learning as measured by water maze performance (figure below-left). Furthermore, sections of the brain were stained with tyrosine hydroxylase (TH), wherein TH stains only live cells. The amounts of TH immunoreactivity in the whole striatum of the brain slices were measured. The rats treated with all 3 doses of ANVS-405 showed a statistically significant increase in the number of surviving cells in the ipsilateral area of the brain over the vehicle treated animals (figure below-right). Thus, ANVS-405 protects the striatum following FPI in rats.



*Effects of ANVS-405 treatment on rats subjected to FPI. Left: performance in a water maze: Sham vs. FPI-vehicle: *p<0.05 by two-way ANOVA, Bonferroni comparison, and FPI-Vehicle vs. FPI-10mg/kg ANVS-405: #p<0.05 by one-way ANOVA, Bonferroni comparison. Right: TH immunoreactivity in the ipsilateral area of rats. Sham vs. FPI-vehicle: *p<0.05 by two-way ANOVA, Bonferroni comparison, and FPI-Vehicle vs. FPI-all ANVS-405 doses: #p<0.05 by one-way ANOVA, Bonferroni comparison.*

Because FPI can induce microglial activation, we next checked whether ANVS-405 would reverse this pathology. Microglial activation was assessed by quantitative measurement of the diameter of IBA-1-positive cells (ionized calcium adaptor binding protein). Microglia with cell body diameters less than 5 µm had a resting morphology characterized by multiple ramified processes. Hyper-ramified microglia/partially activated microglia had a mean cell body diameter of 5-6 µ m. Fully activated amoeboid microglia had a mean cell body diameter of 7-14 µ m. ANVS-405 increases the number of resting microglia and reduces the number of activated microglia.

Effect of 10mg/kg ANVS-405 on Microgilial Activation



Effect of treatment with 10mg/kg ANVS-405 on microglial activation following FPI in rats.

Collectively, these data prove ANVS-405's efficacy in reversing the toxic effects of neurotoxic aggregating proteins *in vivo* , in several animal models of both chronic and acute neurodegeneration.

Reproducible Results Across Species—Mouse, Rat, Human

As mentioned, ANVS-401 reduces and normalizes APP, tau and α SYN; this has been shown in spinal fluid of humans as well as brains of mice and rats.

Furthermore, ANVS-401 reduces inflammation: again, this has been shown in spinal fluid of humans and in brains of rats.

Our data show conclusively that ANVS-401 reduces neurotoxic proteins and inflammation in humans and animals, thereby normalizing whatever function is affected.

As discussed, ANVS-401's unique mechanism of action allows it to inhibit the translation and to reduce the levels of APP, tau and α SYN, which play a central role in the pathogenesis of both AD and PD. That, in combination with our supporting data showing efficacy in AD-DS, AD and PD mouse models, and reversal of the toxic effects of neurotoxic proteins, leads us to believe that ANVS-401 is a promising drug for the treatment of both diseases. Therefore, our approach is innovative in that we do not have a single therapeutic target for a single disease; instead, we have one drug that targets the conserved IRE element of the RNAs of multiple neurotoxic aggregating proteins, applicable to multiple diseases.

The fact that the data are reproducible across species and disease models gives us confidence that the efficacy results will translate to human.

Markets

With a potential market for neurodegenerative diseases estimated at more than $100 billion annually, most pharma companies have a program studying some aspect of nerve and brain

degeneration. None of these approaches have resulted in a drug that improves cognition. Some newer approaches target tau, whose expression is more closely associated with cognitive decline. Similarly, for PD, several companies are trying to inhibit alpha-synuclein. So far neither drugs attacking tau nor alpha-synuclein have been tested in Phase 3. Hence there is an enormous need for a different disease-modifying strategy. There is more than one neurotoxic aggregating protein in the brain of AD and of PD patients, and the same neurotoxic aggregating proteins are involved in the pathogenesis of AD and PD. In fact, a significant portion of AD patients' brains display mixed PD pathology and vice versa. Therefore, just attacking one of these proteins may result in no or lower efficacy than attacking them all. We are unaware of any other person or entity that is working on inhibiting more than one neurotoxic aggregating protein and tackling more than one neurodegenerative disorder at the same time. To prove that this approach is possible, we want to study the effects of ANVS-401 on the levels of several neurotoxic aggregating proteins and other surrogate markers, in parallel, in AD and PD patients. Within 18 to 24 months we believe we will have two Phase 2a studies, one in AD and one in PD patients, showing that ANVS-401 works in both diseases.

Alzheimer's Disease Associated with Down Syndrome—AD-DS Market

Down syndrome (DS) or trisomy 21 is one of the most common causes of intellectual disability and recent national prevalence estimates suggest that 13.65 per 10,000 live births are infants with DS leading to 5,429, on average, annual DS births in the United States. Worldwide the occurrence of DS is about 4 to 5 times that.

DS, life expectancy has increased dramatically; for children with DS born in 2010, median life expectancy is estimated to be 65 years. However, along with this longer lifespan comes the prospect of a considerable increase in the risk of developing dementia associated with AD, with a prevalence of nearly 80% for those with DS who are older than 65 years. In comparison normal individuals have a risk of 40 to 50% by the time they are 90 years old.

Just like in sporadic AD there is a prodromal or asymptomatic phase in DS when AD pathology progressively accumulates (30-40 years) but clinical signs of dementia may be delayed by up to a decade if not longer. This provides a therapeutic window or an opportunity for prevention that is unique to adults with Down syndrome. AD-DS is an orphan indication with identical symptoms to sporadic AD, but in a much younger population with accelerated disease progression.

In the US AD-DS is an orphan indication, because about 50,000 DS people have AD and about 120,000 are at risk to develop AD in the next 5 to 10 years.

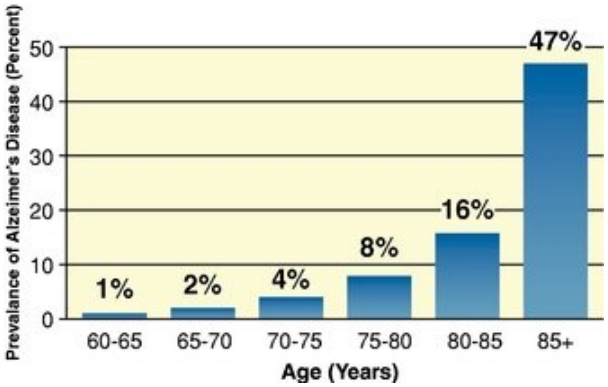
A key challenge for adults with DS as they age is the increasing risk for developing clinical symptoms of AD and dementia. A recent report suggests that by 59 years of age, up to 55% may be demented. Although based on smaller sample sizes, the range of individuals affected by dementia over the age of 60 years is up to 77%. Further, estimated ages of onset in those individuals with dementia also appear to range from 48 to 56 years with a subset of individuals showing an earlier age of onset. Decline in function in specific cognitive domains may be sensitive to early dysfunction and may occur at a younger age than a diagnosis of dementia. The pattern and sequence of cognitive impairments in adults with DS exhibit characteristics similar to AD in the general population.

In parallel with the age-dependent increased risk for developing dementia virtually all adults with DS over the age of 40 years have sufficient plaques and tangles for a neuropathologically based diagnosis of AD, because trisomy 21 leads to the overexpression of APP. Between the ages of 30 and 40 years, neuropathology rapidly accumulates until it reaches levels sufficient for a diagnosis of AD by 40 years and there is an acceleration phase to disease development.

Alzheimer's Disease Market

AD is a neurodegenerative disorder with cognitive, functional, and behavioral alterations. AD is age related, and its incidence is increasing with the aging of the population. It is estimated that currently 44 million victims of AD dementia exist in the world and by 2050, more than 100 million people worldwide will be living with AD. Nearly eightfold as many people have preclinical AD as have symptomatic AD and are at risk for progressing to manifest disease. DMTs that will prevent or delay the onset or slow the progression of AD are urgently needed. A modest one-year delay in onset by 2020 would result in there being 9.2 million fewer cases in 2050. Similarly, medications to effectively improve cognition or ameliorate neuropsychiatric symptoms of patients in the symptomatic phases of AD are needed to improve memory and behavior.

Increase in Incidence of AD with the Aging of the Population



AD is becoming increasingly common as the global population ages and as the health system in developing countries gets better. We urgently need to identify drugs that prevent, delay the onset, slow the progression, or improve the symptoms of AD.

Parkinson's Disease Market

PD is also a progressive neurodegenerative disorder with movement and non-movement symptoms, functional, behavioral and cognitive alterations. PD, like AD, is age related and is becoming markedly more common with the aging of the world's population. PD affects about 1% of the population over the age of 60, while in individuals over the age of 85, this prevalence reaches 5%, highlighting the impact that advancing age has on the risk of developing this condition.

PD affects about 10 million people worldwide of which one million are in the US. There are 60,000 new cases of PD diagnosed each year in the US. The incidence is expected to double by 2040.

The National Parkinson's Foundation estimates that the economic burden of PD is at least $25 billion a year in the United States.

To date, there are no available treatments capable of curing PD, with current therapies seeking only to ameliorate dopamine-related motor symptoms of the disease. No treatments to date address non-motor symptoms. There is a clear and unmet medical need for new disease modifying therapies that can slow or prevent PD progression.

Mixed Pathologies Market

In addition to the unmet need of AD and PD patients, however, about 50% of patients exhibit with mixed pathologies with some pathologies resembling AD and some resembling PD. These patients'

needs are not addressed at all by the drugs presently in development for AD or PD, because those drugs target only one or the other neurotoxic protein.

Dementia is increasingly being recognized in cases of PD; such cases are termed PD dementia (PDD). The spread of fibrillar α SYN pathology from the brainstem to limbic and neocortical structures seems to be the strongest neuropathological correlate of emerging dementia in PD. Up to 50% of patients with PDD develop sufficient numbers of Aâ plaques and tau-containing neurofibrillary tangles for a secondary diagnosis of Alzheimer's disease, and these pathologies may act synergistically with α SYN pathology to confer a worse prognosis. An understanding of the relationships between these three distinct pathologies and their resultant clinical phenotypes is crucial for the development of effective disease-modifying treatments for PD and PDD.

Another study looking at the incidence of mixed pathologies diagnosed community-dwelling older persons. Those with dementia most often have multiple brain pathologies, which greatly increases the odds of dementia. Specifically, in people with dementia, over 50% had multiple diagnoses (AD, PD/LBD, PDD or infarcts). After accounting for age, persons with multiple diagnoses were almost three times more likely to exhibit dementia compared to those with one pathologic diagnosis.

A therapy that only addressed Aâ, tau or α SYN won't help people with mixed pathologies. Since ANVS-401 inhibits more than one neurotoxic aggregating protein, it is possible that by halting the cascade of toxic proteins, it might stop or slow AD, PD and mixed pathology diseases at all stages of development.

Approaches and Competition

Alzheimer's Disease in Orphan Indications

There are two orphan indications that represent AD: one is AD in Down syndrome (AD-DS) and the other is early onset familial AD (EOFAD).

To date very little work has been done in these indications. Roche/Genentech/AC Immune are conducting one study in EOFAD in a Colombian extended family and AC Immune is working on a vaccine for AD-DS.

Anti-Abeta Antibody Phase 3 Study in Colombian EOFAD

In 2012, Genentech, a Roche company, initiated the first-ever study of cognitively healthy individuals who are likely to develop Alzheimer's disease due to their genetic history. The landmark trial is the first to assess the potential of an investigational medicine to stop Alzheimer's before it starts. The study involves a humanized monoclonal antibody made by AC Immune, which is designed to bind to A β , the main constituent of amyloid plaques in the brains of patients with AD. A β is proposed to be causative in the development of the disease.

The prevention trial may provide the most effective test to date of the amyloid hypothesis. Two groups of patients, totaling as many as 324 people, are involved in the study. They live in the Antioquia region of Colombia, which is home to nearly 5,000 people who share the risk for a rare genetic mutation. This mutation, presenilin 1 (PSEN1), causes early-onset Alzheimer's in any individual who is a carrier.

Participants in the trial are 30 or older and within 15 years of the age when their parent's symptoms began. Typically, mild cognitive impairment due to AD begins in these Colombian families around 45. The study is ongoing and moving slower than expected, so we do not know, when the data is due.

Anti Abeta Vaccine Phase 1b Study for Alzheimer's Disease in Down Syndrome

AC Immune has completed recruitment for the high-dose cohort of the ACI-24 Phase 1b study for the treatment of Alzheimer's disease-like characteristics in adults with Down Syndrome (DS). The first low-dose and the second high-dose cohorts have been fully recruited in August 2017 and in July 2018 respectively, and the primary outcome is expected in 2020. In addition to cognitive dysfunction beginning in childhood, individuals with DS are genetically predisposed to develop Abeta-related cognitive decline at a much younger age and with much greater probability than the general population.

AC Immune is expected to start the Phase 2 study with ACI-24 in DS patients with mild AD. The aim of this double-blind, randomized, placebo-controlled study with an adaptive design is to assess the safety, tolerability, immunogenicity, target engagement, biomarkers and clinical efficacy of ACI-24. The trial will seek to confirm the positive trends on Abeta PET* imaging and clinical measurement (CDR-SB°) of the previous Phase 1 safety study. The Phase 2 trial will be conducted in several European countries

Alzheimer's Disease Approaches

Drug development for AD has proven to be very difficult. Five drugs are approved for the treatment of AD including four cholinesterase inhibitors (tacrine, donepezil, rivastigmine, galantamine) and an N-methyl-D-aspartate (NMDA) receptor antagonist (memantine). No new treatments have been approved for AD since 2003. Many failures in AD drug development have occurred, with both small molecules and immunotherapies failing to show a drug/placebo difference or having unacceptable toxicity.

Clinicaltrials.gov is a public website that lists all clinical trials conducted or recruiting. Today there are a total of 112 agents in the pipeline as shown on clinicaltrials.gov. Among the DMTs, most addressed amyloid targets.

Since A β accumulates for years before the symptoms of AD are visible, some pharmaceutical companies are testing their drugs earlier, including cognitively normal people or those who have genetic profiles that place them at high risk for developing AD (table below). In Phase 3, there were six

prevention trials enrolling cognitively normal participants and 12 trials of patients with prodromal AD/MCI or prodromal/mild AD.

Phase	Agent	Trial	Sponsor	Means of defining risk for AD dementia
III	Solanezumab	A4	Eli Lilly	Amyloid PET
II/III	CAD106, CNP520	Generation S1	Novartis	Homozygous APOE4
II/III	CNP520	Generation S2	Novartis	Amyloid PET or CSF
II/III	Icosapent ethyl (IPE)	BRAVE- EPA	VA Office of Research and Development	Parental history of AD and increased prevalence of APOE4 allele
II/III	JNJ-54861911	Early	Janssen	Amyloid PET or CSF
II/III	Gantenerumab, solanezumab, JNJ-54861911	DIAN-TU	Eli Lilly, Roche, Janssen, NIA	Family history of autosomal dominant AD
II	Crenezumab	GN28352	Genentech	Presenilin-1 E280 A mutation
I/II	Probucol	DEPEND	Douglas Mental Health University	Family history of AD
I	Telmisartan	HEART	Emory University	Parental history of AD

An increasing number of agents are directed at tau-related targets. Neurofibrillary tangles are one of two major pathological hallmarks of AD. Correlation studies conducted by Braak and Braak, demonstrating that neurofibrillary tangle burden more closely correlates with cognitive decline than amyloid plaque load. Tau remains an important but largely untested target for disease modification in AD. The first anti-tau programs were directed at reducing tau aggregation. The preliminary results of these studies were largely disappointing, and agents directed against tau aggregation are being re-evaluated.

In summary, at present there are no disease-modifying agents on the market. The first large effort to develop a DMD for AD has targeted A β 42, but all A β 42 approaches to date have failed. A few companies are moving to fighting tau and a lot of companies have pulled out of AD research and are waiting to see what approach might have a better outcome. Since the AD brain contains a number of neurotoxic aggregating proteins—amyloid precursor protein and its toxic fragment A β 42 and IC99, a well as tau and alpha-synuclein—a DMD drug needs to target more than just one toxic protein to be efficacious. ANVS-401 is the only drug that satisfies this criterion.

A concerning observation derived from this AD pipeline review is the lack of agents targeting the moderate to advanced stages of AD. Only 26 trials permit inclusion of participants with scores of 14 or less, and only 12 include participants with scores of 10 or less. Together, these studies intend to enroll only 1,720 participants. With over 15 million people affected by AD dementia worldwide, there is an urgent need to develop more effective symptomatic treatments for moderate to advanced stage disease. The paucity of agents directed at this population represents a significant weakness of the AD drug development pipeline.

Parkinson's Disease Approaches

Levodopa (L-DOPA) was introduced for use in treating PD more than 40 years ago and remains the mainstay of therapy for improving the symptoms of the disease. Unlike dopamine, which cannot cross the blood—brain barrier, L-DOPA is effectively absorbed into the brain, where it metabolizes into dopamine. It is typically administered five times a day and works well in controlling symptoms for 1-5 years. Unfortunately, the effects of L-DOPA in any patient diminish with time.

There are several other drugs available to treat PD, which also seek to modulate dopamine levels. Commonly prescribed dopamine agonists that directly activate dopamine receptors include agents such as Mirapex (pramipexole/BI) and Requip (ropinirole/GlaxoSmithKline).

Combination drug therapy is common in PD. For instance, the use of other drug classes such as the catechol-O-methyltransferase (COMT) inhibitors and the monoamine oxidase (MAO) inhibitors allow patients to reduce L-DOPA dosing levels. A number of MAO inhibitors are approved for PD therapy, including Zelapar (selegiline/Valeant) and Azilect (rasagiline; Teva/Lundbeck).

In 2012, the market for PD drugs was about $2.3 billion worldwide, despite high-volume generics. The most important current therapy for PD, L-DOPA, is prescribed as a generic. While volume growth in the category is expected to remain healthy, dollar growth will likely remain relatively flat as some of the category's larger brands (Requip, Mirapex) contend with generic inroads. The size of the current market reflects the absence of innovative branded therapies more than it does the medical need.

Disease-Modifying Compounds Targeting α-Synuclein for the Treatment of PD in Clinical Trials

So far, all products are at early stages of clinical development and no products have yet shown efficacy in PD patients. The table lists all α SYN approaches in development right now.

Product	Company	MOA	Ph	Status/ Outcome
PRX002	Prothena/Roche	Anti- α SYN-mAb	2	Good safety profile, CSF/Serum 0.3%. P2 primary outcome (MDS UPURS at 52w) is expected in 2020
BIIB054	Neurimmune/Biogen	Anti- α SYN-mAb	2	Good safety profile, CSF/Serum 0.2%. P2 primary outcome (safety, PD at 52w) is expected 2021
Kenterin	Enterin	Shark-derived α SYN inhibitor	2	Primary outcome (safety, PKPD, efficacy) of phase 1/2 a study results expected in 2019
Affiris	Affiris	Therapeutic vaccine for α SYN	1	Good safety profile with immune responses. Responses were shown in several efficacy outcomes (PR: no details reported).
PD03	Affiris	Therapeutic vaccine for α SYN	1	Dose-dependent immune response and good safety profile shown in phase 1 study
NPT088	Proclara	Ig fusion protein (GAIM dimers)	1	Phase 1 study is ongoing
NPT200-11	Neuropore/UCB	Small molecule that reduces α SYN	1	Phase 1 study completed in 2016 but results not reported
MEDI1341	AstraZeneca Takeda	Anti- α SYN-mAb	1	Phase 1 study completion expected in 2019

Although several of the listed drugs have shown potential neuroprotective ability in preclinical studies, demonstrating these effects in clinical studies remains a challenge. Beyond drug therapies, a number of cell and gene therapy approaches are also being explored. Progress across these newer technology platforms has been slow. A notable failure in the cell therapy area was spheramine (Bayer/Titan), a cell therapy in which human retinal cells were injected into the brain to directly produce L-DOPA in the brain, which did not meet its primary and secondary endpoints in a Phase 2b study concluded in 2008.

More recently, neuroprotective development efforts have switched to gene therapies. Targets in the gene therapy area include: neurturin, which is a naturally occurring protein that is known to repair damaged and dying dopaminergic neurons; glutamic acid decarboxylase, which alleviates abnormal brain activity associated with the motor deficits that characterize PD; and aromatic L-amino acid decarboxylase (AADC), tyrosine hydroxylase (TH) and GTP cyclohydrolase 1 (GCH1), which naturally control dopamine levels in the brain by reprogramming transduced cells to manufacture and secrete dopamine.

Progress on this front has also been frustrating. Ceregene's CERE-120, which was an adeno-associated virus vector carrying the gene neurturin, failed in a recently reported Phase 2 trial. Ceregene was recently acquired by Sangamo, which terminated

Intellectual Property

We strive to protect and enhance the proprietary technologies, inventions and improvements that we believe are important to our business, including seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. Our policy is to seek to protect our proprietary position by, among other methods, pursuing and obtaining patent protection in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements, platforms and our product candidates that are important to the development and implementation of our business.

As of March 31, 2019, our portfolio of owned and licensed patents totaled 41 issued or pending patents consisting of seven issued U.S. patents, three pending U.S. patent applications, 17 issued foreign patents and 14 pending foreign applications. These include licensed patents co-owned by Horizon and the PHS with claims directed to a composition of matter, a method of inhibiting production of amyloid precursor protein and a method of treating Alzheimer's disease and dementia via the administration of ANVS-401; a process for producing phenserine and analogs thereof, including ANVS-401; and a method of treating Down syndrome via the administration of (-) phenserine or (+)phenserine (ANVS-401) and combinations thereof. The world-wide exclusive license we have with Horizon comprises the patents co-owned by Horizon and the PHS; the patents have expiration dates between 2021 and 2026.

Annovis has filed three classes of patent applications to prolong the patent life of ANVS-401. The pending patent applications were invented and filed by Annovis and include claims directed to:

- a method of treating neurodegenerative diseases such as AD and PD;
- a method of treating and/or preventing acute brain and nerve injuries; and
- a method of prevention and treatment of disease states due to metal dis-homeostasis such as AD or PD as well as other acute or chronic neurodegenerative diseases.

Unless these applications are approved by the U.S. and international patent offices, the patent life of ANVS- 401 is limited. However, on June 25, 2019, we received a Notice of Allowance from the U.S. Patent and Trademark Office for the first of our Annovis patents covering Parkinson's disease and associated diseases. We have paid the issue fee and expect the patent to issue by the end of August 2019. We are filing one or more continuation applications in order to capture further patentable subject matter in this application.

The patent portfolio licensed from Horizon relating to our product candidate ANVS-401 includes three patent families and more specifically claims:

- The first of these patent families relates to a composition of matter for ANVS-401 tartrate, a method of inhibiting production of amyloid precursor protein and a method of treating Alzheimer's and dementia via the administration of ANVS-401 and 257 analogs. This patent family includes granted patents in the United States, Europe, Australia and Canada. We expect patents in this family to expire in 2021 in non-U.S. jurisdictions and in 2021-2022 in the United States.

- The second of these patent families relates to a process for producing the two enantiomers (–) phenserine and (+) phenserine = ANVS-401 from physostigmine compounds by hydrolysis to form an eseroline compound which is then condensed with an isocyanate. This patent family includes granted patents in the United States, Europe, Canada and South Korea. We expect patents in this family to expire in 2022 in non-U.S. jurisdictions and in 2022 in the United States.

- The third of these patent families relates to a method of treating Down syndrome via the administration of phenserine, (+)phenserine (=ANVS-401), (+)9-N-phenylcarbinol eseroline and combinations thereof. This patent family includes two granted patents in the United States. We expect patents in this family to expire in 2025-2026 in the United States.

The patent and patent application portfolio invented and filed by Annovis relating to ANVS-401 and ANVS-405 includes three patent families and more specifically claims:

- The first of these patent families relates to a method of reducing the amount of a neurotoxic aggregating protein in a human(s) by administering a pharmaceutical composition which includes ANVS-401 or a pharmaceutically acceptable salt thereof in an amount which is surprisingly less than previously reported and administered on a once a day basis. This patent family includes patent applications pending in the United States, Europe, Japan, Canada and South Korea. If granted, we expect patents in this family to expire in 2032 in non-U.S. jurisdictions and in 2032 in the United States. This patent family covers Alzheimer's and Parkinson's disease as well as Huntington's disease, Prion's disease, Amyloid Lateral Sclerosis, tauopathies and Frontotemporal dementia. On June 25, 2019, we received a Notice of Allowance from the U.S. Patent and Trademark Office for the first of our Annovis patents covering Parkinson's disease and associated diseases. We have paid the issue fee and expect the patent to issue by the end of August 2019. We are filing one or more continuation applications in order to capture further patentable subject matter in this application.

- The second of these patent families relates to a method of treating or preventing acute brain or nerve injury in humans in need of such treatment, via the administration of an effective amount of ANVS-401. The acute brain or nerve injury may be, e.g., traumatic brain injury, stroke, acute brain injury induced by brain ischemia, acute brain injury induced by insufficient oxygen supply to the brain, acute brain injury induced by anoxia or hypoxia, micro infarcts, acute brain injury induced by concussion, post-operative cognitive decline resulting from anesthesia or surgery-induced inflammation, acute brain injury induced by drowning, acute brain injury associated with whip lash, acute brain injury associated with bicycle crashes, acute brain injury associated with automobile accidents, shaken baby syndrome, acute brain injury induced by falling, acute brain injury associated with physical impact of the head, or acute angle-closure glaucoma. This patent family includes patent applications pending in the United States and an international application under the Patent Cooperation Treaty which will allow national phase applications to be filed in a broad list of foreign member countries. If granted, we expect patents in this family to expire in 2036 in non-U.S. jurisdictions and in 2036 in the United States.

- The third of these patent families relates to a method of restoring heavy metal homeostasis to a healthy human or restoring heavy metal homeostasis in a sick human patient, comprising chronically administering ANVS-401 in a therapeutically effective amount to maintain heavy metal homeostasis in the healthy human patient or restore heavy metal homeostasis in the sick human patient. The sick human patient may be, e.g., suffering from a neurodegenerative disease, such as Alzheimer's or Parkinson's disease, or a cancerous disease or condition, a cardiovascular disease, or a disease of a vital organ. This patent family further relates to the surprising fact that ANVS-401 may prevent, control, delay or slow the onset of such diseases by maintaining heavy metal homeostasis. Further, Annovis has now recognized that while heavy metal dis-homeostasis is responsible for neurodegenerative disorders, such as Alzheimer's and Parkinson's disease, in

other conditions cells of the human patient can be stressed (e.g., have high heavy metal concentrations such as iron) and react with cardiovascular diseases or conditions of vital organ failure. These diseases may be prevented, controlled, delayed or slowed by the chronic administration of effective amounts of ANVS-401 to maintain heavy metal homeostasis. This patent family includes patent applications pending in the United States, Australia, Canada, China, Europe, Hong Kong, and Japan. If granted, we expect patents in this family to expire in 2038 in non-U.S. jurisdictions and in 2038 in the United States.

Individual patents extend for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued for regularly filed applications in the United States are granted a term of 20 years from the earliest effective non-provisional filing date. In addition, in certain instances, a patent term can be extended to recapture a portion of the U.S. Patent and Trademark Office, or USPTO, delay in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective filing date. However, the actual protection afforded by a patent varies on a product by product basis, from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

Furthermore, we rely upon trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our collaborators, employees and consultants and invention assignment agreements with our employees. We also have confidentiality agreements or invention assignment agreements with our collaborators and selected consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our drugs or processes, obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future drugs may have an adverse impact on us. If third parties have prepared and filed patent applications prior to March 16, 2013 in the United States that also claim technology to which we have rights, we may have to participate in interference proceedings in the USPTO, to determine priority of invention. For more information, please see "Risk Factors—Risks Related to Our Intellectual Property."

Future Development

ANVS-401 may have utility in other neurodegenerative diseases beyond AD and PD patients and protect nerve cells in all chronic and acute neurodegenerative disorders.

Material Agreements

In November 2008 we entered into an exclusive world-wide agreement, as amended in November 2011 and May 2012, with a subsidiary of Horizon Therapeutics PLC (Horizon), which is the successor

to TorreyPines Therapeutics, Inc., for the rights to ANVS-401 and its analogs. We have a worldwide exclusive license to ANVS-401 and its analogs, subject to standard reservation of rights under federal law.

The license agreement requires us to pay a minimum annual fee, milestone payments, royalties and a portion of any sublicense income we may receive. The minimum yearly fee of $46,000 may be deferred until we raise $2 million in equity financing. We have been accruing the yearly fee. At December 31, 2018, we had accrued $460,000 which is included in accrued liabilities in our financial statements. Milestone payments are payable upon the first attainment of the commencement of a Phase 2 efficacy study ($230,000); the commencement of a Phase 3 pivotal study ($575,000); filing of an NDA for regulatory approval ($1,150,000); receipt of regulatory approval in the U.S. ($5,750,000); and receipt of regulatory approval outside the U.S ($5,750,000). Royalties must be paid in an amount equal to 5.75% of net sales of licensed products. Should we be required to obtain a license from a third party in order to sell a licensed product, we may deduct 50% of the royalties on such licensed product paid to the third party, subject to certain minimums. In addition to the royalties, we must pay the licensor 9.2% of all sublicense income attributable to licensed products.

The agreement also provides us a buy-out option which we may exercise at any time. The option price is as follows: $500,000 if exercised prior to the commencement of the first Phase 2 clinical trial; $1,000,000 if exercised on or after the commencement of the first Phase 2 clinical trial and prior to the commencement of the first Phase 3 clinical trial; $5,000,000 if exercised on or after the commencement of the first Phase 3 clinical trial and prior to the filing of a New Drug Application ("NDA") with the FDA for the first licensed product; and $8,000,000 if exercised on or after the filing of an NDA for the first licensed product.

We have the right to terminate the agreement at any time by giving 90 days advance notice subject to the payment of any amounts due under the agreement at that time. If we do not terminate the agreement or exercise the buy-out option, the term of the agreement will continue until the expiration of our obligation to make royalty payments. Such royalty payments continue for each product in each country until the later of the expiration of the related patent or 10 years after the initial sale of the product in the respective country. The agreement may also be terminated for cause by either party upon the breach of the material obligations of the other party or the bankruptcy or liquidation of the other party.

Sales and Marketing

Once ANVS-401 is approved for AD or PD, we plan to enter into sales and marketing agreements with one or several pharmaceutical companies to sell to neurologists, geriatric specialists and to primary care physicians.

Manufacturing

ANVS-401 is a small molecule that is manufactured using a 4-step patented process. We rely on third-party contractors for manufacturing clinical supplies and plan to do so for commercial amounts also. Presently we are working with an overseas supplier for the manufacture of the cGMP API and with a local supplier for the storage stability, encapsulating, blister packing, blinding and distribution of the capsules or pills to the clinical sites.

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs, such as those we are developing. These agencies and other federal, state and local entities regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record

keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of our product candidates.

U.S. Government Regulation of Drug Products

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- Completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations.
- Submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials may begin.
- Approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated.
- Performance of adequate and well-controlled human clinical trials in accordance with good clinical practice, or GCP, requirements to establish the safety and efficacy of the proposed drug product for each indication.
- Submission to the FDA of an NDA.
- Satisfactory completion of an FDA advisory committee review, if applicable.
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practice, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity.
- Satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data.
- Payment of user fees and securing FDA approval of the NDA.
- Compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some preclinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND

sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to initiate.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it initiates at that institution. Information about certain clinical trials must be submitted within specific timeframes to the NIH for public dissemination on their www.clinicaltrials.gov website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.

- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA, for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision.

In addition, under the Pediatric Research Equity Act of 2003, or PREA, as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. An Agreed Initial Pediatric Study Plan requesting a waiver from the requirement to conduct clinical studies has been submitted to the FDA.

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, plan to ensure that the benefits of the drug outweigh its risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, which reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and

profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Special FDA Expedited Review and Approval Programs

The FDA has various programs, including fast track designation, accelerated approval, priority review, and breakthrough therapy designation, which are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life-threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. The FDA may review sections of the NDA for a fast track product on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

The FDA may give a priority review designation to drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. Under the current PDUFA agreement, these six- and ten-month review periods are measured from the "filing" date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review.

In addition, products tested for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on IMM or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures.

Moreover, under the provisions of the Food and Drug Administration Safety and Innovation Act, or FDASIA, passed in July 2012, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and

providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy. At the completion of our two Phase 2 trials, one in PD and one in AD, Annovis will petition the FDA to classify ANVS-401 as a breakthrough therapy.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. We may explore some of these opportunities for our product candidates as appropriate.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long, and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the

cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will be receiving orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same active ingredient for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. Further, the FDA may approve more than one product for the same orphan indication or disease as long as the products contain different active ingredients. Moreover, competitors may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There are continuing, annual program user fee requirements for any marketed products.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval of a drug or medical device is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or

imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- Restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls.
- Fines, warning letters or holds on post-approval clinical trials.
- Refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals.
- Product seizure or detention, or refusal to permit the import or export of products.
- Injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs or devices may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

U.S. Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of our product candidate, ANVS-401, or any other for which we may seek regulatory approval. Sales in the U.S. will depend in part on the availability of adequate financial coverage and reimbursement from third-party payors, which include government health programs such as Medicare, Medicaid, TRICARE and the Veterans Administration, as well as managed care organizations and private health insurers. Prices at which we or our customers seek reimbursement for our product candidates can be subject to challenge, reduction or denial by payors.

The process for determining whether a payor will provide coverage for a product is typically separate from the process for setting the reimbursement rate that the payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list or formulary, which might not include all of the FDA-approved products for a particular indication. Also, third-party payors may refuse to include a particular branded drug on their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or another alternative is available. Medicare Part D, Medicare's outpatient prescription drug benefit, contains protections to ensure coverage and reimbursement for oral oncology products, and all Part D prescription drug plans are required to cover substantially all oral anti-cancer agents. However, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be available. Private payors often rely on the lead of the governmental payors in rendering coverage and reimbursement determinations. Sales of ANVS-401 or any other product candidates will therefore depend substantially on the extent to which the costs of our products will be paid by third-party payors. Achieving favorable coverage and reimbursement from the Centers for Medicare and Medicaid Services ("CMS") and/or the Medicare Administrative Contractors is typically a significant gating issue for successful introduction of a new product.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for marketing, we may need to conduct studies in order to demonstrate the medical necessity and cost-effectiveness of any products, which would be in addition to the costs expended to obtain regulatory approvals. Third-party payors may not consider our product candidates to be medically necessary or cost-effective compared to other available therapies, or the rebate percentages required to secure favorable coverage may not yield

an adequate margin over cost or may not enable us to maintain price levels sufficient to realize an appropriate return on our investment in drug development.

U.S. Healthcare Fraud and Abuse Laws and Compliance Requirements

We are subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales and marketing programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our operations include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from soliciting, receiving, offering or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs. The term "remuneration" has been broadly interpreted to include anything of value;

- federal false claims and civil monetary penalties laws, including the federal civil False Claims Act, which prohibits anyone from, among other things, knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services that are false or fraudulent;

- provisions of HIPAA, which created new federal criminal statutes that prohibit, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program or making false statements in connection with the delivery of or payment for healthcare benefits, items or services. In addition, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, impose certain requirements relating to the privacy, security and transmission of individually identifiable health information; and

- the federal Physician Payment Sunshine Act requirements, under the Patient Protection and Affordable Care Act, which require manufacturers of certain drugs and biologics to track and report to CMS payments and other transfers of value they make to U.S. physicians and teaching hospitals as well as physician ownership and investment interests in the manufacturer.

Regulation Outside the United States

To the extent that any of our product candidates, once approved, are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals.

To market our future products in the EEA (which is comprised of the 28 Member States of the EU plus Norway, Iceland and Liechtenstein) and many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EEA, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

- The Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use of the European Medicines Agency, or EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products and medicinal products indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral

diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU; and

- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member State through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA assess the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Data and Marketing Exclusivity

In the EEA, new products authorized for marketing, or reference products, qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial authorization of the reference product in the EU. The 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those 10 years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

Orphan Drug Designation

In the EEA, a medicinal product can be designated as an orphan drug if its sponsor can establish that the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or that the product is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that the marketing of the drug in the EU would generate sufficient return to justify the necessary investment in development. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the drug will be of significant benefit to those affected by that condition.

In the EEA, an application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. During this market exclusivity period, the EMA or the member state competent authorities, cannot accept another application for a marketing authorization, or grant a marketing authorization, for a similar medicinal product for the same indication. The period of market exclusivity is extended by two years for medicines that have also complied with an agreed PIP.

This period may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation, for example because the

product is sufficiently profitable not to justify market exclusivity. Market exclusivity can be revoked only in very selected cases, such as consent from the marketing authorization holder, inability to supply sufficient quantities of the product, demonstration of "clinical superiority" by a similar medicinal product, or, after a review by the Committee for Orphan Medicinal Products, requested by a member state in the fifth year of the marketing exclusivity period (if the designation criteria are believed to no longer apply). Medicinal products designated as orphan drugs are eligible for incentives made available by the EU and its Member States to support research into, and the development and availability of, orphan drugs.

Employees

As of , 2019, we had 3 employees.

Facilities

Our offices are located in Berwyn, Pennsylvania, where we have leased and have access to 1,500 square feet of office space. We believe that our facilities are adequate to meet our current needs.

Legal Proceedings

From time to time we may be involved in claims that arise during the ordinary course of business. Although the results of litigation and claims cannot be predicted with certainty, we do not currently have any pending litigation to which we are a party or to which our property is subject that we believe to be material. Regardless of the outcome, litigation can be costly and time consuming, and it can divert management's attention from important business matters and initiatives, negatively impacting our overall operations.

MANAGEMENT

The following table sets forth the name, age and position of each of our executive officers and directors as of the date of this prospectus.

Name	Age	Position
Executive Officers		
Maria Maccecchini	68	Founder, President and CEO and director
Jeffrey Cummings	70	Chief Medical Officer
Jeffrey McGroarty	49	Chief Financial Officer
Directors		
Michael Hoffman	69	Chairman of the Board(2)
Claudine Bruck	64	Board Member
Robert Whelan	67	Board Member(1)(2)
Mark White	63	Board Member(1)

(1) Member of the audit committee.

(2) Member of the compensation committee.

(3) Member of the nominating and corporate governance committee.

Executive Officers

Maria L. Maccecchini PhD
Founder, President and CEO

Dr. Maccecchini founded Annovis, formerly QR Pharma, and has served as President and CEO since May 2008. She has over 30 years of experience in neuroscience and the workings of the brain. She was partner and director of two angel groups, Robin Hood Ventures, from 2002 to 2009, and MidAtlantic Angel Group, from 2005 to 2009. In 1992, she founded and became chief executive officer of Symphony Pharmaceuticals/Annovis, a biotech company, which was sold in 2001 to Transgenomic. Prior to that, from 1987 to 1991 she was General Manager of Bachem Bioscience, the US subsidiary of Bachem AG, Switzerland and Head of Molecular Biology at Mallinckrodt. Dr. Maccecchini conducted post-doctoral research at Caltech and the Roche Institute of Immunology. She earned a Ph.D. in biochemistry is from the Biocenter of Basel with a two-year visiting fellowship at The Rockefeller University. Dr. Maccecchini serves on several boards of biotechnology companies, organizations that promote entrepreneurship, international trade, women and charitable organizations. She has been a lecturer at Wharton Business School since 2016. We believe that Dr. Maccecchini's experience in the life science industry, including as principal executive officer and manager of companies in the pharmaceutical development business, qualifies her to serve as our CEO and a director.

Jeffrey L. Cummings MD
Chief Medical Officer

Dr. Cummings has served as our Chief Medical Officer since January 2019. Dr. Cummings was Director and Chair of the Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas, Nevada, Cleveland, Ohio, and Westin, Florida from 2010 until 2018 and joined Annovis as CMO in 2019, because of the interesting mechanism of action of our lead compound, ANVS-401. The Lou Ruvo Center for Brain Health is a clinical care, translational research, and clinical trials enterprise specializing in care of patients with neurocognitive deficits and development of new therapies for neurodegenerative disorders. Dr. Cummings is the author of the Neuropsychiatric Inventory (NPI) which has become the most commonly used tool for characterizing behavioral disturbances in dementia

syndromes and for measuring the effect of antidementia therapies on neuropsychiatric symptoms in Alzheimer's disease and other dementias. Dr. Cummings is an experienced clinical trialist with expertise in clinical trial design and analysis, global trial implementation, and trial outcome measures. He is a member of the Alzheimer's Disease Cooperative Study and of the oversight committee of the NINDS Neuroprotection in Parkinson's Disease program. Dr. Cummings completed Neurology residency and a Fellowship in Behavioral Neurology at Boston University, Boston, Massachusetts. US training was followed by a Research Fellowship in Neuropathology and Neuropsychiatry at the National Hospital for Nervous Diseases, Queen Square, London, England. Dr. Cummings was formerly Professor of Neurology and Psychiatry at UCLA, director of the Mary S. Easton Center for Alzheimer's Disease Research at UCLA, and director of the Deane F. Johnson Center for Neurotherapeutics at UCLA.

Jeffrey McGroarty
Chief Financial Officer

Mr. McGroarty has been our Chief Financial Officer since April 2019. Prior to joining Annovis, Mr. McGroarty served as Senior Vice President and Chief Financial Officer of Safeguard Scientifics, Inc. from 2013 to 2018. Mr. McGroarty joined Safeguard Scientifics in 2005 as Vice President and Corporate Controller subsequently became Vice President—Finance and Corporate Controller, and served as Senior Vice President—Finance from 2012 to 2013. Mr. McGroarty served as Interim Controller of Cephalon, Inc. in 2005; Vice President-Financial Planning & Analysis and previously Assistant Controller at Exide Technologies from 2002 to 2005; and, previously, with PricewaterhouseCoopers from 1991 to 2001. Mr. McGroarty earned his Bachelor's degree from The Pennsylvania State University and his MBA from The Wharton School of The University of Pennsylvania.

Key Collaborators

William Mobley, M.D., Ph.D.
Distinguished Professor, UC San Diego

Dr. Mobley is our Chief Scientific Consultant, who discovered that ANVS-401 prevents nerve cell death by restoring axonal vesicle transport and by restoring homeostasis in the dysfunctional nerve cell. Dr. Mobley is the distinguished Professor, Department of Neurosciences Florence Riford Chair for Alzheimer Research and Associate Dean for Neurosciences Initiatives. He is a member of the National Academy of Medicine. His research focuses on the neurobiology of neurotrophic factor actions/signaling and on the hypothesis that dysfunction of such signaling mechanisms contribute to neuronal dysfunction in developmental and age-related disorders of the neurosystem.

Nigel Greig, Ph.D.

Nigel Greig, Ph.D., Drug Design & Development Section, Intramural Research Program, National Institute on Aging (NIA), at the National Institutes of Health (NIH). Dr. Greig is the inventor of our compounds. He has been officially approved by the NIH Ethics Committee and by the NIA/NIH Executive Board to work with Annovis. He has been a tenured scientist at NIA since 1991, his research has evolved into his present interest, Alzheimer's disease and diabetes. Ongoing research within his program is focused on intervening in common biochemical cascades leading to cell death that are shared between degenerative diseases. His research has culminated in some 300 publications, which includes some 20 patent applications.

Dr. Mobley and Dr. Greig are not compensated for their roles as collaborators and are not parties to any agreement with us. However, we have a collaborative agreement with UCSD and Dr. Mobley's laboratory to conduct his work on DS animals and axonal transport, the results of which are currently in manuscript form for publication.

Directors

Michael M. B. Hoffman
Chairman of the Board

Mr. Hoffman has served as Chairman of the Board of Directors and a member of our Board of Directors since 2014. Since 2018, he has been the founder and partner at Stone Capital Partners, a private equity firm focused on power and renewable energy. From 2003 to 2018, Mr. Hoffman was a partner of Riverstone Holdings LLC, or Riverstone, where he was principally responsible for investments in power and renewable energy. Before joining Riverstone, Mr. Hoffman was senior managing director and head of the mergers and acquisitions advisory business of The Blackstone Group L.P., or Blackstone, where he also served on the firm's principal group investment committee as well as its executive committee. Prior to joining Blackstone, Mr. Hoffman was managing director and co-head of the mergers and acquisitions department at Smith Barney, Harris Upham & Co. Mr. Hoffman currently serves as a director of Onconova Therapeutics, Inc. Mr. Hoffman also serves on the Board of Directors of Curative Biotherapeutics, Inc. and various private companies sponsored by Riverstone. His non-profit board affiliations include Rockefeller University. Mr. Hoffman received his Bachelor's and Master's Degrees from Northwestern University and his M.B.A. from the Harvard Business School. We believe Mr. Hoffman's investment and transactional experience, including as director of other life sciences companies, qualifies him to serve on our board of directors.

Claudine E. Bruck Ph.D.

Dr. Bruck has served as a member of our Board of Directors since 2015. Dr. Bruck is co-founder and has served as Chief Executive Officer of Prolifagen LLC, a start-up company developing a microRNA-based medicine for tissue regeneration, since June 2016. She is also a course Director at University of Pennsylvania's Institute of Translational Medicine and Therapeutics and a project leader for BioMotiv LLC. Dr. Bruck joined GlaxoSmithKline, or GSK, to build GSK's HIV vaccine program in 1985. In her role in GSK's vaccine group, Dr. Bruck was instrumental in the development of GSK's HPV vaccine (Cervarix), and headed their cancer vaccine program from inception to Phase 2 before joining the drug discovery group of GSK. She held several roles in the drug discovery group, from Head of Clinical Immunology (2004-2005) to VP and Head of Biology for the Center of Excellence for External Drug Discovery (2005-2008), to VP and Head of a newly formed ophthalmology R&D group (2008-2015). Since 2018, Dr. Bruck has served as a director of Navidea Biopharmaceuticals, Inc. Dr. Bruck has a Ph.D. in Biochemistry from the University of Brussels. She was a post-doctoral student at Harvard University Medical School and an Assistant Professor at Tufts Medical School. We believe Dr. Bruck's experience and training in the pharmaceutical industry and serving as executive and directors of companies in the pharmaceutical and biotechnology industries, qualifies her to serve on our board of directors.

Robert M. Whelan, Jr.

Mr. Whelan has served as a member of our Board of Directors since 2016. Mr. Whelan has been the President of Whelan & Company, LLC, which provides business and financial consulting and strategic services to a broad range of companies, since 2001. On January 1, 2018, Mr. Whelan joined the firm of Black Point Partners, Inc., which provides financial advisory, capital raising and mergers and acquisition services to technology companies, as a managing director. From 2001 to 2005, Mr. Whelan also served as Managing Director of Valuation Perspectives, Inc., a consulting firm. Prior to 2001, Mr. Whelan held a number of senior-level positions at various investment banking and brokerage firms. Among other positions, Mr. Whelan was Vice Chairman of Prudential Volpe Technology Group, the technology investment banking and research division of Prudential Securities, and prior to that, he was Chief Operating Officer, Managing Director, Head of Investment Banking, and a board member of Volpe Brown Whelan & Company, a private technology and healthcare investment banking, brokerage

and asset management firm acquired by Prudential Securities in 1999. Mr. Whelan serves as a director of Aspen Technology, Inc.. a leading global supplier of asset optimization solutions that optimize asset design, operations and maintenance in complex, industrial environments, and has served as a director of ARIAD Pharmaceuticals, Inc., a developer of small-molecule drugs to treat patients with aggressive cancers, from April 2010 through September 2014. Mr. Whelan holds a B.A. in History from Dartmouth College and an M.B.A. from Stanford University Graduate School of Business. We believe Mr. Whelan's experience as a business and financial advisor, as well as his service as executive and director of companies in the financial services and pharmaceutical industries, qualifies him to serve on our board of directors.

Mark White

Mr. White has served as a member of our Board of Directors since 2016. Since 2014, he has been an independent consultant, specializing in new product commercialization, marketing, business development and strategy. He served as chief executive officer of Neurokine Therapeutics, which focused on neurodegenerative disorders, from 2015-2016 and as chief executive officer of Neurokappa Therapeutics, which focused on rare diseases. Prior to that, he served as vice president, worldwide marketing and other capacities with Pfizer, Inc. from 2002 to 2014, as senior director, marketing and business development with Bracco Diagnostics, a diagnostic pharmaceutical business with radiology and cardiology applications, from 1998-2002 and as director, business development of i-Stat, Inc., a medical device company, from 1995 to 1998. He holds a B.S. and M.Ed. from the University of Missouri and M.B.A. from the University of Chicago Booth School of Business. We believe Mr. White's experience as a business consultant and his service as executive of companies in the pharmaceutical industry qualifies him to serve on our board of directors.

Board Composition and Election of Directors

Director Independence

Our board of directors currently consists of five members. Our board of directors has determined that directors Bruck, Hoffman, Whelan and White do not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of the director and that each of these directors is "independent" as that term is defined under the rules of The Nasdaq Stock Market LLC, or Nasdaq. There are no family relationships among any of our directors or executive officers.

In accordance with current as well as our restated certificate of incorporation and amended and restated bylaws that will go into effect upon the closing of this offering, our board of directors will be elected once a year.

Our restated certificate of incorporation that will go into effect upon the closing of this offering will provide that the authorized number of directors may be changed only by resolution of the board of directors.

In selecting board members, our board may consider many factors, such as personal and professional integrity, ethics and values; experience in corporate management, such as serving as an officer or former officer of a publicly held company; experience as a board member or executive officer of another publicly held company; diversity of expertise and experience in substantive matters pertaining to our business relative to other board members; and diversity of background and perspective, including, but not limited to, with respect to age, gender, race, place of residence and specialized experience.

Board Leadership Structure

Role of the Board in Risk Oversight

One of the key functions of our board of directors is informed oversight of our risk management process. Our board of directors does not have a standing risk management committee, but rather administers this oversight function directly through our board of directors as a whole, as well as through various standing committees of our board of directors that address risks inherent in their respective areas of oversight. In particular, our board of directors is responsible for monitoring and assessing strategic risk exposure and our audit committee has the responsibility to consider and discuss our major financial risk exposures and the steps our management has taken to monitor and control these exposures, including guidelines and policies to govern the process by which risk assessment and management is undertaken. Our audit committee also monitors compliance with legal and regulatory requirements. Our nominating and corporate governance committee when establishment, will monitor the effectiveness of our corporate governance practices, including whether they are successful in preventing illegal or improper liability-creating conduct. Our compensation committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking. While each committee is responsible for evaluating certain risks and overseeing the management of such risks, our entire board of directors is regularly informed through committee reports about such risks.

Director Nominations

The board of directors as a whole will consider director candidates recommended for nomination by our stockholders during such times as they are seeking proposed nominees to stand for election at the next annual meeting of stockholders (or, if applicable, a special meeting of stockholders). Our stockholders that wish to nominate a director for election to our board of directors should follow the procedures set forth in our bylaws.

We have not formally established any specific, minimum qualifications that must be met or skills that are necessary for directors to possess. In general, in identifying and evaluating nominees for director, our board of directors considers educational background, diversity of professional experience, knowledge of our business, integrity, professional reputation, independence, wisdom, and the ability to represent the best interests of our stockholders,

Board Committees

Our board of directors has established two standing committees—audit and compensation—each of which operates under a charter that has been approved by our board of directors. Upon our listing on Nasdaq, Annovis will also establish a nomination and corporate governance committee. Each committee's charter will be available under the Corporate Governance section of our website at *www.annovis.com* . The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider it to be a part of this prospectus.

Audit Committee

Our audit committee will assist our board of directors in its oversight of our accounting and financial reporting process and the audits of our financial statements. We will adopt an audit committee charter, which will detail the principal functions of the audit committee, including:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;

- overseeing the work of our registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and the registered public accounting firm our annual and quarterly financial statements and related disclosures;
- coordinating our board of directors' oversight of our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- discussing our risk management policies;
- meeting independently with our internal auditing staff, if any, registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by SEC rules.

The members of our audit committee are Robert Whelan and Mark White. All members of our audit committee meet the requirements for financial literacy under the applicable listing rules of Nasdaq, or the Nasdaq rules, and meet the independence requirements of Rule 10A-3 under the Exchange Act and the applicable Nasdaq rules. Mr. Whelan qualifies as an audit committee financial expert under Item 407 of Regulation S-K.

Compensation Committee

Our compensation committee will assist our board of directors in the discharge of its responsibilities relating to the compensation of our executive officers. We will adopt a compensation committee charter, which will detail the principal functions of the compensation committee, including.

- reviewing and approving, or recommending for approval by the board of directors, the compensation of our Chief Executive Officer and our other executive officers;
- overseeing and administering our cash and equity incentive plans;
- reviewing and making recommendations to our board of directors with respect to director compensation;
- reviewing and discussing annually with management our "Compensation Discussion and Analysis" to the extent required; and
- preparing the annual compensation committee report required by SEC rules, to the extent required.

The members of our compensation committee are Michael Hoffman and Robert Whelan. Hoffman serves as the chairperson of the committee. Our board of directors has determined that Hoffman and Whelan are independent under the applicable Nasdaq rules, including the Nasdaq rules specific to membership on the compensation committee, and is a "non-employee director" as defined in Rule 16b-3 promulgated under the Exchange Act.

Compensation Committee Interlocks and Insider Participation

No member of our compensation committee is or has been our current or former officer or employee. None of our executive officers served as a director or a member of a compensation committee (or other committee serving an equivalent function) of any other entity.

Code of Ethics and Code of Conduct

We intend to adopt a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Upon our listing on Nasdaq, our code of business conduct and ethics will be available under the Corporate Governance section of our website at *www.annovis.com* . In addition, we intend to post on our website all disclosures that are required by law or the Nasdaq rules concerning any amendments to, or waivers from, any provision of the code. The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider it to be a part of this prospectus.

Legal Proceedings

We are not aware of any of our directors or officers being involved in any legal proceedings in the past 10 years relating to bankruptcy, insolvency or criminal proceedings (other than traffic and other minor offenses) or being subject to any of the items set forth under Item 401(f) of Regulation S-K.

EXECUTIVE AND DIRECTOR COMPENSATION

As an emerging growth company under the JOBS Act we have opted to comply with the executive compensation disclosure rules applicable to "smaller reporting companies," which require compensation disclosure for our principal executive officer and the two most highly compensated executive officers (other than our principal executive officer) serving as executive officers at the end of the fiscal year. This section describes the executive compensation program in place for our named executive officers the year ended December 31, 2018, who are the individuals who served as our principal executive officer and two most highly compensated executive officers.

This section discusses the material components of the executive compensation program for our executive officers who are named in the "2018 Summary Compensation Table" below and the non-employee members of our board of directors. In 2018, our "named executive officers" and their positions were:

- Maria Maccecchini, President and Chief Operating Officer
- Jeffrey Cummings, Chief Medical Officer

This discussion may contain forward-looking statements that are based on our current plans, considerations, expectations and determinations regarding future compensation programs. Actual compensation programs that we adopt following the completion of this offering may differ materially from the currently planned programs summarized in this discussion.

2018 Summary Compensation Table

The following table sets forth information concerning the compensation of our named executive officers for the year ended December 31, 2018.

Name and Principal Position	Year	Salary ($)	Option Awards ($)(1)	Total ($)
Maria Maccecchini *President and Chief Executive Officer*	2018	120,000	35,165	155,165
Jeffrey Cummings *Chief Medical Officer*	2018	—	3,374	3,374

(1) Amounts reflect the full grant date fair value of stock options granted during 2018 computed in accordance with ASC Topic 718, rather than the amounts paid to or realized by the named individual. We provide information regarding the assumptions used to calculate the value of the option awards in Note 8 to our financial statements included in this prospectus.

2018 Bonuses

Our named executive officers did not participate in an annual cash bonus program or receive bonuses for 2018.

Equity Compensation

In connection with this offering, we intend to adopt a 2019 Incentive Award Plan, which we refer to as the 2019 Plan, in order to facilitate the grant of cash and equity incentives to our directors, employees and consultants (including our named executive officers) and to enable us to obtain and retain services of these individuals, which we believe is essential to our long-term success. Following the effective date of the 2019 Plan, we will not make any further grants under our 2018 Plan. However, the

2018 Plan will continue to govern the terms and conditions of the outstanding awards granted under it. For additional information about the 2019 Plan, please see the section titled "Incentive Compensation Plans" below.

Retirement, Health and Welfare Plans

Maria Maccecchini is covered by a medical plan. No other plans are covered by the Company.

Outstanding Equity Awards at 2018 Fiscal Year-End

The following table summarizes the number of shares of common stock underlying outstanding equity incentive plan awards for each named executive officer as of December 31, 2018.

		Option Awards			
Name	Grant Date	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable(1)	Option Exercise Price ($)	Option Expiration Date
Maria Maccecchini	4/1/2017	120,000	—	$ 0.10	4/1/2027
	4/6/2018	70,000	—	$ 0.18	4/5/2028
Jeffrey Cummings	6/24/2015	10,000	—	$ 0.10	6/23/2025
	4/1/2017	6,666	—	$ 0.10	4/1/2027
	4/6/2018	6,666	—	$ 0.18	4/5/2028

Employment Agreement

Dr. Maccecchini has an amended and restated employment agreement dated as of May 10, 2019. Under the employment agreement, we agree to pay her an annual base salary of $120,000 and an annual performance bonus in an amount of up to 50% of the base salary based upon objectives established annually by the board of directors. The agreement may be terminated by either party upon ten business days' prior written notice. The agreement contains standard non-disclosure and non-competition provisions and disclosure and assignment and transfer of inventions, as defined in the agreement. In the event we terminate the employment agreement other than for cause, as defined in the agreement, or Dr. Maccecchini terminates the agreement for good reason, as defined in the agreement, we will pay her the then effective base salary for twelve months after termination in accordance with our regular payroll practices, subject to her execution of a release satisfactory to us and her continued compliance with the provisions of the agreement that survive termination of the agreement.

Mr. McGroarty was appointed our chief financial officer in April 2019 and is working as a consultant. Upon the closing of this offering, we intend to enter into an employment agreement with Mr. McGroarty.

Director Compensation

Directors who are also our employees do not receive compensation for their service on our board of directors. Historically, our non-employee directors have not received compensation for their service on our board of directors other than awards of stock options.

2018 Director Compensation Table

Name	Option Awards ($)(1)	Total ($)
Michael Hoffman	5,062	5,062
Robert Whelan	5,062	5,062
Mark White	5,062	5,062
Claudine Bruck	5,062	5,062

(1) Amounts reflect the full grant date fair value of stock options granted during 2018 computed in accordance with ASC Topic 718, rather than the amounts paid to or realized by the named individual. We will provide information regarding the assumptions used to calculate the value of the option awards in Note 8 to our financial statements included in this prospectus. The stock options were granted with an exercise price equal to the fair market value of our common stock on the date of grant, as determined by our board of directors, and vest as to 25% of the underlying shares in equal quarterly installments beginning June 30, 2018.

Scientific Advisory Board Compensation

Historically, our non-employee scientific advisors have not received compensation for their service other than awards of stock options.

2018 Scientific Advisor Compensation Table

Name	Option Awards ($)(1)	Total ($)
Jeffrey Cummings	3,374	3,374
Peter Davies	3,374	3,374
Sidney Strickland	5,062	5,062
Gregory Petsko	5,062	5,062
Rudy Tanzi	5,062	5,062

(1) Amounts reflect the full grant date fair value of stock options granted during 2018 computed in accordance with ASC Topic 718, rather than the amounts paid to or realized by the named individual. We provide information regarding the assumptions used to calculate the value of the option awards in Note 8 to our financial statements included in this prospectus. The stock options were granted with an exercise price equal to the fair market value of our common stock on the date of grant, as determined by our board of directors, and vest as to 25% of the underlying shares in equal quarterly installments beginning June 30, 2018.

Limitations of Liability and Indemnification

Our restated certificate of incorporation, which will become effective upon the closing of this offering, limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the Delaware General Corporation Law, or the DGCL, and provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty as a director. However, these provisions do not eliminate or limit the liability of any of our directors:

- for any breach of the director's duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;

- for voting for or assenting to unlawful payments of dividends, stock repurchases or other distributions; or
- for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act, omission or claim that occurred or arose prior to such amendment or repeal. If the DGCL is amended to provide for further limitations on the personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the DGCL.

In addition, our restated certificate of incorporation, which will become effective upon the closing of this offering, provides that we must indemnify our directors and officers and we must advance expenses, including attorneys' fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

We maintain a general liability insurance policy that covers specified liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers. In addition, we have entered into indemnification agreements with our directors, and we intend to enter into new indemnification agreements with our directors and executive officers prior to the completion of this offering. These indemnification agreements may require us, among other things, to indemnify each such executive officer or director for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by him or her in any action or proceeding arising out of his or her service as one of our executive officers or directors.

Some of our non-employee directors may, through their relationships with their employers, be insured or indemnified against specified liabilities incurred in their capacities as members of our board of directors.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, or the Securities Act, may be permitted to directors, executive officers or persons controlling us, in the opinion of the Securities and Exchange Commission, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Equity Compensation Plans

Our 2018 Equity Incentive Plan, or the Plan, provides for grants of stock options and stock awards. Our directors, officers and consultants are eligible for grants under the 2018 Equity Incentive Plan.

The purpose of the Plan is to encourage the participants to contribute materially to the growth of the Company, thereby benefitting the Company's stockholders, and will align the economic interests of the participants with those of the stockholders.

Administration. The Plan is administered by the board of directors or a committee appointed by the board. The board has the sole authority to (i) determine the individuals to whom grants shall be made under the Plan, (ii) determine the type, size and terms of the grants to be made to each such individual, (iii) determine the time when the grants will be made and the duration of any applicable exercise or restriction period, including the criteria for exercisability and the acceleration of exercisability, (iv) amend the terms of any previously issued grant, and (v) deal with any other matters arising under the Plan.

Available shares. The aggregate number of shares of our common stock that may be issued pursuant to awards under the Plan is 526,525 shares.

If there is any change in the number or kind of shares of our stock outstanding (i) by reason of a stock dividend, spinoff, recapitalization, stock split, or combination or exchange of shares, (ii) by reason

of a merger, reorganization or consolidation, (iii) by reason of a reclassification or change in par value, or (iv) by reason of any other extraordinary or unusual event affecting the outstanding stock as a class without the receipt of consideration, or if the value of outstanding shares of our stock is substantially reduced as a result of a spinoff or our payment of an extraordinary dividend or distribution, the maximum number of shares of our stock available for grants under the Pla, the maximum number of shares of our stock that any individual participating in this Plan may be granted in any year, the number of shares covered by outstanding grants, the kind of shares issued under this Plan, and the price per share of such grants shall be appropriately adjusted by the board to reflect any increase or decrease in the number of, or change in the kind or value of, issued shares of our stock to preclude, to the extent practicable, the enlargement or dilution of rights and benefits under such Grants; provided, however, that any fractional shares resulting from such adjustment shall be eliminated. Any adjustments determined by the Board shall be final, binding and conclusive.

Eligibility for participation. Members of our board of directors, as well as employees of, and consultants and advisors to, us or any of our subsidiaries and affiliates will be eligible to receive awards under the Plan.

Award agreements. Awards granted under the Plan are evidenced by award agreements, which need not be identical, and that provide additional terms, conditions, restrictions or limitations covering the grant of the award, including, without limitation, additional terms providing for the acceleration of exercisability or vesting of awards in the event of a Change in Control (as defined in the Plan) or conditions regarding the participant's employment, as determined by the committee.

Stock options. The committee may grant nonqualified stock options to any individuals eligible to participate in the Plan and incentive stock options to purchase shares of our common stock only to eligible employees. The committee will determine: (i) the number of shares of our common stock subject to each option; (ii) the term of each option, which may not exceed ten years, or five years in the case of an incentive stock option granted to a 10.0% or greater stockholder; (iii) the exercise price; (iv) the vesting schedule, if any and (v) the other material terms of each option. No incentive stock option or nonqualified stock option may have an exercise price less than the fair market value of a share of our common stock at the time of grant or, in the case of an incentive stock option granted to a 10.0% or greater stockholder, 110.0% of such share's fair market value. Options will be exercisable at such time or times and subject to such terms and conditions as determined by the committee at the time of grant and the exercisability of such options may be accelerated by the committee.

Stock awards. The board may issue shares of our to an employee, non-employee director or advisor under a stock award, upon such terms as the Board deems appropriate. Shares of our stock issued pursuant to stock awards may be issued for consideration or for no consideration, and subject to restrictions or no restrictions, as determined by the board. The board may establish conditions under which restrictions on stock awards shall lapse over a period of time or according to such other criteria as the board deems appropriate.

Change in Control. Upon a change of control where we are not the surviving corporation (or survives only as a subsidiary of another corporation), unless the board determines otherwise, all outstanding options that are not exercised shall be assumed by, or replaced with comparable options by the surviving corporation (or a parent or subsidiary of the surviving corporation), and outstanding stock awards shall be converted to stock awards of the surviving corporation (or a parent or subsidiary of the surviving corporation). In the event of a Change of Control, the board may take any of the following actions with respect to any or all outstanding grants: the Board may (i) determine that outstanding options shall accelerate and become exercisable, in whole or in part, upon the change of control or upon such other event as the board determines, (ii) determine that the restrictions and conditions on outstanding stock awards shall lapse, in whole or in part, upon the change of control or upon such other event as the board determines, (iii) require that grantees surrender their outstanding options in

exchange for a payment by us, in cash or stock as determined by the board, in an amount equal to the amount by which the then fair market value of the shares of our stock subject to the grantee's unexercised options exceeds the exercise price of the options or (iv) after giving grantees an opportunity to exercise their outstanding options, terminate any or all unexercised options at such time as the board deems appropriate. Such surrender or termination shall take place as of the date of the change of control or such other date as the board may specify. The board shall have no obligation to take any of the foregoing actions, and, in the absence of any such actions, outstanding Options and Stock Awards shall continue in effect according to their terms (subject to any assumption pursuant to as described in the first sentence of this paragraph).

As used in the Plan, a "Change of Control" shall mean:

- any merger or consolidation in which our voting securities possessing more than 50% of the total combined voting power of our outstanding securities are transferred to a person or persons different from the person holding those securities immediately prior to such transaction and the composition of the board following such transaction is such that our directors prior to the transaction constitute less than 50% of the board membership following the transaction;

- any acquisition, directly or indirectly, by a person or related group of persons (other than the Company or a person that directly or indirectly controls, is controlled by, or is under common control with, the Company) of beneficial ownership of our voting securities possessing more than 50% of the total combined voting power of our outstanding securities; provided, however, that, no Change of Control shall be deemed to occur by reason of the acquisition of shares of our capital stock by an investor in us in a capital-raising transaction;

- any acquisition, directly or indirectly, by a person or related group of persons of the right to appoint a majority of our directors or otherwise directly or indirectly control our management, affairs and business;

- any sale, transfer or other disposition of all or substantially all of our assets; or

- a complete liquidation or dissolution of us.

The term "transfer" includes any sale, exchange, assignment, gift, bequest, disposition, mortgage, charge, pledge, encumbrance, grant of a security interest or other arrangement by which possession, legal title or beneficial ownership passes from one person to another, or to the same person in a different capacity, whether or not voluntarily and whether or not for value, and including without limitation any merger or amalgamation and any agreement to effect any of the foregoing.

Stockholder rights. Except as otherwise provided in the applicable award agreement, and with respect to an award of restricted stock, a participant will have no rights as a stockholder with respect to shares of our common stock covered by any award until the participant becomes the record holder of such shares.

Amendment and termination. Notwithstanding any other provision of the Plan, our board of directors may at any time amend any or all of the provisions of the Plan.

Transferability. Awards granted under the Plan generally will be nontransferable, other than by will or the laws of descent and distribution, except that the committee may provide for the transferability of nonqualified stock options at the time of grant or thereafter to certain family members.

CERTAIN RELATIONSHIPS AND RELATED PERSON TRANSACTIONS

The following includes a summary of transactions (before giving effect to our 1-for- reverse stock split) since January 1, 2017 to which we have been a party in which the amount involved exceeded or will exceed the lesser of $120,000 or one percent of the average of our total assets as of December 31, 2018 and 2017, and in which any of our directors, executive officers or, to our knowledge, beneficial owners of more than 5% of our capital stock or any member of the immediate family of any of the foregoing persons had or will have a direct or indirect material interest, other than equity and other compensation, termination, change in control and other arrangements, which are described under "Executive and Director Compensation." We also describe below certain other transactions with our directors, executive officers and stockholders.

Preferred Stock and Convertible Note Financings

Issuance of Series A-1 Convertible Preferred Stock

In December 2017 and March 2018, we issued and sold an aggregate of 630,722 shares of series A-1 convertible preferred stock at a purchase price per share of $.90, for an aggregate purchase price of approximately $0.568 million. The following persons who hold more than 5.0% of our outstanding capital stock and our directors purchased the following shares in this private offering:

- Paul Hoffman, Inc. (Michael Hoffman, affiliate) purchased an aggregate of 222,222 shares for $200,000
- Robert Whelan purchased an aggregate of 83,333 shares for $75,000
- Maria Maccecchini purchased an aggregate of 11,111 shares for $10,000
- Claudine Bruck purchased an aggregate of 5,556 shares for $5,000

Issuance of Convertible Promissory Notes

In March 2019, we issued and sold an aggregate of $530,000 principal amount of our convertible promissory notes, which will convert upon the closing of this offering into shares of our common stock at 20% discount to the public offering price. The following persons who hold more than 5.0% of our outstanding capital stock and our directors purchased the following notes in this private offering:

- Paul Hoffman, Inc. (Michael Hoffman, affiliate) purchased an aggregate of $250,000
- Robert Whelan purchased an aggregate of $50,000
- Claudine Bruck purchased an aggregate of $5,000

Policies and Procedures for Related Person Transactions

Our board of directors intends to adopt a written related person transaction policy, to be effective upon the closing of this offering, setting forth the policies and procedures for the review and approval or ratification of related person transactions. This policy will cover, with certain exceptions set forth in Item 404 of Regulation S-K under the Securities Act, any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we were or are to be a participant, where the amount involved exceeds the lesser of $120,000 or one percent of the average of our total assets as of December 31, 2018 and 2017 and a related person had, has or will have a direct or indirect material interest, including without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person. In reviewing and approving any such transactions, our audit committee is tasked to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction and the extent of the related person's interest in the transaction. All of the transactions described in this section occurred prior to the adoption of this policy.

PRINCIPAL STOCKHOLDERS

The following table sets forth information with respect to the beneficial ownership of our common stock, as of , 2019 by:

- each person or group of affiliated persons known by us to beneficially own more than 5% of our common stock;
- each of our named executive officers;
- each of our directors; and
- all of our executive officers and directors as a group.

The number of shares beneficially owned by each stockholder is determined under rules issued by the SEC. Under these rules, beneficial ownership includes any shares as to which the individual or entity has sole or shared voting power or investment power. Applicable percentage ownership is based on 6,159,534 shares of common stock outstanding as of , 2019, assuming the conversion of all outstanding shares of preferred stock into common stock. In computing the number of shares beneficially owned by an individual or entity and the percentage ownership of that person, shares of common stock subject to the exercise of options, warrants or other rights held by such person that are currently exercisable or will become exercisable within 60 days of , 2019 and shares of our common stock that will be issued upon conversion of our $530,000 principal amount convertible promissory notes upon the closing of this offering into shares of our common stock at a 20% discount to the public offering price are considered outstanding, although these shares are not considered outstanding for purposes of computing the percentage ownership of any other person. Unless noted otherwise, the address of all listed stockholders is . Each of the stockholders listed has sole voting and investment power with respect to the shares beneficially owned by the stockholder unless noted otherwise, subject to community property laws where applicable.

Name of Beneficial Owner	Number of Shares Beneficially Owned Prior to Offering	Percentage of Shares Beneficially Owned	
		Prior to Offering	After Offering
5% or Greater Stockholders			
Michael Hoffman	1,825,340(1)	29.6%	
Maria Maccecchini	1,558,043(2)	24.5%	
Ben Franklin Technology Partners	323,387(3)	5.3%	
Named Executive Officers and Directors Other Than 5% or Greater Stockholders			
Robert Whelan	118,333(4)	1.9%	
Claudine Bruck	50,556(5)	*%	
Mark White	94,667(6)	1.5%	
Jeffrey McGroarty	—	*%	
Jeffrey Cummings	23,332(7)	*%	
All Executive Officer and Directors as a Group (7 persons)	3,670,271(8)	56.5%	

* Less than 1%.

(1) Includes (i) currently exercisable stock options to purchase 10,000 shares at an exercise price of $0.18 per share and (ii) shares of our common stock that will be issued upon conversion of $250,000 principal amount of our convertible promissory notes upon the closing of this offering into shares of our common stock at a 20% discount to the public offering price.

(2) Includes currently exercisable stock options to purchase 120,000 shares at an exercise price of $0.10 per share and 70,000 shares at an exercise price of $0.18 per share.

(3) RoseAnn B. Rosenthal, the President and Chief Executive Officer of Ben Franklin Technology Partners, has sole voting and investment power with respect to these securities.

(4) Includes (i) currently exercisable stock options to purchase 25,000 shares at an exercise price of $0.10 per share and 10,000 shares at an exercise price of $0.18 per share and (ii) [ ] shares of our common stock that will be issued upon conversion of $50,000 principal amount of our convertible promissory notes upon the closing of this offering into shares of our common stock at a 20% discount to the public offering price.

(5) Includes (i) currently exercisable stock options to purchase 35,000 shares at an exercise price of $0.10 per share and 10,000 shares at an exercise price of $0.18 per share and (ii) [ ] shares of our common stock that will be issued upon conversion of $5,000 principal amount of our convertible promissory notes upon the closing of this offering into shares of our common stock at a 20% discount to the public offering price.

(6) Includes currently exercisable stock options to purchase 20,000 shares at an exercise price of $0.10 per share and 10,000 shares at an exercise price of $0.18 per share.

(7) Includes currently exercisable stock options to purchase 16,666 shares at an exercise price of $0.10 per share and 6,666 shares at an exercise price of $0.18 per share.

(8) Includes (i) currently exercisable stock options to purchase 216,666 shares at an exercise price of $0.10 per share and 116,666 shares at an exercise price of $0.18 per share and (ii) [ ] shares of our common stock that will be issued upon conversion of $305,000 principal amount of our convertible promissory notes upon the closing of this offering into shares of our common stock at a 20% discount to the public offering price.

DESCRIPTION OF CAPITAL STOCK

General

The following description summarizes some of the terms of our restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering. Because it is only a summary, it does not contain all the information that may be important to you. For a complete description, you should refer to our restated certificate of incorporation and amended and restated bylaws, copies of which have been or will be filed as exhibits to the registration statement of which this prospectus is a part. The description of our common stock and preferred stock reflects changes to our capital structure that will occur immediately prior to the closing of this offering.

Following the closing of this offering, our authorized capital stock will consist of million shares of common stock, par value $0.0001 per share, and 10 million shares of preferred stock, par value $0.0001 per share.

Common Stock

As of , 2019, there were 395,653 shares of our common stock issued and outstanding and 5,763,881 shares of our common stock issuable upon the automatic conversion of all outstanding shares of our preferred stock upon the closing of this offering.

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote in the election. Subject to the supermajority votes for some matters, other matters shall be decided by the affirmative vote of our stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of any series of preferred stock that we may designate and issue in the future.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive on a pro rata basis our net assets available for distribution to stockholders after the payment of all debts and other liabilities, subject to the prior rights of any holders of outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. Our outstanding shares of common stock are, and the shares offered by us in this offering will be, when issued and paid for, validly issued, fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

Under the terms of our amended and restated certificate of incorporation that will become effective upon the closing of this offering, our board of directors is authorized to direct us to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our

outstanding voting stock. Upon the closing of this offering, there will be no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

Options

Registration Rights

Under our registration rights agreement dated as of December 19, 2014, the holders of approximately shares of common stock, or their transferees, will have the right to require us to register their shares under the Securities Act so that those shares may be publicly resold, or to include their shares in any registration statement we file, in each case as further described below.

Demand Registration Rights

Commencing on the earlier of (i) December 19, 2019 or (ii) 180 days after the effective date of an initial public offering of the our common stock, if holders of more than 50% of the registrable securities request us to file a registration statement under the Securities Act for a public offering of such shares of registrable securities having an aggregate offering price of at least $10,000,000, we must, within ten days after the receipt of such notice, notify all holders of registrable securities of such request and shall use its reasonably diligent efforts to register under the Securities Act the registrable securities of all holders who so request within 90 days after the date of our notice; provided, however, that we are obligated to register only shares of common stock pursuant to the agreement. We are obligated to effect a maximum of two such demand registrations.

Piggyback/Incidental Registration Rights

Whenever we propose to register any common stock for our own or others' account under the Securities Act for a public offering for cash, other than a registration relating to employee benefit plans, we must give each holder of registrable securities prompt written notice of its intent to do so. Upon the written request of any such holder given within 10 days after receipt of such notice, we will cause to be included in such registration all of the registrable securities that such holder requests; provided, however, that we are obligated to register only shares of our common stock pursuant to the agreement. If we are advised in writing by any managing underwriter of the securities being offered pursuant to any registration statement that the number of shares to be sold by persons other than us is greater than the number of such shares that can be offered without adversely affecting the offering, we may reduce pro rata the number of shares of registrable securities offered for the accounts of such persons to a number deemed satisfactory by such managing underwriter; and a managing underwriter will have the right to exclude registrable securities entirely pursuant to the preceding clause.

Form S-3 Registration Rights

If, at a time when Form S-3 (or any successor thereto) is available for such registration, we receive from holders of more than 15% of the Registrable Securities a written request or requests that we effect a registration on Form S-3 of Registrable Securities having an aggregate offering price of at least $5,000,000 (based on the then current public market price), we will promptly give written notice of the proposed registration to all other holders of Registrable Securities and, as soon as reasonably practicable, effect such registration and all such related qualifications and compliances as may be requested and as would permit the sale and distribution of all Registrable Securities as are specified in such request and any written requests of other holders given within 10 days after receipt of such notice; provided, however, that the Company shall not be obligated to effect any such registration pursuant to the agreement: (i) if Form S-3 is not available for such offering by the applicable holders; or (ii) if we furnish to the applicable holders a certificate signed by the chief executive officer stating that in the good faith judgment of the board of directors, it would be seriously detrimental to us and our

stockholders for such Form S-3 registration to be effected at such time, in which event we will have the right to defer the filing of the Form S-3 registration statement for a period of not more than 120 days after receipt of the request of the holder or holders; provided, however, that we may not utilize this right more than twice in any 12-month period. We are not obligated to file more than two registrations under this provision.

Other Provisions and Expenses

A registrable security will cease to be a registrable security when (i) a registration statement covering such registrable security has been declared effective by the SEC and it has been disposed of pursuant to such effective registration statement; or (ii) such registrable security could be sold pursuant to Rule 144 (or any successor or comparable provision) without any volume restriction.

Other than underwriting discounts and commissions and certain other expenses, we will be required to pay all expenses incurred by us related to any registration effected pursuant to the exercise of these registration rights. These expenses may include all registration and filing fees, printing expenses, fees and disbursements of our counsel, reasonable fees and disbursements of a counsel for the selling securityholders and blue sky fees and expenses.

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

Some provisions of Delaware law, our restated certificate of incorporation and our amended and restated bylaws that will be in effect upon the consummation of this offering could make the following transactions more difficult: an acquisition of us by means of a tender offer; an acquisition of us by means of a proxy contest or otherwise; or the removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions which provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Authorized by Unissued Shares

Our authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval. These additional shares may be utilized for a variety of corporate purposes, including future public offerings to raise additional capital and corporate acquisitions. The existence of authorized but unissued shares of common stock and preferred stock could render more difficult or discourage an attempt to obtain control of a majority of our common stock by means of a proxy contest, tender offer, merger or otherwise.

Stockholder Meetings

Any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide advance notice in writing, and also specify requirements as to the form and content of a stockholder's notice.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the General Corporation Law of the State of Delaware, which prohibits persons deemed to be "interested stockholders" from engaging in a "business combination" with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors.

Choice of Forum

The Court of Chancery of the State of Delaware is the exclusive forum in which we and our directors may be sued by our stockholders, to the fullest extent permitted by law, for:

- any derivative action or proceeding brought on our behalf;
- any action asserting a breach of fiduciary duty;
- any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation, or our amended and restated bylaws; or
- or any action asserting a claim against us that is governed by the internal affairs doctrine.

Nothing in our amended and restated bylaws will preclude stockholders that assert claims under the Securities Act from bringing such claims in state or federal court, subject to applicable law, or actions under the Exchange Act.

These choice of forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, or other employees, which may discourage lawsuits with respect to such claims. Alternatively, if a court were to find either choice of forum provision contained in our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business, results of operations, and financial condition.

Advance Notice Requirements

Our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to the board of directors. Stockholders at an annual meeting will only be able to consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors or by a stockholder who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given our Secretary timely written notice, in proper form, of the stockholder's intention to bring that business before the meeting. Although our bylaws do not give the board of directors the power to approve or disapprove stockholder nominations

of candidates or proposals regarding other business to be conducted at a special or annual meeting, our bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of us.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

National Securities Exchange Listing

We intend to apply to have our common stock listed on The Nasdaq Capital Market under the symbol "ANVS."

SHARES ELIGIBLE FOR FUTURE SALE

Immediately prior to this offering, there was no public market for our common stock. Future sales of substantial amounts of common stock in the public market, or the perception that such sales may occur, could adversely affect the market price of our common stock.

Upon the closing of this offering, we will have outstanding an aggregate of shares of common stock, assuming the issuance of shares of common stock offered by us in this offering, the automatic conversion of all outstanding shares of our preferred stock into shares of our common stock and no exercise of options after December 31, 2018. Of these shares, all shares sold in this offering will be freely tradable without restriction or further registration under the Securities Act, except for any shares purchased by our "affiliates," as that term is defined in Rule 144 under the Securities Act, whose sales would be subject to the Rule 144 resale restrictions described below, other than the holding period requirement. Additionally, the Representatives' Warrants may not be sold, transferred, assigned, pledged, or hypothecated for a 180-day period following the effective date of the registration statement, except to any underwriter and selected dealer participating in the offering and their bona fide officers or partners.

The remaining shares of common stock will be "restricted securities," as that term is defined in Rule 144 under the Securities Act. These restricted securities are eligible for public sale only if they are registered under the Securities Act or if they qualify for an exemption from registration under Rules 144 or 701 under the Securities Act, which are summarized below. We expect that all of these shares will be subject to the 12-month and 180-day lock-up periods under the lock-up agreements described below. Upon expiration of the lock-up periods, we estimate that approximately shares will be available for sale in the public market, subject in some cases to applicable volume limitations under Rule 144.

In addition, of the 495,025 shares of our common stock that were subject to stock options outstanding as of December 31, 2018, options to purchase 477,525 shares of common stock were vested as of December 31, 2018 and, upon exercise, these shares will be eligible for sale subject to the lock-up agreements described below and Rules 144 and 701 under the Securities Act.

Lock-Up Agreements

In connection with this offering, we, our officers and directors and the holders of our outstanding capital stock have agreed with the underwriters, subject to certain exceptions, not to dispose of or hedge any shares of our common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of the lock-up agreement continuing through the date 12 months, in the case of our directors and officers, and 180 days, in the case of our stockholders, after the date of this prospectus, except with the prior written consent of ThinkEquity.

Following the lock-up periods set forth in the agreements described above, and assuming that ThinkEquity do not release any parties from these agreements and that there is no extension of the lock-up period, all of the shares of our common stock that are restricted securities or are held by our affiliates as of the date of this prospectus will be eligible for sale in the public market in compliance with Rule 144 under the Securities Act.

Rule 144

Affiliate Resales of Restricted Securities

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is an affiliate of ours, or who was an affiliate at any time during the 90 days before a sale, who has beneficially owned shares of our common stock for at least six months

would be entitled to sell in "broker's transactions" or certain "riskless principal transactions" or to market makers, a number of shares within any three-month period that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately shares immediately after this offering; or
- the average weekly trading volume in our common stock on Nasdaq during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Affiliate resales under Rule 144 are also subject to the availability of current public information about us. In addition, if the number of shares being sold under Rule 144 by an affiliate during any three-month period exceeds 5,000 shares or has an aggregate sale price in excess of $50,000, the seller must file a notice on Form 144 with the Securities and Exchange Commission and Nasdaq concurrently with either the placing of a sale order with the broker or the execution directly with a market maker.

Non-Affiliate Resales of Restricted Securities

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is not an affiliate of ours at the time of sale, and has not been an affiliate at any time during the nine months preceding a sale, and who has beneficially owned shares of our common stock for at least six months but less than a year, is entitled to sell such shares subject only to the availability of current public information about us. If such person has held our shares for at least one year, such person can resell under Rule 144(b)(1) without regard to any Rule 144 restrictions, including the 90-day public company requirement and the current public information requirement.

Non-affiliate resales are not subject to the manner of sale, volume limitation or notice filing provisions of Rule 144.

Rule 701

In general, under Rule 701, any of an issuer's employees, directors, officers, consultants or advisors who purchases shares from an issuer in connection with a compensatory stock or option plan or other written agreement before the effective date of a registration statement under the Securities Act is entitled to sell such shares 90 days after such effective date in reliance on Rule 144. An affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding period requirement, and non-affiliates of the issuer can resell shares in reliance on Rule 144 without having to comply with the current public information and holding period requirements.

The Securities and Exchange Commission has indicated that Rule 701 will apply to typical stock options granted by an issuer before it becomes subject to the reporting requirements of the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after an issuer becomes subject to the reporting requirements of the Exchange Act.

Equity Plans

We intend to file one or more registration statements on Form S-8 under the Securities Act to register all shares of common stock subject to outstanding stock options and common stock issued or issuable under our stock plans. We expect to file the registration statement covering shares offered pursuant to our stock plans shortly after the date of this prospectus, permitting the resale of such shares by nonaffiliates in the public market without restriction under the Securities Act and the sale by affiliates in the public market, subject to compliance with the resale provisions of Rule 144.

Registration Rights

The holders of shares of common stock are entitled to certain rights with respect to the registration of the offer and sale of common stock issuable upon conversion of such shares of common stock under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. See the section titled "Description of Capital Stock-Registration Rights" for additional information.

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following discussion is a summary of the material U.S. federal income tax consequences to non-U.S. holders (as defined below) of the purchase, ownership and disposition of the shares of common stock issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local or foreign tax laws are not discussed. This discussion is based on the Internal Revenue Code of 1986, as amended, or the Code, Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service, or IRS, in effect as of the date of this offering. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a non-U.S. holder of our common stock. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position regarding the tax consequences of the purchase, ownership and disposition of our common stock.

This discussion is limited to non-U.S. holders that hold our common stock as a "capital asset" within the meaning of Section 1221 of the Code (property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a non-U.S. holder's particular circumstances, including the impact of the alternative minimum tax or the unearned income Medicare contribution tax. In addition, it does not address consequences relevant to holders subject to particular rules, including, without limitation:

- U.S. expatriates and certain former citizens or long-term residents of the United States;
- persons holding our common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- regulated investment companies or real estate investment trusts;
- brokers, dealers or traders in securities or currencies;
- controlled foreign corporations, "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);
- tax-exempt organizations or governmental organizations;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons for whom our common stock constitutes "qualified small business stock" within the meaning of Section 1202 of the Code or as "Section 1244 stock" for purposes of Section 1244 of the Code;
- persons subject to special tax accounting rules as a result of any item of gross income with respect to our common stock being taken into account in an "applicable financial statement" (as defined in the Code);
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation; and
- tax-qualified retirement plans.

If a partnership (or other entity treated as a partnership for U.S. federal income tax purposes) holds our common stock, the tax treatment of a partner in the partnership will depend on the status of

the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

THIS DISCUSSION IS FOR INFORMATION PURPOSES ONLY AND IS NOT INTENDED AS LEGAL OR TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

Definition of a Non-U.S. Holder

For purposes of this discussion, a "non-U.S. holder" is any beneficial owner of our common stock that is not a "U.S. person," a partnership or an entity disregarded as separate from its owner, each for United States federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is:

- an individual who is a citizen or resident of the United States;
- a corporation (or other entity treated as a corporation for U.S. federal income tax purposes) created or organized under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. court and the control of one or more United States persons (within the meaning of Section 7701(a)(30) of the Code), or (2) has made a valid election under applicable Treasury Regulations to continue to be treated as a United States person.

Distributions

As described in the section entitled "Dividend Policy," we do not anticipate declaring or paying dividends to holders of our common stock in the foreseeable future. However, if we do make distributions on our common stock, such distributions of cash or property on our common stock will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a non-U.S. holder's adjusted tax basis in its common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below in the section relating to the sale or disposition of our common stock. Because we may not know the extent to which a distribution is a dividend for U.S. federal income tax purposes at the time it is made, for purposes of the withholding rules discussed below we or the applicable withholding agent may treat the entire distribution as a dividend.

Subject to the discussion below on backup withholding and foreign accounts, dividends paid to a non-U.S. holder of our common stock that are not effectively connected with the non-U.S. holder's conduct of a trade or business within the United States will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty).

Non-U.S. holders will be entitled to a reduction in or an exemption from withholding on dividends as a result of either (a) an applicable income tax treaty or (b) the non-U.S. holder holding our

common stock in connection with the conduct of a trade or business within the United States and dividends being effectively connected with that trade or business. To claim such a reduction in or exemption from withholding, the non-U.S. holder must provide the applicable withholding agent with a properly executed (a) IRS Form W-8BEN or W-8BEN-E (or other applicable documentation) claiming an exemption from or reduction of the withholding tax under the benefit of an income tax treaty between the United States and the country in which the non-U.S. holder resides or is established, or (b) IRS Form W-8ECI stating that the dividends are not subject to withholding tax because they are effectively connected with the conduct by the non-U.S. holder of a trade or business within the United States, as may be applicable. These certifications must be provided to the applicable withholding agent prior to the payment of dividends and must be updated periodically. Non-U.S. holders that do not timely provide the applicable withholding agent with the required certification, but that qualify for a reduced rate under an applicable income tax treaty, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS.

If dividends paid to a non-U.S. holder are effectively connected with the non-U.S. holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the United States to which such dividends are attributable), then, although exempt from U.S. federal withholding tax (provided the non-U.S. holder provides appropriate certification, as described above), the non-U.S. holder will be subject to U.S. federal income tax on such dividends on a net income basis at the regular graduated U.S. federal income tax rates. In addition, a non-U.S. holder that is a corporation may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on its effectively connected earnings and profits for the taxable year that are attributable to such dividends, as adjusted for certain items. Non-U.S. holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaty.

Sale or Other Disposition of Common Stock

Subject to the discussions below on backup withholding and foreign accounts, a non-U.S. holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the United States to which such gain is attributable);
- the non-U.S. holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition and certain other requirements are met; or
- our common stock constitutes U.S. real property interests, or USRPIs, by reason of our status as a U.S. real property holding corporation, or USRPHC, for U.S. federal income tax purposes.

Gain described in the first bullet point above will generally be subject to U.S. federal income tax on a net income basis at the regular graduated U.S. federal income tax rates. A non-U.S. holder that is a foreign corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

A non-U.S. holder described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on any gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder (even though the individual is not considered a resident of the United States) provided the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we are not currently and do not anticipate becoming a USRPHC. Because the determination of whether we are a USRPHC depends on the fair market value of our USRPIs relative to the fair market value of our other business assets and our non-U.S. real property interests, however, there can be no assurance we are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition by a non-U.S. holder of our common stock will not be subject to U.S. federal income tax if our common stock is "regularly traded," as defined by applicable Treasury Regulations, on an established securities market, and such non-U.S. holder owned, actually and constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other taxable disposition or the non-U.S. holder's holding period. If we are a USRPHC and either our common stock is not regularly traded on an established securities market or a non-U.S. holder holds more than 5% of our outstanding common stock, directly or indirectly, during the applicable testing period, such non-U.S. holder's gain on the disposition of shares of our common stock generally will be taxed in the same manner as gain that is effectively connected with the conduct of a U.S. trade or business, except that the branch profits tax generally will not apply. If we are a USRPHC and our common stock is not regularly traded on an established securities market, a non-U.S. holder's proceeds received on the disposition of shares will also generally be subject to withholding at a rate of 15%. Prospective investors are encouraged to consult their tax advisors regarding the possible consequences to them if we are, or were to become, a USRPHC.

Non-U.S. holders should consult their tax advisors regarding potentially applicable income tax treaties that may provide for different rules.

Information Reporting and Backup Withholding

Subject to the discussion below on foreign accounts, a non-U.S. holder will not be subject to backup withholding (currently at a rate of 24%) with respect to distributions on our common stock we make to the non-U.S. holder, provided the applicable withholding agent does not have actual knowledge or reason to know such holder is a United States person and the holder certifies its non-U.S. status, such as by providing a valid IRS Form W-8BEN, W-8BEN-E or W-8ECI, or other applicable certification. However, information returns generally will be filed with the IRS in connection with any distributions (including deemed distributions) made on our common stock to the non-U.S. holder, regardless of whether any tax was actually withheld. Copies of these information returns may also be made available under the provisions of a specific treaty or agreement to the tax authorities of the country in which the non-U.S. holder resides or is established.

Information reporting and backup withholding may apply to the proceeds of a sale or other taxable disposition of our common stock within the United States, and information reporting may (although backup withholding generally will not) apply to the proceeds of a sale or other taxable disposition of our common stock outside the United States conducted through certain U.S.-related financial intermediaries, in each case, unless the beneficial owner certifies under penalty of perjury that it is a non-U.S. holder on IRS Form W-8BEN or W-8BEN-E, or other applicable form (and the payor does not have actual knowledge or reason to know that the beneficial owner is a U.S. person) or such owner otherwise establishes an exemption. Proceeds of a disposition of our common stock conducted through a non-U.S. office of a non-U.S. broker generally will not be subject to backup withholding or information reporting.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a non-U.S. holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

Additional Withholding Tax on Payments Made to Foreign Accounts

Withholding taxes may be imposed under the Foreign Account Tax Compliance Act, or FATCA, on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends (including deemed dividends) paid on our common stock, or gross proceeds from the sale or other disposition of our common stock paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain "specified United States persons" or "United States-owned foreign entities" (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

Under the applicable Treasury Regulations and administrative guidance, withholding under FATCA generally applies to payments of dividends (including deemed dividends) paid on our common stock, and will apply to payments of gross proceeds from the sale or other disposition of common stock on or after January 1, 2019. Because we may not know the extent to which a distribution is a dividend for U.S. federal income tax purposes at the time it is made, for purposes of these withholding rules we or the applicable withholding agent may treat the entire distribution as a dividend. Prospective investors should consult their tax advisors regarding the potential application of these withholding provisions.

UNDERWRITING

ThinkEquity, a division of Fordham Financial Management, Inc. ("ThinkEquity"), is acting as representative of the underwriters of this offering. We have entered into an underwriting agreement dated , 2019, with the representative. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to each underwriter named below, and each underwriter named below has severally agreed to purchase from us, at the public offering price less the underwriting discounts set forth on the cover page of this prospectus, the number of common shares listed next to its name in the following table:

Underwriters	Number of Shares
ThinkEquity, a division of Fordham Financial Management, Inc.	
Total	

The underwriters are committed to purchase all shares offered by us other than those covered by the over-allotment option described below, if any are purchased. The obligations of the underwriters may be terminated upon the occurrence of certain events specified in the underwriting agreement. Furthermore, pursuant to the underwriting agreement, the underwriters' obligations are subject to customary conditions, representations and warranties contained in the underwriting agreement, such as receipt by the underwriters of officers' certificates and legal opinions.

The underwriters are offering the shares subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, and other conditions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

The underwriters propose to offer the shares offered by us to the public at the public offering price set forth on the cover of the prospectus. After the shares are released for sale to the public, the underwriters may change the offering price and other selling terms at various times

Over-Allotment Option

We have granted the underwriters an over-allotment option. This option, which is exercisable for up to 45 days after the date of this prospectus, permits the representative to purchase a maximum of additional shares of common stock (15% of the shares sold in this offering) from us to cover over-allotments, if any. If the representative exercises all or part of this option, it will purchase shares covered by the option at the public offering price per share that appears on the cover page of this prospectus, less the underwriting discount. If this option is exercised in full, the total offering price to the public will be $ and the total net proceeds, before expenses, to us will be $.

Discount

The following table shows the public offering price, underwriting discounts and proceeds, before expenses, to us. The information assumes either no exercise or full exercise by the underwriters of their over-allotment option.

	Per Share	Total Without Over-Allotment Option	Total With Over-Allotment Option
Public offering price	$	$	$
Underwriting discount(1)	$	$	$
Proceeds, before expense, to us	$	$	$

(1) We have agreed to pay the underwriters a commission of % of the gross proceeds of this offering.

We have agreed to pay a non-accountable expense allowance to the underwriters equal to 1.0% of the gross proceeds received in this offering (excluding proceeds received from exercise of the underwriters' over-allotment option).

We have paid an expense deposit of $35,000 to the representative for out-of-pocket-accountable expenses, which will be returned to us to the extent such out-of-pocket accountable expenses are not actually incurred in accordance with FINRA Rule 5110(f)(2)(C).

In addition, we have agreed to pay the following expenses of the underwriters relating to the offering: (a) all fees, expenses and disbursements relating to background checks of our officers and directors in an amount not to exceed $15,000 in the aggregate; (b) all filing fees and communication expenses associated with the review of this offering by FINRA; (c) all fees, expenses and disbursements relating to the registration or qualification of the shares under the "blue sky" securities laws in an amount not to exceed $5,000; (d) $29,500 for the underwriters' use of Ipreo's book-building, prospectus tracking and compliance software for this offering; (e) the underwriters' legal fees incurred in connection with this offering in an amount up to $125,000; (f) up to $20,000 of the Representatives' actual accountable road show expenses for the offering; (g) $10,000 for data services and communications expenses; and (h) up to $3,000 for the costs associated with bound volumes of the public offering materials as well as commemorative mementos and Lucite tombstones.

We estimate that the total expenses of the offering payable by us, excluding the total underwriting discount and non-accountable expense allowance, will be approximately $.

Representative's Warrants

We have agreed to issue to the representative warrants to purchase up to a total of shares of our common stock (5% of the aggregate number of shares of common stock sold in this offering, excluding shares of common stock sold upon exercise of underwriters' the over-allotment option) (the "Representative's Warrants"), for an aggregate purchase price of $100.00. The Representative's Warrants will be exercisable at a per share exercise price equal to 125% of the public offering price per share of the shares of common stock sold in this offering. The Representative's Warrants are exercisable at any time, from time to time, in whole or in part, during the four year period commencing one year from the effective date of the registration statement related to this offering.

The Representative's Warrants and the shares of common stock underlying the Representative's Warrants have been deemed compensation by FINRA and are, therefore, subject to a 180-day lock-up pursuant to FINRA Rule 5110(g)(1). The Representative or permitted assignees under such rule may not sell, transfer, assign, pledge, or hypothecate the Representative's Warrants or the securities underlying the Representative's Warrants, nor will the representative engage in any hedging, short sale, derivative, put, or call transaction that would result in the effective economic disposition of the Representative's Warrants or the underlying shares of common stock for a period of 180 days from the effective date of the registration statement. Additionally, the Representative's Warrants may not be sold, transferred, assigned, pledged, or hypothecated for a 180-day period following the effective date of the registration statement, except to any underwriter and selected dealer participating in the offering and their bona fide officers or partners. The Representative's Warrants provide for registration rights upon request, in certain cases. The demand registration right provided will not be greater than five years from the effective date of this registration statement in compliance with FINRA Rule 5110(f)(2)(G)(iv). The piggyback registration right provided will not be greater than seven years from the effective date of this registration statement in compliance with FINRA Rule 5110(f)(2)(G)(v). We will bear all fees and expenses attendant to registering the securities issuable on exercise of the warrants other than underwriting commissions incurred and payable by the holders. The exercise price and number of shares issuable upon exercise of the warrants may be adjusted in certain circumstances including in the event of a stock dividend or our recapitalization, reorganization, merger or

consolidation. However, the warrant exercise price or underlying shares will not be adjusted for issuances of shares of common stock at a price below the warrant exercise price.

Discretionary Accounts

The underwriters do not intend to confirm sales of the securities offered hereby to any accounts over which they have discretionary authority.

Lock-Up Agreement

Pursuant to certain "lock-up" agreements, we, our executive officers and directors and our stockholders, have agreed not to, without the prior written consent of the representative, offer, sell, assign, transfer, pledge, contract to sell, or otherwise dispose of or announce the intention to otherwise dispose of, or enter into any swap, hedge or similar agreement or arrangement that transfers, in whole or in part, the economic risk of ownership of, directly or indirectly, engage in any short selling of any common stock or securities convertible into or exchangeable or exercisable for any common stock, whether currently owned or subsequently acquired, for a period of 12 months, in the case of our officers and directors, and 180 days from the date of this prospectus, in the case of us and all other stockholders.

Right of First Refusal

Subject to certain limited exceptions, until 18 months after the closing of this initial public offering, ThinkEquity has a right of first refusal to act as sole investment banker, sole book-runner and/or sole placement agent, at ThinkEquity's sole discretion, for each and every future public and private equity and debt offering, including all equity-linked offerings, by us or any of our successors or subsidiaries during such 18-month period on terms customary to the representative.

Indemnification

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make for these liabilities.

Electronic Offer, Sale and Distribution of Shares

A prospectus in electronic format may be made available on the websites maintained by one or more underwriters or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representative may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters and selling group members that will make internet distributions on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' websites is not part of, nor incorporated by reference into, this prospectus or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

Stabilization

In connection with this offering, the underwriters may engage in stabilizing transactions, over-allotment transactions, syndicate-covering transactions, penalty bids and purchases to cover positions created by short sales.

Stabilizing transactions permit bids to purchase securities so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the securities while the offering is in progress.

Over-allotment transactions involve sales by the underwriters of securities in excess of the number of securities that underwriters are obligated to purchase. This creates a syndicate short position which may be either a covered short position or a naked short position. In a covered short position, the number of securities over-allotted by the underwriters is not greater than the number of securities that they may purchase in the over-allotment option. In a naked short position, the number of securities involved is greater than the number of securities in the over-allotment option. The underwriters may close out any short position by exercising their over-allotment option and/or purchasing securities in the open market.

Syndicate covering transactions involve purchases of securities in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of securities to close out the short position, the underwriters will consider, among other things, the price of securities available for purchase in the open market as compared with the price at which they may purchase securities through exercise of the over-allotment option. If the underwriters sell more securities than could be covered by exercise of the over-allotment option and, therefore, have a naked short position, the position can be closed out only by buying securities in the open market. A naked short position is more likely to be created if the underwriters are concerned that after pricing there could be downward pressure on the price of the securities in the open market that could adversely affect investors who purchase in the offering.

Penalty bids permit the representative to reclaim a selling concession from a syndicate member when the securities originally sold by that syndicate member are purchased in stabilizing or syndicate covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our securities or preventing or retarding a decline in the market price of our securities. As a result, the price of our securities in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of our securities. These transactions may be effected on The Nasdaq Capital Market, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

Passive Market Making

In connection with this offering, underwriters and selling group members may engage in passive market making transactions in our common stock on The Nasdaq Capital Market or on the OTCQB in accordance with Rule 103 of Regulation M under the Exchange Act, during a period before the commencement of offers or sales of the securities and extending through the completion of the distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, then that bid must then be lowered when specified purchase limits are exceeded.

Other Relationships

Certain of the underwriters and their affiliates may provide in the future, various advisory, investment and commercial banking and other services to us in the ordinary course of business, for which they may receive customary fees and commissions. However, we have not yet had, and have no present arrangements with any of the underwriters for any further services.

Pricing of the Offering

Prior to this offering, there has been no established public market for our common stock. The initial public offering price will be determined by negotiations among us and the representative of the underwriters. In addition to prevailing market conditions, among the factors to be considered in determining the initial public offering price of our common stock will be:

- the information included in this prospectus and otherwise available to the representative;
- our historical performance;
- estimates of our business potential and our earnings prospects;
- an assessment of our management;
- and the consideration of the above factors in relation to market valuation of companies in related businesses.

The estimated initial public offering price range set forth on the cover page of this prospectus is subject to change as a result of market conditions and other factors. An active trading market for the shares of our common stock may not develop. It is also possible that the shares will not trade in the public market at or above the initial public offering price following the closing of this offering.

We intend to apply to have our common stock approved for listing on The Nasdaq Capital Market under the trading symbol "ANVS."

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Duane Morris LLP. Certain legal matters will be passed upon for the underwriters by Venable LLP.

EXPERTS

The financial statements of Annovis Bio, Inc. as of December 31, 2018 and 2017, and for the years then ended have been included herein and in this prospectus in reliance upon the report of Withum Smith+Brown, PC, independent registered public accounting firm, appearing elsewhere in the registration statement, upon the authority of said firm as experts in accounting and auditing.

No expert named in the registration statement of which this prospectus forms a part as having prepared or certified any part thereof (or named as having prepared or certified a report or valuation for use in connection with such registration statement) or counsel named in this prospectus as having given an opinion upon the validity of the securities being offered pursuant to this prospectus or upon other legal matters in connection with the registration or offering of such securities was employed for such purpose on a contingency basis. At the time of such preparation, certification or opinion or at any time thereafter, through the date of effectiveness of such registration statement or that part of such registration statement to which such preparation, certification or opinion relates, no such person had, or is to receive, in connection with the offering, a substantial interest, direct or indirect, in our Company or any of its parents or subsidiaries. Nor was any such person connected with our Company or any of its parents or subsidiaries as a promoter, managing or principal underwriter, voting trustee, director, officer or employee.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the Securities and Exchange Commission a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information about us and the common stock offered hereby, we refer you to the registration statement and the exhibits and schedules filed thereto. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. Upon completion of this offering, we will be required to file periodic reports, proxy statements, and other information with the Securities and Exchange Commission pursuant to the Securities Exchange Act of 1934. Securities and Exchange Commission also maintains an Internet website that contains reports, proxy statements and other information about registrants, like us, that file electronically with the Securities and Exchange Commission. The address of that site is *www.sec.gov* .

ANNOVIS BIO, INC.

Table of Contents

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders of Annovis Bio, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Annovis Bio, Inc. (the "Company"), as of December 31, 2018 and 2017, and the related statements of operations, statements of redeemable convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the two years in the period ended December 31, 2018 and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2018, in conformity with accounting principles generally accepted in the United States of America.

Restatement of Previously Issued Financial Statements

As discussed in Note 12 to the financial statements, the Company has restated its 2018 and 2017 financial statements for an error in expense classifications in the statements of operations and other disclosures.

Substantial Doubt Regarding Going Concern

The accompanying financial statements have been prepared assuming that the entity will continue as a going concern. As discussed in Note 1 to the financial statements, the entity has suffered recurring losses from operations, has experienced cash used from operations in excess of its current cash position, and has an accumulated deficit, that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty. Our opinion is not modified with respect to this matter.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

WithumSmith+Brown, PC

We have served as the Company's auditor since 2019.

East Brunswick, New Jersey
May 15, 2019, except for the effects on the financial statements of the restatement described in Note 12, as to which the date is July 2, 2019.

ANNOVIS BIO INC.

Balance Sheets

December 31, 2018 and 2017

	2018	2017
Assets		
Current assets:		
Cash and cash equivalents	$ 35,312	$ 347,472
Prepaid expenses and other current assets	15,680	10,491
Total current assets	50,992	357,963
Total assets	$ 50,992	$ 357,963
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 68,425	$ 71,107
Accrued expenses	499,518	419,113
Total current liabilities	567,943	490,220
Total liabilities	567,943	490,220
Redeemable convertible preferred stock—$0.0001 par value		
Series A, –5,133,159 shares authorized, issued and outstanding at December 31, 2018 and 2017	6,509,303	6,509,303
Series A-1, –1,111,111 shares authorized at December 31, 2018 and 2017, and 630,722 and 360,000 shares issued and outstanding at December 31, 2018 and 2017, respectively	567,649	324,000
Stockholders' equity (deficit):		
Common stock—$0.0001 par value, 10,150,000 shares authorized at December 31, 2018 and 2017, and 395,653 and 375,653 shares outstanding at December 31, 2018 and 2017, respectively	40	38
Additional paid-in capital	192,105	106,579
Accumulated deficit	(7,786,048)	(7,072,177)
Total stockholders' equity (deficit)	(7,593,903)	(6,965,560)
Total liabilities and stockholders' equity (deficit)	$ 50,992	$ 357,963

See accompanying notes to financial statements.

ANNOVIS BIO INC.

Statements of Operations

Years ended December 31, 2018 and 2017

	2018 (As Restated)	2017 (As Restated)
Operating expenses:		
Research and development	$ 111,608	$ 273,370
General and administrative	602,329	409,063
Total operating expenses	713,937	682,433
Operating loss	(713,937)	(682,433)
Other income (expense):		
Interest income, net	66	84
Total other income (expense)	66	84
Loss before income taxes	(713,871)	(682,349)
Income tax expense (benefit)	—	—
Net loss	$ (713,871)	$ (682,349)
Basic and Diluted loss per common share	$ (1.84)	$ (1.90)
Weighted average number of comon shares outstanding, basic and diluted	388,612	358,599

See accompanying notes to financial statements.

ANNOVIS BIO INC.
Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)
Years ended December 31, 2018 and 2017

	Redeemable Convertible Preferred Stock				Stockholders' Equity (Deficit)				
	Series A		Series A-1		Common Stock		Additional Paid-In Capital	Accumulated deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount			
Balance, December 31, 2016	5,133,159	$ 6,509,303	—	$ —	305,474	$ 31	$ 49,596	$ (6,389,828)	$ (6,340,201)
Proceeds from the issuance of preferred shares	—	—	360,000	324,000	—	—	—	—	—
Proceeds from the issuance of common shares	—	—	—	—	70,179	7	8,488	—	8,495
Share-based compensation expense	—	—	—	—	—	—	48,495	—	48,495
Net loss	—	—	—	—	—	—	—	(682,349)	(682,349)
Balance, December 31, 2017	5,133,159	6,509,303	360,000	324,000	375,653	38	106,579	(7,072,177)	(6,965,560)
Proceeds from the issuance of preferred shares	—	—	270,722	243,649	—	—	—	—	—
Proceeds from the issuance of comon shares	—	—	—	—	20,000	2	2,798	—	2,800
Share-based compensation expense	—	—	—	—	—	—	82,728	—	82,728
Net loss	—	—	—	—	—	—	—	(713,871)	(713,871)
Balance, December 31, 2018	5,133,159	$ 6,509,303	630,722	$ 567,649	395,653	$ 40	$ 192,105	$ (7,786,048)	$ (7,593,903)

See accompanying notes to financial statements.

ANNOVIS BIO INC.

Statements of Cash Flow

Years ended December 31, 2018 and 2017

	2018	2017
Cash flows from operating activities:		
Net loss	$ (713,871)	$ (682,349)
Adjustments to reconcile net loss to net cash used in operating activities:		
Share-based compensation expense	82,728	48,495
Changes in assets and liabilities:		
Prepaid expenses and other current assets	(5,189)	(2,368)
Accounts payable and accrued expenses	(2,682)	61,827
Accrued expenses	80,405	36,914
Net cash used in operating activities	(558,609)	(537,481)
Cash flows from financing activities:		
Proceeds from issuance of common shares	2,800	8,495
Proceeds from issurance of preferred shares	243,649	324,000
Net cash provided by financing activities	246,449	332,495
Net decrease in cash	(312,160)	(204,986)
Cash and cash equivalents, beginning of year	347,472	552,458
Cash and cash equivalents, end of year	$ 35,312	$ 347,472

See accompanying notes to financial statements.

Annovis Bio, Inc.

Notes to Financial Statements

December 31, 2018 and 2017

(1) Nature of Business and Liquidity

Annovis Bio, Inc. (the "Company" or "Annovis") was incorporated on April 29, 2008, under the laws of the State of Delaware as QR Pharma, Inc. On March 21, 2019, the Board of Directors of the Company (the "Board") approved the name change to Annovis Bio, Inc. Annovis is a clinical stage pharmaceutical company focused on developing and commercializing innovative drugs for the treatment of Parkinson's ("PD") and Alzheimer's ("AD") diseases and other neurodegenerative diseases. The Company's lead compound, ANVS-401, is a small molecule administered orally that attacks neurodegeneration by entering the brain and inhibiting the translation of neurotoxic proteins thereby improving and normalizing axonal vesicle transport.

Since its founding, the Company has been engaged in organizational activities, including raising capital, and research and development activities. The Company has not generated substantial revenues and has not yet achieved profitable operations, nor has it ever generated positive cash flows from operations. There is no assurance that profitable operations, if achieved, could be sustained on a continuing basis. The Company is subject to those risks associated with any clinical stage pharmaceutical company that has substantial expenditures for research and development. There can be no assurance that the Company's research and development projects will be successful, that products developed will obtain necessary regulatory approval, or that any approved product will be commercially viable. In addition, the Company operates in an environment of rapid technological change and is largely dependent on the services of its employees and consultants. Further, the Company's future operations are dependent on the success of the Company's efforts to raise additional capital.

These uncertainties raise substantial doubt about the Company's ability to continue as a going concern for 12 months after the issuance date of these financial statements. The accompanying financial statements have been prepared on a going-concern basis which contemplates the continuation of operations, realization of assets and liquidation of liabilities in the ordinary course of business. The Company incurred a net loss of $713,871 and $682,349 for the years ended December 31, 2018 and 2017, respectively, and had an accumulated deficit of $7,786,048 as of December 31, 2018. The Company anticipates incurring additional losses until such time, if ever, that it can generate significant revenue from its product candidates currently in development. The Company's primary source of capital has been the issuance of equity securities.

In January 2019, the Company received proceeds of $530,000 from the issuance of Convertible Promissory Notes (See Note 13—Subsequent Events). Management believes that current cash and cash equivalents are sufficient to fund operations and capital requirements for the first half of 2019. Additional financings will be needed by the Company to fund its operations, to complete clinical development of and to commercially develop its product candidates. There is no assurance that such financing will be available when needed or on acceptable terms.

(2) Summary of Significant Accounting Policies

(a) Basis of Presentation

The accompanying financial statements have been prepared in conformity with U.S. generally accepted accounting principles (U.S. GAAP). Any reference in these notes to applicable guidance is meant to refer to U.S. GAAP as found in the Accounting Standards Codification (ASC) and Accounting Standards Update (ASU) of the Financial Accounting Standards Board (FASB).

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(2) Summary of Significant Accounting Policies (Continued)

(b) Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, including disclosure of contingent assets and liabilities, at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting period. Due to the uncertainty of factors surrounding the estimates or judgments used in the preparation of the financial statements, actual results may materially vary from these estimates.

Significant items subject to such estimates and assumptions include the valuation of equity-based compensation, and contingent liabilities. Future events and their effects cannot be predicted with certainty; accordingly, accounting estimates require the exercise of judgment. Accounting estimates used in the preparation of these financial statements change as new events occur, as more experience is acquired, as additional information is obtained and as the operating environment changes.

(c) Basic and Diluted Earnings (Loss) per Share

Basic net loss per share is determined using the weighted average number of shares of common stock outstanding during each period. Diluted net income per share includes the effect, if any, from the potential exercise or conversion of securities, such as redeemable convertible preferred stock and stock options, which would result in the issuance of incremental shares of common stock. The computation of diluted net loss per shares does not include the conversion of securities that would have an anti-dilutive effect. The basic and dilutive computations of net loss per share for the Company are the same because the dilutive effects of the Company's convertible securities would be anti-dilutive.

(d) Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less to be cash equivalents. At times, the Company's cash balances may exceed the current insured amounts under the Federal Deposit Insurance Corporation (FDIC). There were no accounts that exceeded federally insured limits at December 31, 2018. Total cash was $347,472 as of December 31, 2017, which exceeded the FDIC coverage limit of $250,000 by $97,472.

(e) Fair Value of Financial Instruments

The carrying amounts of the Company's financial instruments, including cash and accounts payable approximate fair value due to the short-term nature of those instruments.

(f) Research and Development

Research and development costs are expensed as incurred and are primarily comprised of external research and development expenses incurred under arrangements with third parties, such as contract research organizations ("CROs") and consultants. At the end of each reporting period, the Company compares the payments made to each service provider to the estimated progress towards completion of the related project. Factors that the Company considers in preparing these estimates include the number of patients enrolled in studies, milestones achieved, and other criteria related to the efforts of its vendors. These estimates will be subject to change as additional information becomes available.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(2) Summary of Significant Accounting Policies (Continued)

Depending on the timing of payments to vendors and estimated services provided, the Company will record net prepaid or accrued expenses related to these costs. As of December 31, 2018 and 2017, the Company had no outstanding payables to CROs.

(g) Share-Based Compensation

Share-based compensation cost is measured at the grant date based on the fair value of the award and is recognized as expense over the requisite service period, which is generally the vesting period. The Company early adopted ASU 2018-07 on January 1, 2017 which permits the valuation of stock-based awards granted to non-employees to be measured at fair value at the grant date rather than on an accelerated attribution basis over the vesting period.

Determining the appropriate fair value of share-based awards requires the use of subjective assumptions, including the fair value of the Company's common shares, and for options, the expected life of the option and expected share price volatility. The Company uses the Black-Scholes option pricing model to value its option awards. The assumptions used in calculating the fair value of share-based awards represent management's best estimates and involve inherent uncertainties and the application of management's judgment. As a result, if factors change and management uses different assumptions, share-based compensation expense could be materially different for future awards.

The expected life of options was estimated using the simplified method, as the Company has limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment.

(h) Income Taxes

The Company provides for income taxes using the asset and liability approach. Deferred tax assets and liabilities are recorded based on the differences between the financial statement and tax bases of assets and liabilities and the tax rates in effect when these differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance if, based on the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. As of December 31, 2018 and 2017, the Company had a full valuation allowance against deferred tax assets.

The Company is subject to the provisions of ASC 740-10-25, Income Taxes (ASC 740). ASC 740 prescribes a more likely-than-not threshold for the financial statement recognition of uncertain tax positions. ASC 740 clarifies the accounting for income taxes by prescribing a minimum recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. There are currently no open Federal or State tax audits. The Company has not recorded any liability for uncertain tax positions at December 31, 2018 or December 31, 2017.

The Tax Cuts and Jobs Act (the "Tax Act"), enacted on December 22, 2017, among other things, permanently lowered the statutory federal corporate tax rate from 35% to 21%, effective for tax years including or beginning January 1, 2018. Although in the normal course of business the Company is required to make estimates and assumptions for certain tax items which cannot be fully determined at period end, the Company did not identify items for which the income tax effects of the Tax Act have

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(2) Summary of Significant Accounting Policies (Continued)

not been completed as of December 31, 2017 and, therefore, considers its accounting for the tax effects of the Tax Act on its deferred tax assets and liabilities to be complete as of December 31, 2017.

(i) Recent Accounting Pronouncements

In February 2016, the FASB issued its final standard on lease accounting, ASU No. 2016-02, "Leases (Topic 842)," which superseded Topic 840, "Leases," which was further modified in ASU No. 2018-10, "Codification Improvements to Topic 842, Leases," ASU No. 2018-11, "Leases (Topic 842) Targeted Improvements" and ASU No. 2019-01 "Leases (Topic 842) Codification Improvements" to clarify the implementation guidance. The new pronouncement requires the recognition on the balance sheet of right-of-use assets and lease liabilities for all long-term leases, including operating leases, on the balance sheet. The pronouncement requires that lease arrangements longer than 12 months result in an entity classifying leases as finance or operating leases. However, unlike current U.S. GAAP, which requires only capital leases to be recognized on the balance sheet, ASU 2016-02 will require both types of leases to be recognized on the balance sheet. ASU 2016-02 also requires disclosures about the amount, timing, and uncertainty of cash flows arising from leases. These disclosures include qualitative and quantitative requirements, providing additional information about the amounts recorded in the financial statements.

The pronouncement is effective for all public business entities for interim and annual periods beginning after December 15, 2018 and for non-public business entities with annual periods beginning after December 15, 2019 with early adoption permitted. In July 2018, the FASB issued ASU No. 2018-11, which provides targeted improvements to the new lease standard, including an option to apply the transition provisions at its adoption date instead of at the earliest comparative period presented in its financial statements. The Company adopted the new leasing standards using a modified retrospective transition approach to be applied to leases existing as of or entered into after January 1, 2019. The adoption of this guidance did not have a material impact on the Company's financial statements.

In May 2014, the FASB issued ASU 2014-09, Revenue from Contracts with Customers (Topic 606), requiring an entity to recognize the amount of revenue to which it expects to be entitled for the transfer of promised goods or services to customers. ASU 2014-09 supersedes nearly all existing revenue recognition guidance under U.S. GAAP and requires revenue to be recognized when promised goods or services are transferred to customers in an amount that reflects the consideration that is expected to be received for those goods or services. Additionally, qualitative and quantitative disclosures are required about customer contracts, significant judgments and changes in judgments, and assets recognized from the costs to obtain or fulfill a contract.

The FASB also issued the following amendments to ASU No. 2014-09 to provide clarification on the guidance:

- ASU No. 2015-14, Revenue from Contracts with Customers (Topic 606)—Deferral of the Effective Date
- ASU No. 2016-08, Revenue from Contracts with Customers (Topic 606)—Principal versus Agent (Reporting Revenue Gross vs. Net)

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(2) Summary of Significant Accounting Policies (Continued)

- ASU No. 2016-10, Revenue from Contracts with Customers (Topic 606)—Identifying Performance Obligations and Licensing
- ASU No. 2016-12, Revenue from Contracts with Customers (Topic 606)—Narrow-Scope Improvements and Practical Expedients

The Company has elected to early adopt ASU 2014-09 effective January 1, 2017. The standard did not have an impact on the Company's financial statements.

In August 2016, the FASB issued ASU 2016-15, Classification of Certain Cash Receipts and Cash Payments, which provides specific guidance related to eight cash flow classification issues. The pronouncement is effective for interim and annual periods beginning after December 15, 2018, and interim periods within fiscal years beginning after December 15, 2019. The Company elected to early adopt the new pronouncement in the first quarter of 2019. Such early adoption of ASU 2016-15 in the first quarter of 2019 will not have an impact on the Company's financial statements.

In November 2016, the FASB issued ASU 2016-18, Restricted Cash, which requires changes in restricted cash and restricted cash equivalents to be explained on the statement of cash flows by including restricted cash and restricted cash equivalents in the beginning-of-period and end-of-period total cash and cash equivalents shown on the statement of cash flows. The pronouncement is effective for interim and annual periods beginning after December 15, 2018, and interim periods within fiscal years beginning after December 15, 2019. Early adoption is permitted, including adoption in an interim period. If an entity early adopts the amendments in an interim period, any adjustments should be reflected as of the beginning of the fiscal year that includes that interim period. The Company elected to early adopt ASU 2016-18. The early adoption of ASU 2016-18 in the first quarter of 2019 will not have an impact on the Company's financial statements.

In March 2018, the FASB issued ASU 2018-5—Income Taxes (Topic 740): Amendments to SEC Paragraphs pursuant to SEC Staff Accounting Bulletin No. 118. This ASU provided guidance related to Securities and Exchange Commission ("SEC") Staff Accounting Bulletin No. 118 ("SAB 118"), which addresses the accounting implications of the Tax Act. SAB 118 allows a company to record provisional amounts during a measurement period not to extend beyond one year of the enactment date and was effective upon issuance. The Company has analyzed the Tax Act, and in certain areas, has made reasonable estimates of the effects on its financial statements and tax disclosures.

In June 2018, the FASB issued ASU 2018-07, Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting. The new guidance expands the scope of Topic 718 to include share-based payments granted to nonemployees in exchange for goods or services used or consumed in an entity's own operations, and supersedes the guidance in ASC 505-50, Equity-Based Payments to Non-Employees. The most significant change resulting from this update is that stock-based awards granted to non-employees will no longer need to be re-measured at fair value at each financial reporting date until performance is complete, as these awards will be measured at fair value at the grant date. The guidance is effective January 1, 2019 with early adoption permitted, including in an interim period for which financial statements have not been issued. The Company has elected to apply the provisions of this ASU in the Company's financial statements effective January 1, 2017.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(2) Summary of Significant Accounting Policies (Continued)

In August 2018, the FASB issued ASU No. 2018-13, Fair Value Measurement (Topic 820)—Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement. The new guidance improves and clarifies the fair value measurement disclosure requirement of ASC 820. The new disclosure requirements include the changes in unrealized gains or losses included in other comprehensive income for recurring Level 3 fair value measurement held at the end of reporting period and the explicit requirement to disclose the range and weighted average used to develop significant unobservable inputs for Level 3 fair value measurements. The other provisions of ASU 2018-13 also include eliminated and modified disclosure requirements. The guidance is effective for fiscal years beginning after December 15, 2019 with early adoption permitted, including in an interim period for which financial statements have not been issued or made available for issuance. The Company has evaluated the impact of adoption of this ASU and determined that it will not have a significant impact on its financial statements.

(3) Fair Value Measurements

The Company measures certain assets and liabilities at fair value in accordance with Accounting Standards Codification ("ASC") 820, Fair Value Measurements and Disclosures. ASC 820 defines fair value as the price that would be received to sell an asset or paid to transfer a liability (the exit price) in an orderly transaction between market participants at the measurement date. The guidance in ASC 820 outlines a valuation framework and creates a fair value hierarchy that serves to increase the consistency and comparability of fair value measurements and the related disclosures. In determining fair value, the Company maximizes the use of quoted prices and observable inputs. Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from independent sources. The fair value hierarchy is broken down into three levels based on the source of inputs as follows:

Level 1—Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities.

Level 2—Valuations based on observable inputs and quoted prices in active markets for similar assets and liabilities.

Level 3—Valuations based on unobservable inputs and models that are supported by little or no market activity.

The Company's financial assets which are measured at fair value on a recurring basis were comprised of cash and cash equivalents of $35,312 and $347,472 at December 31, 2018 and 2017, respectively, based on Level 1 inputs.

(4) Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following:

	December 31, 2018	December 31, 2017
Prepaid rent	$ 1,904	$ 1,795
Prepaid research and development	4,976	4,896
Prepaid expenses	5,000	—
Security deposit	3,800	3,800
Total prepaid expenses and other current assets	$ 15,680	$ 10,491

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(5) Accrued Expenses

Accrued expenses consisted of the following:

	December 31,	
	2018	2017
Payroll and related benefits	$ 21,640	$ 3,765
Accrued professional fees	17,878	1,348
Accrued license payments	460,000	414,000
	$ 499,518	$ 419,113

See Note 6—Commitments for further detail on the accrued license payments.

(6) Commitments

(a) Leases

The Company leases its office facilities under a month-to-month operating lease. Total rental expense was $22,372 and $21,723 for the years ended December 31, 2018 and 2017, respectively.

(b) License Agreements

In November 2008, the Company licensed the rights to certain chemical compounds, know-how and intellectual property rights that may be suitable for the development of human therapeutics. Currently, the intellectual property rights are owned by a subsidiary of Horizon Therapeutics, PLC ("Licensor"). Payments by the Company under the license agreement include a one-time non-refundable fee of $50,000, a minimum annual commitment of $40,000 commencing in 2009, milestone payments upon attainment of certain milestone events, royalties based on net sales of products covered by the patent-related rights and a portion of any sublicense income received by the Company. The Company is responsible for the development and commercialization of the licensed products.

In May 2012, such license agreement was amended. The minimum annual commitment was increased to $46,000 and may be deferred by the Company until the Company raises at least $2 million in equity financing, then the aggregate annual payments of all amounts will become payable.

At December 31, 2018, the Company had accrued $460,000 in license payments under the term of this license, included in accrued liabilities, of which no amounts have been paid to date.

In further consideration for the licenses granted, the Company shall make the following milestone payments to Licensor based upon the attainment of each milestone event indicated below.

Milestone Event	Amount
Commencement of Phase II	$ 230,000
Commencement of Phase III	$ 575,000
Filing of an NDA for Regulatory Approval (or equivalent in Europe or Japan	$ 1,150,000
Receipt of Regulatory Approval in the United States	$ 5,750,000
Receipt of Regulatory Approval outside United States	$ 5,750,000

No milestones have been achieved as of December 31, 2018.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(6) Commitments (Continued)

Royalties shall be paid to Licensor assessed on net sales of licensed products on a country-by-country basis in an amount equal to 5.75%. Should the Company be required to obtain a license from a third party in order to sell a licensed product, the Company may deduct 50% of the royalties on such licensed product paid to the third party subject to certain minimums.

In addition to the royalties the Company shall pay licensor 9.2% of all sublicense income attributable to licensed products.

The Licensor also granted the Company a buy-out option which may be exercised at any time during the term of the agreement. The option price will be as follows: $500,000 if exercised prior to the commencement of the first Phase II clinical trial; $1,000,000 if exercised on or after the commencement of the first Phase II clinical trial and prior to the commencement of the first Phase III clinical trial; $5,000,000 if exercised on or after the commencement of the first Phase III clinical trial and prior to the filing of a New Drug Application ("NDA") with the FDA for the first licensed product; and $8,000,000 if exercised on or after the filing of an NDA for the first licensed product.

The Company has the right to terminate the agreement at any time by giving 90 days advance notice subject to the payment of any amounts due under the agreement at that time. If the Company does not terminate the agreement or exercise the buy-out option, the term of the agreement shall continue until the expiration of the Company's obligation to make royalty payments. Such royalty payments continue for each product in each country until the later of the expiration of the related patent or 10 years after the initial sale of the product in the respective country. The agreement may also be terminated for cause by either party upon the breach of the material obligations of the other party or the bankruptcy or liquidation of the other party.

(c) Employment Agreements

The Company has entered into an amended and restated employment agreement with the President and Chief Executive Officer (the "CEO") of the Company, effective May 10, 2019. The term of the agreement will continue in effect until notice is provided 10 business days prior to the termination by either party. Upon termination of the agreement by the Company for any reason other than for cause, death or disability or by the CEO for good reason, the Company shall pay the CEO's base salary, currently $120,000, for a period of one year.

(d) Litigation

The Company is subject, from time to time, to claims by third parties under various legal disputes. The defense of such claims, or any adverse outcome relating to any such claims, could have a material adverse effect on the Company's liquidity, financial condition and cash flows. At December 31, 2018 and December 31, 2017, the Company did not have any pending legal actions.

(7) Redeemable Convertible Preferred Stock and Stockholders' Equity

a) Overview:

The Company's Certificate of Incorporation, originally filed on April 29, 2008, was most recently amended by the Amended and Restated Certificate of Incorporation filed on December 14, 2017, which authorized the issuance of two classes of stock to be designated, respectively, "Common Stock"

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(7) Redeemable Convertible Preferred Stock and Stockholders' Equity (Continued)

and "Preferred Stock". The total number of shares which the Company is authorized to issue is 16,394,270, each with a par value of $0.0001 per share. Of these shares, 10,150,000 shall be Common Stock and 6,244,270 shall be Preferred Stock.

Pursuant to the Series A Stock Purchase Agreement as of December 19, 2014 ("Series A Purchase Agreement"), the Company was permitted to issue 1,000,000 shares of the Company's Series A Convertible Preferred Stock ("Series A"), par value $0.0001 per share, and was permitted to issue an additional 1,000,000 shares of Series A at additional closings at a price per share of $0.50. In addition, at the initial closing all of the outstanding convertible promissory notes of the Company were converted into 1,400,000 shares of Series A. The conversion of the promissory notes was treated as a capital transaction and the excess of the carrying value of the promissory notes over the issuance price of the Series A was reflected in the carrying value of the Series A. The Series A Purchase Agreement was amended on February 16, 2015 to increase the additional share amount to 2,000,000. Pursuant to the Series A Purchase Agreement, as amended, 1,000,000 shares of Series A were issued on December 19, 2014 and 1,134,718 shares were issued and sold at additional closings held on March 15, 2015 and May 22, 2015.

On September 16, 2016 the Company entered into a second amendment to the Series A Purchase Agreement to permit the Company to issue and sell up to 1,400,000 additional Series A shares and extend the date for additional closings to October 31, 2016. On October 11, 2016, the Company entered into a third amendment to the Series A Purchase Agreement to increase the additional shares that could be sold through October 31, 2016 to 1,600,000, thus increasing the total shares available for sale under the Series A Purchase Agreement, as amended, to 2,734,718. During October 2016, 1,598,441 additional shares were issued resulting in a total of 5,133,159 Series A shares issued and outstanding as of the years ended December 31, 2018 and 2017.

Pursuant to the Series A-1 Stock Purchase Agreement dated as of December 15, 2017 ("Series A-1 Purchase Agreement") the Company sold and issued 360,000 shares of the Company's Series A-1 Convertible Preferred Stock ("Series A-1"), par value $0.0001 per share, and was permitted to issue an additional 751,111 shares of Series A-1 at additional closings at a price per share of $0.90. At an additional closing in March, 2018, 270,722 additional shares were sold and issued by the Company. 630,722 and 360,000 Series A-1 shares were issued and outstanding as of December 31, 2018 and 2017, respectively.

b) Common Stock:

a. Dividends:

Subject to the rights of holders of Preferred Stock, the holders of the Common Stock are entitled to receive dividends as declared from time to time by the Board.

b. Liquidation:

Subject to the rights of holders of Preferred Stock as to liquidation, upon the liquidation, dissolution or winding up of the Corporation, the remaining assets of the Corporation will be distributed to the holders of Common Stock.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(7) Redeemable Convertible Preferred Stock and Stockholders' Equity (Continued)

c. Voting:

The holders of the Common Stock are entitled to one vote for each share of Common Stock held but shall not be entitled to vote on any amendment to the Certificate of Incorporation that relates solely to the terms of one or more outstanding series of Preferred Stock. There is no cumulative voting.

c) Redeemable Convertible Preferred stock:

The authorized Preferred stock is designated as Series A Preferred (5,133,159 shares) and Series A-1 Preferred (1,111,111 shares). The Series A-1 Preferred stock shall rank equal with the Series A Preferred Stock and each shall rank senior to the Common Stock in regard to payment of dividends, distributions of assets upon a liquidation or Liquidity Event.

a. Dividends:

The holders of the Series A and Series A-1 Preferred Stock (known collectively as the "Preferred Stock") are entitled to receive dividends, when and as declared by the Board.

b. Liquidation:

The holders of the Preferred Stock shall be entitled to receive, prior and in preference to any distribution of any assets of the Company to the Common holders a liquidation preference. The Series A-1 Preferred Stock and Series A Preferred Stock shall be entitled to an amount per share equal to the Series A-1 original issue price and Series A original issue prices respectively, plus an amount equal to all declared but unpaid dividends.

If there is insufficient funds to pay the full amount of the Preferred Stock liquidation preference than the holders of Preferred Stock shall share in any distribution in proportion to the respective liquidation preference.

All remaining assets after payment of the Preferred Stock liquidation preference shall be distributed among the holders of Common Stock in proportion to their number of shares and the holders of Preferred Stock have no further rights.

A Liquidity Event is defined as any sale, license or other transfer, in a single transaction or a series of related tranactions of substantially all of the assets of the Company in which the holders of the Company's oustanding capital stock immediately after such transaction represents less than 50% of the voting owner of the entity. As a Liquidity Event, which is outside the control of the Company, may result in redemption of the Preferred Stock, the Preferred Stock is classified outside of Stockholders' Equity (Deficit) as temporary equity.

Unless at least fifty percent (50%) of the holders of Preferred Stock elect otherwise, a Liquidity Event shall be treated as a liquidation.

c. Conversion:

Each share of Preferred Stock is convertible, at the option of the holder, into the number of shares of Common Stock determined by dividing the original issue price by the applicable conversion price. The Series A-1 conversion price is initially equal to $0.90 and the Series A conversion price is initially equal to $0.50.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(7) Redeemable Convertible Preferred Stock and Stockholders' Equity (Continued)

The conversion price shall be adjusted for diluting issues such as issuance of: any options or convertilble securities, additional shares of common stock less than the Preferred Stock conversion price in effect prior to the issue, stock splits and combinations, certain dividends and distributions, and merger or reorganizaiton.

In the event of a liquidation, dissolution or winding up of the Company, the conversion rights shall terminate.

Upon the closing of a sale of Common Stock pursuant to an intial public offering ("IPO") with gross proceeds of at least $20,000,000 all ouststanding share of Preferred Stock will be automatically converted into Common Stock at the applicable conversion rate.

d. Protective Provisions:

The Company may not take any of the following actions, without the consent of the holders of at least a majority of the outstanding shares of Preferred Stock: amend the Certificate of Incorporation, create any new series or class of shares having a preference or on parity as to dividends or assets with the Preferred Stock, apply any assets to the redemption of any shares of Common Stock, authorize or effect the payment of any dividend to any holders of capital stock.

e. Voting:

The holder of each share of Preferred Stock shall have the right to one vote for each share of Common Stock into which such Preferred Stock could then be converted, and with respect to such vote, such holder shall have full voting rights and powers equal to the voting rights and powers of the holders of Common Stock, shall be entitled to notice of any stockholders' meeting in accordance with the Bylaws of the Company, and shall be entitled to vote, together with holders of Common Stock, with respect to any question upon which holders of Common Stock have the right to vote.

Additionally the holders of Preferred Stock, voting together as a single class, shall be entitled to elect three members of the Board. The holders of the Common Stock voting together as a single class, shall be entitled to elect one member of the Board. The holders of the Common Stock and Preferred Stock, voting together as a single class on an as-converted basis, shall be entitled to elect the remaining members of the Board.

(8) Share-Based Compensation

In 2008, the Board approved the QR Pharma, Inc. 2008 Equity Incentive Plan (the "2008 Plan") initially authorizing 500,000 options to be issued which was subsequently increased to 624,424. On April 12, 2018, the 2008 Plan was succeeded by the QR Pharma, Inc. 2018 Equity Incentive Plan (the "2018 Plan") authorizing 526,525 shares to be issued (the 26,525 shares remaining available for issuance under the prior plan as of the effective date plus 500,000 additional shares). The 2008 Plan had 522,246 shares outstanding as of the effective date of the 2018 Plan. The Company currently maintains the 2018 Plan, which provides for grants of equity to employees, board of directors, officers and consultants of the Company, in the form of stock awards and stock options. The amount and terms of grants are determined by the Company's Board. The equity awards granted under the 2018 Plan vest over various periods. In the case of some non-employee awards, vesting is based on hours of service. The terms are ten (10) years after date of grant and are exercisable in cash or as otherwise determined

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(8) Share-Based Compensation (Continued)

by the Board. As of December 31, 2018, and 2017, 533,746 and 199,857 stock options were available for future grants.

As of December 31, 2018, and 2017, options to purchase common shares of the Company outstanding under the Plan were as follows:

	Number of shares	Weighted average exercise price	Weighted average remaining contractual term (years)
Outstanding at December 31, 2016	206,689	$ 0.14	8.2
Granted	216,666	0.10	—
Exercised	(70,179)	0.14	—
Forfeited	(4,262)	0.55	—
Outstanding at December 31, 2017	348,914	$ 0.11	8.5
Granted	173,332	0.18	—
Exercised	(20,000)	0.14	—
Forfeited	(7,221)	0.06	
Outstanding at December 31, 2018	495,025	$ 0.13	8.2
Vested and exercisable	477,525		
Vested and expected to vest at December 31, 2018	495,025		

The intrinsic value of the outstanding shares as of December 31, 2018 and 2017 was $235,299 and $54,704 respectively.

The fair value of the options was estimated on the date of grant using a Black-Scholes option pricing model with the following assumptions:

	2018	2017
Risk-free interest rate	2.58%	1.94%
Expected life	5.15	5.38
Expected volatility	75%	75%
Expected dividend yield	—	—

The weighted average grant date fair value of the options for the years ended December 31, 2018 and 2017 was $0.50 and $0.20 per share, respectively.

Compensation expense related to options granted for the years ended December 31, 2018 and 2017 was $82,728 and $48,495, respectively. At December 31, 2018 and 2017, there was $8,859 and $91,587, respectively, of unrecognized compensation expense related to unvested employee and nonemployee options that are expected to vest over a weighted average period of 0.25 and 1 year for 2018 and 2017, respectively.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(9) Net Loss Per Share

The Company has reported a net loss for the years ended December 31, 2018 and 2017, and the basic and diluted net loss per share attributable to common stockholders are the same for both years because all redeemable convertible preferred stock and stock options have been excluded from the computation of diluted weighted-average shares outstanding because such securities would have an antidilutive impact.

The following table sets forth the computation of basic and diluted net loss per share:

	For the Year Ended December 31,	
	2018	2017
Numerator		
Net loss	$ (713,871)	$ (682,349)
Denominator		
Weighted-average common shares outstanding, basic and diluted	388,612	358,599
Net loss per share attributable to common stockholders, basic and diluted	$ (1.84)	$ (1.90)

Potential common shares issuable upon conversion of preferred stock and exercise of stock options that are excluded from the computation of diluted weighted-average shares outstanding are as follows:

	For the Year Ended December 31,	
	2018	2017
Redeemable convertible preferred stock	5,763,881	5,493,159
Stock options	495,025	348,914

(10) Income Taxes

On December 22, 2017, the U.S. government enacted the Tax Act. The Tax Act makes broad and complex changes to the U.S. tax code, including, but not limited to, reducing the U.S. federal corporate tax rate from 35 percent to 21 percent; eliminating the corporate alternative minimum tax (AMT) and changing how existing AMT credits can be realized; creating a new limitation on deductible interest expense; changing rules related to uses and limitations of net operating loss carryforwards created in tax years beginning after December 31, 2017; limitations on the deductibility of certain executive compensation; and changes to the calculation of the orphan drug credit.

Upon the enactment of the Tax Act, we recorded a reduction in our deferred income tax assets of $335,717 for the effect of the aforementioned change in the U.S. statutory income tax rate with an offsetting decrease in the valuation allowance established against the deferred tax assets. As a result, there was no change or recognition of an income tax provision or benefit in the consolidated statement of operations for the year ended December 31, 2017.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(10) Income Taxes (Continued)

A reconciliation of income tax benefit computed at the statutory federal income tax rate to income taxes as reflected in the financial statements is as follows:

	December 31, 2018	December 31, 2017
Federal income tax benefit at statutory rate	21.0%	34.0%
State and local tax, net of federal benefit	7.5%	6.3%
Permanent differences	(1.3)%	(1.3)%
Impact of Tax Reform	0.0%	(92.9)%
Change in valuation allowance	(27.1)%	53.8%
Effective Income Tax rate	0.0%	0.0%

Deferred taxes are recognized for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. The significant components of the Company's deferred tax assets are comprised of the following:

	December 31, 2018 (As Restated)	December 31, 2017 (As Restated)
Net operating loss carryforwards	$ 1,181,738	$ 999,650
Stock compensation	19,160	13,043
R&D credit carryforward	137,826	137,826
Total deferred tax assets	1,338,724	1,150,519
Less valuation allowance	(1,338,724)	(1,150,519)
Net deferred taxes	$ —	$ —

As of December 31, 2018, the Company had U.S. federal net operating loss carryforwards of $3,394,475, which may be available to offset future income tax liabilities. Federal net operating loss carryforwards generated in 2017 and prior of $2,764,240 will expire beginning 2028. The remaining $630,235 of federal net operating loss carryforwards generated in 2018, do not expire but are limited 80% of taxable income in future years. As of December 31, 2018, the Company also had U.S. state net operating loss carryforwards of $3,394,475 which may be available to offset future income tax liabilities and will expire beginning in 2028.

The Company has recorded a full valuation allowance against its net deferred tax assets as of December 31, 2018 and 2017 because the Company has determined that is it more likely than not that these assets will not be fully realized due to historic net operating losses incurred. The Company experienced a net change in valuation allowance of $188,205 in the year ended December 31, 2018.

As of December 31, 2018, the Company had federal research and development tax credit carryforwards of $137,826 available to reduce future tax liabilities which expire beginning in 2034.

Under the provisions of the Internal Revenue Code, the net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(10) Income Taxes (Continued)

limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has completed financings since its inception which may have resulted in a change in control as defined by Sections 382 and 383 of the Internal Revenue Code, or could result in a change in control in the future.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. The Company's tax years from 2015 to the present remain open for review. All open years may be examined to the extent that tax credits or net operating loss carryforwards are used in future periods. The Company will recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2018, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's statements of operations.

(11) Related-Party Transactions

The Company had no related party transactions for the years ended December 31, 2018 and 2017.

(12) Restatement of Previously Issued Financial Statements

In connection with the process of filing its Form S-1 Registration Statement, the Company identified misstatements in the historical statements of operations related to the classification of intellectual property legal costs, which consist of attorney fees and fees charged by patent authorities. The Company had previously classified these costs in research and development expenses but determined that these costs should be classified as general and administrative expenses. As a result, the Company has restated its statements of operations as detailed in the tables below:

	Year Ended December 31, 2018			Year Ended December 31, 2017		
	Previously Reported	Adjustments	As Restated	Previously Reported	Adjustments	As Restated
Research and development	$ 323,993	$ (212,385)	$ 111,608	$ 357,651	$ (84,281)	$ 273,370
General and administrative	$ 389,944	$ 212,385	$ 602,329	$ 324,782	$ 84,281	$ 409,063
Total operating expenses	$ 713,937	$ —	$ 713,937	$ 682,433	$ —	$ 682,433

The Company has also corrected its previously reported net operating loss carryforwards to reflect the reduction of tax attributes related to previous years' activity. The deferred tax assets from net operating loss carryforwards as restated as of December 31, 2018 and 2017 were $1,181,738 and $999,650, respectively, compared to the previously reported amounts as of December 31, 2018 and 2017 of $1,716,583 and $1,534,495, respectively. The adjustment of $534,845 was offset by a corresponding change in the valuation allowance.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(13) Subsequent Events

In March 2019, the Company issued unsecured Convertible Promissory Notes (the "Notes") to various investors in the aggregate principal amount of $530,000. Interest accrues at 8% compounded annually on all Notes. The maturity date is the earlier of a Liquidity Event or December 31, 2023. A Liquidity Event is defined as (i) the date of the closing of a merger or reorganization of the Company with another entity (ii) or sale of substantially all of the assets of the Company in which the Company's stockholders own less than 50% of the equity securities after the event or (iii) a liquidation of the Company.

Effective upon the closing of a Qualified Financing, the principal and accrued interest of the notes will convert into the equity security issued by the Company at a 20% discount from the price of the security issued and on the same terms as the security. A Qualified Financing means an IPO with a total offering of at least $8.0 million or the issuance of at least $8.0 million of preferred stock of the Company for new money.

In May 2019, the Company entered into an amended and restated employment agreement with the CEO. See Note 6.

There are no other subsequent events required to be recognized or disclosed in the financial statements other than disclosed herein.

ANNOVIS BIO INC.

Balance Sheets

	March 31, 2019 (unaudited)	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 336,573	$ 35,312
Prepaid expenses and other current assets	63,704	15,680
Total current assets	400,277	50,992
Long-term assets:		
Deferred offering costs	30,986	—
Total long-term assets	30,986	—
Total assets	$ 431,263	$ 50,992
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 10,389	$ 68,425
Accrued expenses	597,514	499,518
Total current liabilities	607,903	567,943
Long-term liabilities:		
Derivative liability	26,500	—
Convertible debt, net of unamortized deferred financing fees of $8,010 and debt discount of $26,135	495,855	—
Total long-term liabilities	522,355	—
Total liabilities	1,130,258	567,943
Redeemable convertible preferred stock—$0.0001 par value		
Series A, –5,133,159 shares authorized, issued and outstanding at March 31, 2019 and December 31, 2018	6,509,303	6,509,303
Series A-1, –1,111,111 shares authorized at March 31, 2019 and December 31, 2018, and 630,722 shares issued and outstanding at March 31, 2019 and December 31, 2018	567,649	567,649
Stockholders' equity (deficit):		
Common stock—$0.0001 par value, 10,150,000 shares authorized at March 31, 2019 and December 31, 2018, and 395,653 and 375,653 shares outstanding at March 31, 2019 and December 31, 2018, respectively	40	40
Additional paid-in capital	200,964	192,105
Accumulated deficit	(7,976,951)	(7,786,048)
Total stockholders' equity (deficit)	(7,775,947)	(7,593,903)
Total liabilities and stockholders' equity (deficit)	$ 431,263	$ 50,992

See accompanying notes to financial statements.

ANNOVIS BIO INC.

Statements of Operations

(Unaudited)

	For the Three Months Ended March 31,	
	2019 (As Restated)	2018 (As Restated)
Operating expenses:		
Research and development	$ 6,021	$ 57,815
General and administrative	180,769	132,151
Total operating expenses	186,790	189,966
Operating loss	(186,790)	(189,966)
Other income (expense):		
Interest income (expense), net	(4,113)	26
Total other income (expense)	(4,113)	26
Loss before income taxes	(190,903)	(189,940)
Income tax expense (benefit)	—	—
Net loss	$ (190,903)	$ (189,940)
Basic and Diluted loss per common share	$ (0.48)	$ (0.51)
Weighted average number of comon shares outstanding, basic and diluted	395,653	375,653

See accompanying notes to financial statements.

ANNOVIS BIO INC.
Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)
(Unaudited)

	Redeemable Convertible Preferred Stock				Stockholders' Equity (Deficit)				
	Series A		Series A-1		Common Stock		Additional Paid-In Capital	Accumulated deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount			
Three Months Ended March 31, 2019									
Balance, December 31, 2018	5,133,159	$ 6,509,303	630,722	$ 567,649	395,653	$ 40	$ 192,105	$ (7,786,048)	$ (7,593,903)
Share-based compensation expense	—	—	—	—	—	—	8,859	—	8,859
Net loss	—	—	—	—	—	—	—	(190,903)	(190,903)
Balance, March 31, 2019	5,133,159	$ 6,509,303	630,722	$ 567,649	395,653	$ 40	$ 200,964	$ (7,976,951)	$ (7,775,947)
Three Months Ended March 31, 2018									
Balance, December 31, 2017	5,133,159	$ 6,509,303	360,000	$ 324,000	375,653	$ 38	$ 106,579	$ (7,072,177)	$ 6,965,560
Proceeds from the issuance of preferred shares	—	—	270,722	243,649	—	—	—	—	—
Share-based compensation expense	—	—	—	—	—	—	3,809	—	3,809
Net loss	—	—	—	—	—	—	—	(189,940)	(189,940)
Balance, March 31, 2018	5,133,159	$ 6,509,303	630,722	$ 567,649	375,653	$ 38	$ 110,388	$ (7,262,117)	$ (7,151,691)

See accompanying notes to financial statements.

ANNOVIS BIO INC.

Statements of Cash Flow

(Unaudited)

	For the Three Months Ended March 31,	
	2019	2018
Cash flows from operating activities:		
Net loss	$ (190,903)	$ (189,940)
Adjustments to reconcile net loss to net cash used in operating activities:		
Amortization of deferred financing fees	112	—
Amortization of debt discount	365	—
Share-based compensation expense	8,859	3,809
Changes in assets and liabilities:		
Prepaid expenses and other current assets	(48,024)	4,896
Accounts payable	(58,036)	(71,107)
Accrued expenses	58,888	95,393
Net cash used in operating activities	(228,739)	(156,949)
Cash flows from financing activities:		
Proceeds from issuance of convertible debt	530,000	—
Proceeds from issuance of preferred shares	—	243,649
Net cash provided by financing activities	530,000	243,649
Net increase in cash	301,261	86,700
Cash and cash equivalents, beginning of period	35,312	347,472
Cash and cash equivalents, end of period	$ 336,573	$ 434,172
Supplemental disclosure of cash flow information		
Deferred offering costs in accrued expenses	$ 30,986	$ —
Deferred financing fees in accrued expenses	$ 8,122	$ —

See accompanying notes to financial statements.

Annovis Bio, Inc.

Notes to Financial Statements

March 31, 2019 and 2018

(Unaudited)

(1) Nature of Business and Liquidity

Annovis Bio, Inc. (the "Company" or "Annovis") was incorporated on April 29, 2008, under the laws of the State of Delaware as QR Pharma, Inc. On March 21, 2019, the Board of Directors of the Company (the "Board") approved the name change to Annovis Bio, Inc. Annovis is a clinical stage pharmaceutical company focused on developing and commercializing innovative drugs for the treatment of Parkinson's ("PD") and Alzheimer's ("AD") diseases and other neurodegenerative diseases. The Company's lead compound, ANVS-401, is a small molecule administered orally that attacks neurodegeneration by entering the brain and inhibiting the translation of neurotoxic proteins thereby improving and normalizing axonal vesicle transport.

Since its founding, the Company has been engaged in organizational activities, including raising capital, and research and development activities. The Company has not generated substantial revenues and has not yet achieved profitable operations, nor has it ever generated positive cash flows from operations. There is no assurance that profitable operations, if achieved, could be sustained on a continuing basis. The Company is subject to those risks associated with any clinical stage pharmaceutical company that has substantial expenditures for research and development. There can be no assurance that the Company's research and development projects will be successful, that products developed will obtain necessary regulatory approval, or that any approved product will be commercially viable. In addition, the Company operates in an environment of rapid technological change and is largely dependent on the services of its employees and consultants. Further, the Company's future operations are dependent on the success of the Company's efforts to raise additional capital.

These uncertainties raise substantial doubt about the Company's ability to continue as a going concern for 12 months after the issuance date of these financial statements. The accompanying financial statements have been prepared on a going-concern basis which contemplates the continuation of operations, realization of assets and liquidation of liabilities in the ordinary course of business. The Company incurred a net loss of $190,303 and $189,940 for the three months ended March 31, 2019 and 2018, respectively, and had an accumulated deficit of $7,976,951 as of March 31, 2019. The Company anticipates incurring additional losses until such time, if ever, that it can generate significant revenue from its product candidates currently in development. The Company's primary source of capital has been the issuance of equity securities.

Management believes that current cash and cash equivalents are sufficient to fund operations and capital requirements for the first half of 2019. Additional financings will be needed by the Company to fund its operations, to complete clinical development of and to commercially develop its product candidates. There is no assurance that such financing will be available when needed or on acceptable terms.

(2) Summary of Significant Accounting Policies

(a) Basis of Presentation of Interim Unaudited Financial Statements

The interim financial statements included herein are unaudited. In the opinion of management, these statements include all adjustments, consisting only of normal, recurring adjustments, necessary for a fair presentation of the financial position of Annovis at March 31, 2019, and its results of operations and its cash flows for the three months ended March 31, 2019 and 2018. The interim results of

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

March 31, 2019 and 2018

(Unaudited)

(2) Summary of Significant Accounting Policies (Continued)

operations are not necessarily indicative of the results to be expected for a full year. These interim unaudited financial statements should be read in conjunction with the audited financial statements for the years ended December 31, 2018 and 2017 and notes thereto. The accompanying financial statements have been prepared in conformity with U.S. generally accepted accounting principles (U.S. GAAP). Any reference in these notes to applicable guidance is meant to refer to U.S. GAAP as found in the Accounting Standards Codification (ASC) and Accounting Standards Update (ASU) of the Financial Accounting Standards Board (FASB). Certain information and note disclosures normally included in financial statements prepared in accordance with U.S. GAAP have been omitted pursuant to such rules and regulations relating to interim financial statements.

(b) Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, including disclosure of contingent assets and liabilities, at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting period. Due to the uncertainty of factors surrounding the estimates or judgments used in the preparation of the financial statements, actual results may materially vary from these estimates.

Significant items subject to such estimates and assumptions include the valuation of equity-based compensation, valuation of a derivative liability and contingent liabilities. Future events and their effects cannot be predicted with certainty; accordingly, accounting estimates require the exercise of judgment. Accounting estimates used in the preparation of these financial statements change as new events occur, as more experience is acquired, as additional information is obtained and as the operating environment changes.

(c) Basic and Diluted Earnings (Loss) per Share

Basic net loss per share is determined using the weighted average number of shares of common stock outstanding during each period. Diluted net income per share includes the effect, if any, from the potential exercise or conversion of securities, such as redeemable convertible preferred stock and stock options, which would result in the issuance of incremental shares of common stock. The computation of diluted net loss per shares does not include the conversion of securities that would have an anti-dilutive effect. The basic and dilutive computations of net loss per share for the Company are the same because the dilutive effects of the Company's convertible securities would be anti-dilutive.

(d) Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less to be cash equivalents. At times, the Company's cash balances may exceed the current insured amounts under the Federal Deposit Insurance Corporation (FDIC). Total cash was $336,573 as of March 31, 2019 which exceeded the FDIC coverage limit of $250,000.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

March 31, 2019 and 2018

(Unaudited)

(2) Summary of Significant Accounting Policies (Continued)

(e) Deferred Offering Costs

Included in long-term assets, are costs incurred in connection with our planned initial public offering ("IPO") and primarily consist of direct incremental legal, printing and accounting fees. These costs are capitalized as incurred and will be offset against proceeds upon consummation of the offering. In the event the offering is terminated or abandoned, deferred offering costs will be expensed in the period such determination has been made. As of March 31, 2019, the deferred offering costs amounted to $30,986. There were no deferred offering costs at December 31, 2018.

(f) Fair Value of Financial Instruments

The Company's financial instruments include, cash and cash equivalents, accounts payable, accrued expenses, a derivative liability and debt. Cash and cash equivalents and the derivative liability are reported at fair value. The recorded carrying amount of accounts payable and accrued expenses reflect their fair value due to their short-term nature. The carrying value of the interest-bearing debt approximates fair value based upon the borrowing rates currently available to the Company for loans with similar terms and maturities.

(g) Research and Development

Research and development costs are expensed as incurred and are primarily comprised of external research and development expenses incurred under arrangements with third parties, such as contract research organizations ("CROs") and consultants. At the end of each reporting period, the Company compares the payments made to each service provider to the estimated progress towards completion of the related project. Factors that the Company considers in preparing these estimates include the number of patients enrolled in studies, milestones achieved, and other criteria related to the efforts of its vendors. These estimates will be subject to change as additional information becomes available. Depending on the timing of payments to vendors and estimated services provided, the Company will record net prepaid or accrued expenses related to these costs. As of March 31, 2019 and December 31, 2018, the Company had no outstanding payables to CROs.

(h) Share-Based Compensation

Share-based compensation cost is measured at the grant date based on the fair value of the award and is recognized as expense over the requisite service period, which is generally the vesting period. The Company early adopted ASU 2018-07 on January 1, 2017 which permits the valuation of stock-based awards granted to non-employees to be measured at fair value at the grant date rather than on an accelerated attribution basis over the vesting period.

Determining the appropriate fair value of share-based awards requires the use of subjective assumptions, including the fair value of the Company's common shares, and for options, the expected life of the option and expected share price volatility. The Company uses the Black-Scholes option pricing model to value its option awards. The assumptions used in calculating the fair value of share-based awards represent management's best estimates and involve inherent uncertainties and the

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

March 31, 2019 and 2018

(Unaudited)

(2) Summary of Significant Accounting Policies (Continued)

application of management's judgment. As a result, if factors change and management uses different assumptions, share-based compensation expense could be materially different for future awards.

The expected life of options was estimated using the simplified method, as the Company has limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment.

(i) Income Taxes

The Company provides for income taxes using the asset and liability approach. Deferred tax assets and liabilities are recorded based on the differences between the financial statement and tax bases of assets and liabilities and the tax rates in effect when these differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance if, based on the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. As of March 31, 2019 and December 31, 2018, the Company had a full valuation allowance against deferred tax assets.

The Company is subject to the provisions of ASC 740-10-25, Income Taxes (ASC 740). ASC 740 prescribes a more likely-than-not threshold for the financial statement recognition of uncertain tax positions. ASC 740 clarifies the accounting for income taxes by prescribing a minimum recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. There are currently no open Federal or State tax audits. The Company has not recorded any liability for uncertain tax positions at March 31, 2019 or 2018.

The Tax Cuts and Jobs Act (the "Tax Act"), enacted on December 22, 2017, among other things, permanently lowered the statutory federal corporate tax rate from 35% to 21%, effective for tax years including or beginning January 1, 2018. Although in the normal course of business the Company is required to make estimates and assumptions for certain tax items which cannot be fully determined at period end, the Company did not identify items for which the income tax effects of the Tax Act have not been completed as of December 31, 2017 and, therefore, considers its accounting for the tax effects of the Tax Act on its deferred tax assets and liabilities to be complete as of December 31, 2017.

(j) Recent Accounting Pronouncements

In February 2016, the FASB issued its final standard on lease accounting, ASU No. 2016-02, "Leases (Topic 842)," which superseded Topic 840, "Leases," which was further modified in ASU No. 2018-10, "Codification Improvements to Topic 842, Leases," ASU No. 2018-11, "Leases (Topic 842) Targeted Improvements" and ASU No. 2019-01 "Leases (Topic 842) Codification Improvements" to clarify the implementation guidance. The new pronouncement requires the recognition on the balance sheet of right-of-use assets and lease liabilities for all long-term leases, including operating leases, on the balance sheet. The pronouncement requires that lease arrangements longer than 12 months result in an entity classifying leases as finance or operating leases. However, unlike current U.S. GAAP, which requires only capital leases to be recognized on the balance sheet, ASU 2016-02 will require both types of leases to be recognized on the balance sheet. ASU 2016-02 also requires disclosures about the amount, timing, and uncertainty of cash flows arising from leases. These disclosures include qualitative and quantitative requirements, providing additional information about the amounts recorded in the financial statements.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

March 31, 2019 and 2018

(Unaudited)

(2) Summary of Significant Accounting Policies (Continued)

The pronouncement is effective for all public business entities for interim and annual periods beginning after December 15, 2018 and for non-public business entities with annual periods beginning after December 15, 2019 with early adoption permitted. In July 2018, the FASB issued ASU No. 2018-11, which provides targeted improvements to the new lease standard, including an option to apply the transition provisions at its adoption date instead of at the earliest comparative period presented in its financial statements. The Company adopted the new leasing standards using a modified retrospective transition approach applied to leases existing as of or entered into after January 1, 2019. The adoption of this guidance did not have any impact on the Company's financial statements due to the short-term nature of our leasing arrangements.

In May 2014, the FASB issued ASU 2014-09, Revenue from Contracts with Customers (Topic 606), requiring an entity to recognize the amount of revenue to which it expects to be entitled for the transfer of promised goods or services to customers. ASU 2014-09 supersedes nearly all existing revenue recognition guidance under U.S. GAAP and requires revenue to be recognized when promised goods or services are transferred to customers in an amount that reflects the consideration that is expected to be received for those goods or services. Additionally, qualitative and quantitative disclosures are required about customer contracts, significant judgments and changes in judgments, and assets recognized from the costs to obtain or fulfill a contract.

The FASB also issued the following amendments to ASU No. 2014-09 to provide clarification on the guidance:

- ASU No. 2015-14, Revenue from Contracts with Customers (Topic 606)—Deferral of the Effective Date
- ASU No. 2016-08, Revenue from Contracts with Customers (Topic 606)—Principal versus Agent (Reporting Revenue Gross vs. Net)
- ASU No. 2016-10, Revenue from Contracts with Customers (Topic 606)—Identifying Performance Obligations and Licensing
- ASU No. 2016-12, Revenue from Contracts with Customers (Topic 606)—Narrow-Scope Improvements and Practical Expedients

The Company elected to early adopt ASU 2014-09 effective January 1, 2017. The standard did not have an impact on the Company's financial statements.

In August 2016, the FASB issued ASU 2016-15, Classification of Certain Cash Receipts and Cash Payments, which provides specific guidance related to eight cash flow classification issues. The pronouncement is effective for interim and annual periods beginning after December 15, 2018, and interim periods within fiscal years beginning after December 15, 2019. The Company elected to early adopt the new pronouncement in the first quarter of 2019. Such early adoption of ASU 2016-15 in the first quarter of 2019 did not have an impact on the Company's financial statements.

In November 2016, the FASB issued ASU 2016-18, Restricted Cash, which requires changes in restricted cash and restricted cash equivalents to be explained on the statement of cash flows by including restricted cash and restricted cash equivalents in the beginning-of-period and end-of-period

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

March 31, 2019 and 2018

(Unaudited)

(2) Summary of Significant Accounting Policies (Continued)

total cash and cash equivalents shown on the statement of cash flows. The pronouncement is effective for interim and annual periods beginning after December 15, 2018, and interim periods within fiscal years beginning after December 15, 2019. Early adoption is permitted, including adoption in an interim period. If an entity early adopts the amendments in an interim period, any adjustments should be reflected as of the beginning of the fiscal year that includes that interim period. The Company elected to early adopt ASU 2016-18. The early adoption of ASU 2016-18 in the first quarter of 2019 did not have an impact on the Company's financial statements.

In March 2018, the FASB issued ASU 2018-5—Income Taxes (Topic 740): Amendments to SEC Paragraphs pursuant to SEC Staff Accounting Bulletin No. 118. This ASU provided guidance related to Securities and Exchange Commission ("SEC") Staff Accounting Bulletin No. 118 ("SAB 118"), which addresses the accounting implications of the Tax Act. SAB 118 allows a company to record provisional amounts during a measurement period not to extend beyond one year of the enactment date and was effective upon issuance. The Company has analyzed the Tax Act, and in certain areas, has made reasonable estimates of the effects on its financial statements and tax disclosures.

In June 2018, the FASB issued ASU 2018-07, Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting. The new guidance expands the scope of Topic 718 to include share-based payments granted to nonemployees in exchange for goods or services used or consumed in an entity's own operations, and supersedes the guidance in ASC 505-50, Equity-Based Payments to Non-Employees. The most significant change resulting from this update is that stock-based awards granted to non-employees will no longer need to be re-measured at fair value at each financial reporting date until performance is complete, as these awards will be measured at fair value at the grant date. The guidance is effective January 1, 2019 with early adoption permitted, including in an interim period for which financial statements have not been issued. The Company elected to apply the provisions of this ASU in the Company's financial statements effective January 1, 2017.

In August 2018, the FASB issued ASU No. 2018-13, Fair Value Measurement (Topic 820)—Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement. The new guidance improves and clarifies the fair value measurement disclosure requirement of ASC 820. The new disclosure requirements include the changes in unrealized gains or losses included in other comprehensive income for recurring Level 3 fair value measurement held at the end of reporting period and the explicit requirement to disclose the range and weighted average used to develop significant unobservable inputs for Level 3 fair value measurements. The other provisions of ASU 2018-13 also include eliminated and modified disclosure requirements. The guidance is effective for fiscal years beginning after December 15, 2019 with early adoption permitted, including in an interim period for which financial statements have not been issued or made available for issuance. The Company has evaluated the impact of adoption of this ASU and determined that it will not have a significant impact on its financial statements.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

March 31, 2019 and 2018

(Unaudited)

(3) Fair Value Measurements

The Company measures certain assets and liabilities at fair value in accordance with Accounting Standards Codification ("ASC") 820, Fair Value Measurements and Disclosures. ASC 820 defines fair value as the price that would be received to sell an asset or paid to transfer a liability (the exit price) in an orderly transaction between market participants at the measurement date. The guidance in ASC 820 outlines a valuation framework and creates a fair value hierarchy that serves to increase the consistency and comparability of fair value measurements and the related disclosures. In determining fair value, the Company maximizes the use of quoted prices and observable inputs. Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from independent sources. The fair value hierarchy is broken down into three levels based on the source of inputs as follows:

Level 1—Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities.

Level 2—Valuations based on observable inputs and quoted prices in active markets for similar assets and liabilities.

Level 3—Valuations based on unobservable inputs and models that are supported by little or no market activity.

The following table provides the carrying value and fair value of certain financial assets and liabilities of the Company measured at fair value on a recurring basis as of March 31, 2019 and December 31, 2018:

		Fair Value Measurement at March 31, 2019		
	Carrying Value	Level 1	Level 2	Level 3
Cash and cash equivalents	$ 336,573	$ 336,573	$ —	$ —
Derivative liability	$ 26,500	$ —	$ —	$ 26,500

		Fair Value Measurement at December 31, 2018		
	Carrying Value	Level 1	Level 2	Level 3
Cash and cash equivalents	$ 35,312	$ 35,212	$ —	$ —
Derivative liability	$ —	$ —	$ —	$ —

The derivative liability was associated with the March 2019 issuance of convertible promissory notes (see Note 6). The Company computed fair value at the date of issuance of $26,500 related to the embedded share settlement feature providing for conversion of the notes at a 20% discount to the price of the shares issued in a Qualified Financing. The Company estimated the fair value using a probability weighted approach. Using the same methodology, the Company determined that there was no change in the fair value of the derivative liability at March 31, 2019.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

March 31, 2019 and 2018

(Unaudited)

(4) Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following:

	March 31, 2019	December 31, 2018
Prepaid rent	$ 1,904	$ 1,904
Prepaid research and development	—	4,976
Prepaid expenses	—	5,000
Prepaid professional fees	58,000	—
Security deposit	3,800	3,800
Total prepaid expenses and other current assets	$ 63,704	$ 15,680

(5) Accrued Expenses

Accrued expenses consisted of the following:

	March 31, 2019	December 31, 2018
Accrued interest	$ 3,651	$ —
Payroll and related benefits	42,237	21,640
Accrued professional fees	80,126	17,878
Accrued license payments	471,500	460,000
	$ 597,514	$ 499,518

See Note 7—Commitments for further detail on the accrued license payments.

(6) Convertible Promissory Notes

In March 2019, the Company issued convertible promissory notes (the "Notes") to various investors in the aggregate principal amount of $530,000. Interest accrues at 8% compounded annually on all Notes. The maturity date is the earlier of a Liquidity Event or upon the written demand of the holders of a majority of the outstanding principal amount of the Notes made any time after December 31, 2023. A Liquidity Event is defined as (i) the date of the closing of a merger or reorganization of the Company with another entity (ii) or sale of substantially all of the assets of the Company in which the Company's stockholders own less than 50% of the equity securities after the event or (iii) a liquidation of the Company.

Effective upon the closing of a Qualified Financing, the principal and accrued interest of the notes will convert into the equity security issued by the Company at a 20% discount from the price of the security issued and on the same terms as the security. A Qualified Financing means an IPO with a total offering of at least $8.0 million or the issuance of at least $8.0 million of preferred stock of the Company for new money. Effective upon any other financing, each holder of the Notes has the right to convert into shares of the security at the same per share purchase price as the security issued.

The Company incurred costs of $8,122 in connection with the issuance of the Notes, which are being amortized to interest expense over the term of the Notes. In addition, on issuance, the Company recognized a discount associated with the Notes of $26,500 related to the fair value of an embedded

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

March 31, 2019 and 2018

(Unaudited)

(6) Convertible Promissory Notes (Continued)

derivative reflecting the share-settlement provision upon the closing of a Qualified Financing. Unamortized deferred financing fees and debt discount are deducted from the face amount of the Notes on the balance sheets.

(7) Commitments

(a) Leases

The Company leases its office facilities under a month-to-month operating lease. Total rental expense was $5,712 and $5,469 for the three months ended March 31, 2019 and 2018, respectively.

(b) License Agreements

In November 2008, the Company licensed the rights to certain chemical compounds, know-how and intellectual property rights that may be suitable for the development of human therapeutics. Currently, the intellectual property rights are owned by a subsidiary of Horizon Therapeutics, PLC ("Licensor"). Payments by the Company under the license agreement include a one-time non-refundable fee of $50,000, a minimum annual commitment of $40,000 commencing in 2009, milestone payments upon attainment of certain milestone events, royalties based on net sales of products covered by the patent-related rights and a portion of any sublicense income received by the Company. The Company is responsible for the development and commercialization of the licensed products.

In May 2012, such license agreement was amended. The minimum annual commitment was increased to $46,000 and may be deferred by the Company until the Company raises equity financing of at least $2 million in equity financing, then the aggregate annual payments of all amounts will become payable.

At March 31, 2019 and December 31, 2018, the Company had accrued $471,500 and $460,000, respectively, in license payments under the term of this license, included in accrued liabilities, of which no amounts have been paid to date.

In further consideration for the licenses granted, the Company shall make the following milestone payments to Licensor based upon the attainment of each milestone event indicated below.

Milestone Event	Amount
Commencement of Phase II	$ 230,000
Commencement of Phase III	$ 575,000
Filing of an NDA for Regulatory Approval (or equivalent in Europe or Japan	$ 1,150,000
Receipt of Regulatory Approval in the United States	$ 5,750,000
Receipt of Regulatory Approval outside United States	$ 5,750,000

No milestones have been achieved as of March 31, 2019.

Royalties shall be paid to Licensor assessed on net sales of licensed products on a country-by-country basis in an amount equal to 5.75%. Should the Company be required to obtain a

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

March 31, 2019 and 2018

(Unaudited)

(7) Commitments (Continued)

license from a third party in order to sell a licensed product, the Company may deduct 50% of the royalties on such licensed product paid to the third party subject to certain minimums.

In addition to the royalties the Company shall pay licensor 9.2% of all sublicense income attributable to licensed products.

The Licensor also granted the Company a buy-out option which may be exercised at any time during the term of the agreement. The option price will be as follows: $500,000 if exercised prior to the commencement of the first Phase II clinical trial; $1,000,000 if exercised on or after the commencement of the first Phase II clinical trial and prior to the commencement of the first Phase III clinical trial; $5,000,000 if exercised on or after the commencement of the first Phase III clinical trial and prior to the filing of a New Drug Application ("NDA") with the FDA for the first licensed product; and $8,000,000 if exercised on or after the filing of an NDA for the first licensed product.

The Company has the right to terminate the agreement at any time by giving 90 days advance notice subject to the payment of any amounts due under the agreement at that time. If the Company does not terminate the agreement or exercise the buy-out option, the term of the agreement shall continue until the expiration of the Company's obligation to make royalty payments. Such royalty payments continue for each product in each country until the later of the expiration of the related patent or 10 years after the initial sale of the product in the respective country. The agreement may also be terminated for cause by either party upon the breach of the material obligations of the other party or the bankruptcy or liquidation of the other party.

(c) Employment Agreements

The Company has entered into an amended and restated employment agreement with the President and Chief Executive Officer (the "CEO") of the Company, effective May 10, 2019. The term of the agreement will continue in effect until notice is provided 10 business days prior to the termination by either party. Upon termination of the agreement by the Company for any reason other than for cause, death or disability or by the CEO for good reason, the Company shall pay the CEO's base salary, currently $120,000, for a period of one year.

(d) Litigation

The Company is subject, from time to time, to claims by third parties under various legal disputes. The defense of such claims, or any adverse outcome relating to any such claims, could have a material adverse effect on the Company's liquidity, financial condition and cash flows. At March 31, 2019, the Company did not have any pending legal actions.

(8) Redeemable Convertible Preferred Stock and Stockholders' Equity

a) Overview:

The Company's Certificate of Incorporation, originally filed on April 29, 2008, was most recently amended by the Amended and Restated Certificate of Incorporation filed on December 14, 2017, which authorized the issuance of two classes of stock to be designated, respectively, "Common Stock" and "Preferred Stock". The total number of shares which the Company is authorized to issue is

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

March 31, 2019 and 2018

(Unaudited)

(8) Redeemable Convertible Preferred Stock and Stockholders' Equity (Continued)

16,394,270, each with a par value of $0.0001 per share. Of these shares, 10,150,000 shall be Common Stock and 6,244,270 shall be Preferred Stock.

Pursuant to the Series A Stock Purchase Agreement as of December 19, 2014 ("Series A Purchase Agreement"), the Company was permitted to issue 1,000,000 shares of the Company's Series A Convertible Preferred Stock ("Series A"), par value $0.0001 per share, and was permitted to issue an additional 1,000,000 shares of Series A at additional closings at a price per share of $0.50. In addition, at the initial closing all of the outstanding convertible promissory notes of the Company were converted into 1,400,000 shares of Series A. The conversion of the promissory notes was treated as a capital transaction and the excess of the carrying value of the promissory notes over the issuance price of the Series A was reflected in the carrying value of the Series A. The Series A Purchase Agreement was amended on February 16, 2015 to increase the additional share amount to 2,000,000. Pursuant to the Series A Purchase Agreement, as amended, 1,000,000 shares of Series A were issued on December 19, 2014 and 1,134,718 shares were issued and sold at additional closings held on March 15, 2015 and May 22, 2015.

On September 16, 2016 the Company entered into a second amendment to the Series A Purchase Agreement to permit the Company to issue and sell up to 1,400,000 additional Series A shares and extend the date for additional closings to October 31, 2016. On October 11, 2016, the Company entered into a third amendment to the Series A Purchase Agreement to increase the additional shares that could be sold through October 31, 2016 to 1,600,000, thus increasing the total shares available for sale under the Series A Purchase Agreement, as amended, to 2,734,718. During October 2016, 1,598,441 additional shares were issued resulting in a total of 5,133,159 Series A shares issued and outstanding as of March 31, 2019 and December 31, 2018.

Pursuant to the Series A-1 Stock Purchase Agreement dated as of December 15, 2017 ("Series A-1 Purchase Agreement") the Company sold and issued 360,000 shares of the Company's Series A-1 Convertible Preferred Stock ("Series A-1"), par value $0.0001 per share, and was permitted to issue an additional 751,111 shares of Series A-1 at additional closings at a price per share of $0.90. At an additional closing in March, 2018, 270,722 additional shares were sold and issued by the Company. 630,722 Series A-1 shares were issued and outstanding as of March 31, 2019 and December 31, 2018.

b) Common Stock:

a. Dividends:

Subject to the rights of holders of Preferred Stock, the holders of the Common Stock are entitled to receive dividends as declared from time to time by the Board.

b. Liquidation:

Subject to the rights of holders of Preferred Stock as to liquidation, upon the liquidation, dissolution or winding up of the Corporation, the remaining assets of the Corporation will be distributed to the holders of Common Stock.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

March 31, 2019 and 2018

(Unaudited)

(8) Redeemable Convertible Preferred Stock and Stockholders' Equity (Continued)

c. Voting:

The holders of the Common Stock are entitled to one vote for each share of Common Stock held but shall not be entitled to vote on any amendment to the Certificate of Incorporation that relates solely to the terms of one or more outstanding series of Preferred Stock. There is no cumulative voting.

c) Redeemable Convertible Preferred stock:

The authorized Preferred stock is designated as Series A Preferred (5,133,159 shares) and Series A-1 Preferred (1,111,111 shares). The Series A-1 Preferred stock shall rank equal with the Series A Preferred Stock and each shall rank senior to the Common Stock in regard to payment of dividends, distributions of assets upon a liquidation or Liquidity Event.

a. Dividends:

The holders of the Series A and Series A-1 Preferred Stock (known collectively as the "Preferred Stock") are entitled to receive dividends, when and as declared by the Board.

b. Liquidation:

The holders of the Preferred Stock shall be entitled to receive, prior and in preference to any distribution of any assets of the Company to the Common holders a liquidation preference. The Series A-1 Preferred Stock and Series A Preferred Stock shall be entitled to an amount per share equal to the Series A-1 original issue price and Series A original issue prices respectively, plus an amount equal to all declared but unpaid dividends.

If there is insufficient funds to pay the full amount of the Preferred Stock liquidation preference than the holders of Preferred Stock shall share in any distribution in proportion to the respective liquidation preference.

All remaining assets after payment of the Preferred Stock liquidation preference shall be distributed among the holders of Common Stock in proportion to their number of shares and the holders of Preferred Stock have no further rights.

A Liquidity Event is defined as any sale, license or other transfer, in a single transaction or a series of related tranactions of substantially all of the assets of the Company in which the holders of the Company's oustanding capital stock immediately after such transaction represents less than 50% of the voting owner of the entity. As a Liquidity Event, which is outside the control of the Company, may result in redemption of the Preferred Stock, the Preferred Stock is classified outside of Stockholders' Equity (Deficit) as temporary equity.

Unless at least fifty percent (50%) of the holders of Preferred Stock elect otherwise, a Liquidity Event shall be treated as a liquidation.

c. Conversion:

Each share of Preferred Stock is convertible, at the option of the holder, into the number of shares of Common Stock determined by dividing the original issue price by the applicable conversion price. The Series A-1 conversion price is initially equal to $0.90 and the Series A conversion price is initially equal to $0.50.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

March 31, 2019 and 2018

(Unaudited)

(8) Redeemable Convertible Preferred Stock and Stockholders' Equity (Continued)

The conversion price shall be adjusted for diluting issues such as issuance of: any options or convertilble securities, additional shares of common stock less than the Preferred Stock conversion price in effect prior to the issue, stock splits and combinations, certain dividends and distributions, and merger or reorganizaiton.

In the event of a liquidation, dissolution or winding up of the Company, the conversion rights shall terminate.

Upon the closing of a sale of Common Stock pursuant to an IPO with gross proceeds of at least $20,000,000 all ouststanding share of Preferred Stock will be automatically converted into Common Stock at the applicable conversion rate.

d. Protective Provisions:

The Company may not take any of the following actions, without the consent of the holders of at least a majority of the outstanding shares of Preferred Stock: amend the Certificate of Incorporation, create any new series or class of shares having a preference or on parity as to dividends or assets with the Preferred Stock, apply any assets to the redemption of any shares of Common Stock, authorize or effect the payment of any dividend to any holders of capital stock.

e. Voting:

The holder of each share of Preferred Stock shall have the right to one vote for each share of Common Stock into which such Preferred Stock could then be converted, and with respect to such vote, such holder shall have full voting rights and powers equal to the voting rights and powers of the holders of Common Stock, shall be entitled to notice of any stockholders' meeting in accordance with the Bylaws of the Company, and shall be entitled to vote, together with holders of Common Stock, with respect to any question upon which holders of Common Stock have the right to vote.

Additionally the holders of Preferred Stock, voting together as a single class, shall be entitled to elect three members of the Board. The holders of the Common Stock voting together as a single class, shall be entitled to elect one member of the Board. The holders of the Common Stock and Preferred Stock, voting together as a single class on an as-converted basis, shall be entitled to elect the remaining members of the Board.

(9) Share-Based Compensation

Share-based compensation expense for the three months ended March 31, 2019 and 2018 was $8,859 and $3,809, respectively.

As of March 31, 2019 and December 31, 2018, 533,746 stock options were available for future grants.

As of March 31, 2019, there were 495,025 options outstanding, all of which were vested and exercisable. As of December 31, 2018, there were 495,025 options outstanding, of which 477,525 were vested and exercisable. The intrinsic value of outstanding options was $235,299 as of March 31, 2019.

There were no options issued during the three months ended March 31, 2019 and 2018.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

March 31, 2019 and 2018

(Unaudited)

(10) Net Loss Per Share

The Company has reported a net loss for the three months ended March 31, 2019 and 2018, and the basic and diluted net loss per share attributable to common stockholders are the same for both periods because all convertible promissory notes, redeemable convertible preferred stock and stock options have been excluded from the computation of diluted weighted-average shares outstanding because such securities would have an antidilutive impact.

The following table sets forth the computation of basic and diluted net loss per share:

	Three Months Ended March 31,	
	2019	2018
Numerator		
Net loss	$ (190,903)	$ (189,940)
Denominator		
Weighted-average common shares outstanding, basic and diluted	395,653	375,653
Net loss per share attributable to common stockholders, basic and diluted	$ (0.48)	$ (0.51)

Potential common shares issuable upon conversion of redeemable convertible preferred stock and exercise of stock options that are excluded from the computation of diluted weighted-average shares outstanding are as follows:

	Three Months Ended March 31,	
	2019	2018
Redeemable convertible preferred stock	5,763,881	5,763,881
Stock options	495,025	321,693

(11) Income Taxes

The Company's consolidated income tax benefit (expense) was $0.0 million for the three months ended March 31, 2019 and 2018. The Company has recorded a valuation allowance to reduce its net deferred tax asset to an amount that is more likely than not to be realized in future years. Accordingly, the benefit of the net operating loss that would have been recognized in the three months ended March 31, 2019 and 2018 was offset by changes in the valuation allowance.

As of March 31, 2019, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's statements of operations.

(12) Related-Party Transactions

As discussed in Note 6, in March 2019 the Company issued Notes in the aggregate principal amount of $530,000. Three of the Company's directors purchased an aggregate of $305,000 of the Notes.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

March 31, 2019 and 2018

(Unaudited)

(13) Restatement of Previously Issued Financial Statements

In connection with the process of filing its Form S-1 Registration Statement, the Company identified misstatements in the historical statements of operations related to the classification of intellectual property legal costs, which consist of attorney fees and fees charged by patent authorities. The Company had previously classified these costs in research and development expenses but determined that these costs should be classified as general and administrative expenses. As a result, the Company has restated its statements of operations as detailed in the tables below:

	Three Months Ended March 31, 2019			Three Months Ended March 31, 2018		
	Previously Reported	Adjustments	As Restated	Previously Reported	Adjustments	As Restated
Research and development	$ 34,735	$ (28,714)	$ 6,021	$ 126,860	$ (69,045)	$ 57,815
General and administrative	$ 152,055	$ 28,714	$ 180,769	$ 63,106	$ 69,045	$ 132,151
Total operating expenses	$ 186,790	$ —	$ 186,790	$ 189,966	$ —	$ 189,966

(14) Subsequent Events

In May 2019, the Company entered into an amended and restated employment agreement with the CEO. See Note 7.

There are no other subsequent events required to be recognized or disclosed in the financial statements other than disclosed herein.

Table of Contents

Shares of Common Stock

ANNOVIS BIO, INC.

PROSPECTUS

ThinkEquity

a division of Fordham Financial Management, Inc.

, 2019

Through and including , 2019 (25 days after the commencement of this offering), all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table indicates the expenses to be incurred in connection with the offering described in this registration statement, other than underwriting discounts and commissions, all of which will be paid by us. All amounts are estimated except the Securities and Exchange Commission registration fee, the Financial Industry Regulatory Authority, Inc., or FINRA, filing fee and the Nasdaq listing fee.

	Amount
Securities and Exchange Commission registration fee	$
FINRA filing fee	
Initial Nasdaq Capital Market listing fee	
Accountants' fees and expenses	
Legal fees and expenses	
Transfer Agent's fees and expenses	
Printing and engraving expenses	
Non-accountable expenses to underwriters	
Miscellaneous	
Total expenses	$

Item 14. Indemnification of Directors and Officers.

Section 102 of the General Corporation Law of the State of Delaware permits a corporation to eliminate the personal liability of directors of a corporation to the corporation or its stockholders for monetary damages for a breach of fiduciary duty as a director, except where the director breached his duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. Our restated certificate of incorporation provides that no director of the Registrant shall be personally liable to it or its stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability, except to the extent that the General Corporation Law of the State of Delaware prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty.

Section 145 of the General Corporation Law of the State of Delaware provides that a corporation has the power to indemnify a director, officer, employee, or agent of the corporation, or a person serving at the request of the corporation for another corporation, partnership, joint venture, trust or other enterprise in related capacities against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he was or is a party or is threatened to be made a party to any threatened, ending or completed action, suit or proceeding by reason of such position, if such person acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

Our restated certificate of incorporation provides that we will indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or

proceeding (other than an action by or in the right of us) by reason of the fact that he or she is or was, or has agreed to become, a director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (all such persons being referred to as an "Indemnitee"), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding and any appeal therefrom, if such Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, and, with respect to any criminal action or proceeding, he or she had no reasonable cause to believe his or her conduct was unlawful. Our restated certificate of incorporation provides that we will indemnify any Indemnitee who was or is a party to an action or suit by or in the right of us to procure a judgment in our favor by reason of the fact that the Indemnitee is or was, or has agreed to become, a director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise, or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding, and any appeal therefrom, if the Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, except that no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to us, unless a court determines that, despite such adjudication but in view of all of the circumstances, he or she is entitled to indemnification of such expenses. Notwithstanding the foregoing, to the extent that any Indemnitee has been successful, on the merits or otherwise, he or she will be indemnified by us against all expenses (including attorneys' fees) actually and reasonably incurred in connection therewith. Expenses must be advanced to an Indemnitee under certain circumstances.

We have entered into indemnification agreements with each of our directors and officers. These indemnification agreements may require us, among other things, to indemnify our directors and officers for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or officer in any action or proceeding arising out of his or her service as one of our directors or officers, or any of our subsidiaries or any other company or enterprise to which the person provides services at our request.

We maintain a general liability insurance policy that covers certain liabilities of directors and officers of our corporation arising out of claims based on acts or omissions in their capacities as directors or officers.

In any underwriting agreement we enter into in connection with the sale of common stock being registered hereby, the underwriters will agree to indemnify, under certain conditions, us, our directors, our officers and persons who control us within the meaning of the Securities Act of 1933, as amended, or the Securities Act, against certain liabilities.

Item 15. Recent Sales of Unregistered Securities.

Set forth below is information regarding shares of capital stock issued by us within the past three years (before giving effect to our 1-for- reverse stock split). Also included is the consideration received by us for such shares and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

(a) Issuance of Capital Stock.

(1) Series A Convertible Preferred Stock: October 2016—1,598,441 shares for gross proceeds of $799,201.

(2) Series A-1 Convertible Preferred Stock: December 2017—360,000 shares for gross proceeds of $324,000; and March 2018—270,722 shares for gross proceeds of $243,649.

(b) Issuance of Convertible Notes

March 2019—$530,000 principal amount of our Convertible Promissory Notes

(c) Stock Option Grants and Exercises

April 2016—stock options to purchase 60,000 shares of our common stock at $0.10 per share

October 2016—stock options to purchase 30,000 shares of our common stock at $0.10 per share

April 2017—stock options to purchase 186,666 shares of our common stock at $0.10 per share

July 2017—stock options to purchase 30,000 shares of our common stock at $0.10 per share

April 2018—stock options to purchase 173,332 shares of our common stock at $0.18 per share

Also, issuances of shares of common stock upon the exercise of outstanding stock options were as follows:

January to March 2017—we issued 44,764 shares of our common stock for proceeds of $4,395;

May 2017—we issued 25,415 shares of our common stock for proceeds of $4,100; and

May 2018—we issued 20,000 shares of our common stock for proceeds of $2,800.

The offers, sales and issuances of the securities described in paragraphs (a)(1) and (2) and (b) above were exempt from registration in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(a)(2) under the Securities Act and under Regulation D of the Securities Act, relative to transactions by an issuer not involving a public offering.

The grants of stock options and issuances of shares upon exercise thereof described in paragraph (c) above were exempt from registration under the Securities Act in reliance on Rule 701 as offers and sales of securities under written compensatory benefit plans and contracts relating to compensation in compliance with Rule 701. Each of the recipients of securities in any transaction exempt from registration either received or had adequate access, through employment, business or other relationships, to information about us.

All purchasers of securities in transactions exempt from registration pursuant to Regulation D described above represented to us in connection with their purchase that they were "accredited investors" and were acquiring the securities for investment purposes only and not with a view to, or for sale in connection with, any distribution thereof and that they could bear the risks of the investment and could hold the securities for an indefinite period of time. The purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration statement or an available exemption from the registration requirements of the Securities Act.

All of the foregoing securities are deemed restricted securities for purposes of the Securities Act. The certificates representing the issued securities described in this Item 15 included appropriate legends setting forth that the applicable securities have not been registered and reciting the applicable restrictions on transfer. There were no underwriters employed in connection with any of the transactions set forth in this Item 15.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

Exhibit Number	Description of Exhibit
1.1*	Form of Underwriting Agreement
3.1	Amended and Restated Certificate of Incorporation of the Registrant, as amended
3.2*	Form of Restated Certificate of Incorporation of the Registrant, to be in effect upon completion of this offering
3.3	Bylaws of the Registrant
3.4*	Form of Amended and Restated Bylaws of the Registrant, to be in effect upon completion of this offering
4.1*	Specimen Certificate evidencing shares of the Registrant's common stock
5.1*	Opinion of Duane Morris LLP regarding the legality of the securities being registered
10.1+	Amended and Restated Employment Agreement dated as of May 10, 2019 between the Registrant and Maria Maccecchini.
10.2+	Annovis Bio, Inc. 2018 Equity Incentive Plan.
10.3	License Agreement dated as of November 10, 2008 between TorreyPines Therapeutics, Inc. and the Registrant.
10.4	License Agreement Amendment dated November 29, 2011 between Raptor Therapeutics, Inc. and the Registrant.
10.5*	Registration Rights Agreement dated as of December 19, 2014 among the Registrant and the signatories thereto.
10.6	License Agreement Amendment No. 2 effective as of May 2, 2012 between Raptor Therapeutics and the Registrant.
10.7	Investigator-Initiated Clinical Trial Agreement dated June 27, 2016 between The Regents of the University of California and the Registrant.
23.1	Consent of Withum Smith+Brown, PC
23.2*	Consent of Duane Morris LLP (to be included in Exhibit 5.1
24.1	Power of Attorney (included on signature page)

* To be filed by amendment.

\+ Indicates management contract or compensatory plan.

(b) Financial Statement Schedules

See index to financial statements on page F-1. All schedules have been omitted because they are not required or are not applicable.

Item 17. Undertakings.

The undersigned registrant hereby undertakes to provide to the underwriters, at the closing specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act, the registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Berwyn, Commonwealth of Pennsylvania, on July 2, 2019.

ANNOVIS BIO, INC.

By: /s/ MARIA MACCECCHINI

Name: Maria Maccecchini
Title: *President and Chief Executive Officer*

POWER OF ATTORNEY

We, the undersigned officers and directors of Annovis Bio, Inc., hereby severally constitute and appoint Maria Maccecchini and Jeffrey McGroarty, and each of them singly (with full power to each of them to act alone), our true and lawful attorneys-in-fact and agents, with full power of substitution and re-substitution in each of them for him or her and in his or her name, place and stead, and in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement (or any other registration statement for the same offering that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933), and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as full to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities held on the dates indicated.

Signature	Title	Date
/s/ MARIA MACCECCHINI Maria Maccecchini	President and Chief Executive Officer (principal executive officer)	July 2, 2019
/s/ JEFFREY MCGROARTY Jeffrey McGroarty	Chief Financial Officer (principal financial and accounting officer)	July 2, 2019
/s/ MICHAEL HOFFMAN Michael Hoffman	Chairman of the Board and Director	July 2, 2019
/s/ CLAUDINE BRUCK Claudine Bruck	Director	July 2, 2019

Signature	Title	Date
/s/ ROBERT WHELAN Robert Whelan	Director	July 2, 2019
/s/ MARK WHITE Mark White	Director	July 2, 2019

Exhibit 3.1

CERTIFICATE OF INCORPORATION
OF
QR PHARMA, INC.

The undersigned, for the purpose of forming a corporation pursuant to the provisions of the General Corporation Law of the State of Delaware (the "DGCL"), does hereby certify as follows:

ARTICLE I

The name of the corporation is QR Pharma, Inc. (the "Corporation").

ARTICLE II

The address of the Corporation's registered office in the State of Delaware is 15 East North Street, Dover, Delaware 19901 in the County of Kent. The name of the Corporation's registered agent at such address is Capitol Corporate Services, Inc.

ARTICLE III

The purpose of the Corporation is to engage in any lawful act or activity for which corporations may be organized under the DGCL.

ARTICLE IV

A. Classes of Stock . The aggregate number of shares which the Corporation shall have the authority to issue is 8,000,000 shares, divided into 6,000,000 shares of Common Stock, par value $.0001 per share (the "Common Stock") and 2,000,000 shares of Preferred Stock, par value $.0001 per share (the "Preferred Stock").

B. Preferred Stock . The Board of Directors of the Corporation (the "Board") shall have the authority to the fullest extent permitted under the DGCL to adopt by resolution from time to time one or more certificates of designation providing for the designation of one or more classes or series of the Preferred Stock and the voting powers, whether full or limited or no voting powers, and such designations, preferences and relative, participating, optional or other special rights and qualifications, limitations or restrictions thereof, and to fix or alter the number of shares comprising any such class or series, subject to any requirements of the DGCL and this Certificate of Incorporation, as amended from time to time (the "Certificate"). Subject to compliance with applicable protective voting rights that may be granted to the Preferred Stock or series thereof in certificates of designation or the Certificate, but notwithstanding any other rights of the Preferred Stock or of series thereof, the rights, preferences, privileges and restrictions of any such additional series or classes of the Preferred Stock may be subordinated to, pari passu with (including, without limitation, in provisions regarding dividend, liquidation and acquisition preferences and/or approval of matters by vote or written consent), or senior to any of those of any present or future class or series of the Preferred Stock or the Common Stock.

C. Common Stock . The Common Stock shall have the following relative rights, preferences, qualifications, privileges, limitations and restrictions:

1. **Dividend Rights** . Subject to the rights of holders of all classes of stock at the time outstanding having rights that are prior to or pari passu with the holders of the Common Stock as to dividends, the holders of the Common Stock shall be entitled to receive, when and as declared by the Board, out of any assets of the Corporation legally available therefor, such dividends as may be declared from time to time by the Board.

2. **Liquidation Rights** . Subject to the rights of holders of all classes of stock at the time outstanding having rights that are prior to or pari passu with the holders of the Common Stock as to liquidation, upon the liquidation, dissolution or winding up of the Corporation, the assets of the Corporation shall be distributed to the holders of Common Stock.

3 **.** **Voting Rights** . The holders of Common Stock shall have the right to one vote for each share of Common Stock, shall be entitled to vote upon such matters and in such manner as may be provided by law and shall be entitled to notice of any meetings of stockholders in accordance with the By-Laws of the Corporation. The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of shares of stock of the Corporation representing a majority of the votes represented by all outstanding shares of stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the DGCL.

ARTICLE V

Except as otherwise provided in the Certificate, in furtherance and not in limitation of the powers conferred by statute, the Board is expressly authorized to make, repeal, alter, amend and rescind any or all of the By-Laws of the Corporation.

ARTICLE VI

A director of the Corporation shall have no personal liability to the Corporation or its stockholders for monetary damages for breach of fiduciary duty as a director except to the extent that Section 102(b)(7) (or any successor provision) of the DGCL expressly provides that the liability of a director may not be eliminated or limited. No amendment or repeal of this Article VI shall apply to or have any effect on the liability or alleged liability of any director of the Corporation for or with respect to any acts or omissions of such director occurring prior to such amendment or repeal.

ARTICLE VII

Whenever a compromise or arrangement is proposed between the Corporation and its creditors or any class of them and/or between the Corporation and its stockholders or any class of them, any court of equitable jurisdiction within the State of Delaware may, on the application in a summary way of the Corporation or of any creditor or stockholder thereof or on the application of any receiver or receivers appointed for the Corporation under the provisions of Section 291 of Title 8 of the Delaware Code or on the application of trustees in dissolution or of any receiver or receivers appointed for the Corporation under the provisions of Section 279 of Title 8 of the Delaware Code, order a meeting of the creditors or class of creditors, and/or of the stockholders or class of stockholders of the Corporation, as the case may be, to be summoned in such manner as the said court directs. If a majority in number representing three-fourths in value of the

creditors or class of creditors, and/or of the stockholders or class of stockholders of the Corporation, as the case may be, agree to any compromise or arrangement and to any reorganization of the Corporation as consequence of such compromise or arrangement, such compromise or arrangement and such reorganization shall, if sanctioned by the court to which the said application has been made, be binding on all the creditors or class of creditors, and/or on all the stockholders or class of stockholders of the Corporation, as the case may be, and also on the Corporation.

ARTICLE VIII

Meetings of stockholders may be held within or without the State of Delaware, as the By-Laws of the Corporation may provide. The books of the Corporation may be kept outside the State of Delaware at such place or places as may be designated from time to time by the Board or in the By-Laws of the Corporation. Subject to any additional vote required by the Certificate, the number of directors of the Corporation shall be determined in a manner set forth in the By-Laws of the Corporation. Election of directors need not be by written ballot unless the By-Laws of the Corporation so provide.

ARTICLE IX

Unless the Certificate is amended or repealed with respect to this Article IX or unless the By-Laws of the Corporation designate otherwise, the Corporation expressly elects not to be governed by Section 203 of the DGCL.

ARTICLE X

A. Indemnification . Each person who was or is made a party or is threatened to be made a party to or is otherwise involved in any action, suit or proceeding, whether civil, criminal administrative or investigative (hereinafter a "proceeding"), by reason of the fact that he or she is or was a director or officer of the Corporation or any of its direct or indirect subsidiaries or is or was serving at the request of the Corporation as a director, officer, employee or agent of any other corporation or of a partnership, joint venture, trust or other enterprise, including service with respect to an employee benefit plan (hereinafter an "indemnitee"), whether the basis of such proceeding is alleged action in an official capacity as a director or officer or in any other capacity while serving as a director or officer, shall be indemnified and be held harmless by the Corporation to the fullest extent permitted by the DGCL, as the same exists or may hereafter be amended (but, in the case of any such amendment, and unless the DGCL or other applicable law otherwise requires, only to the extent that such amendment permits the Corporation to provide broader indemnification rights than permitted prior thereto), against all expense, liability and loss (including attorneys' fees, judgments, fines, excise or other taxes assessed with respect to an employee benefit plan, penalties, and amounts paid in settlement) reasonably incurred or suffered by such indemnitee in connection therewith, and such indemnification shall continue as to an indemnitee who has ceased to be a director or officer and shall inure to the benefit of the indemnitee's heirs, executors, and administrators; provided, however, that, except as provided in Section C of this Article X with respect to proceedings to enforce rights to indemnification, the Corporation shall indemnify any such indemnitee in connection with a proceeding (or part

thereof) initiated by such indemnitee only if such proceeding (or part thereof) was authorized by the Board.

B. Payment of Expenses . The right to indemnification conferred in Section A of this Article X shall include the right to be paid by the Corporation the expenses incurred in defending any proceeding for which such right to indemnification is applicable in advance of its final disposition (hereinafter in "advancement of expenses"); provided, however, that, if the DGCL requires, an advancement of expenses incurred by an indemnitee in his or her capacity as a director or officer (and not in any other capacity in which service was or is rendered by such indemnitee, including, without limitation, service to an employee benefit plan) shall be made only upon delivery to the Corporation of an undertaking (hereinafter an "undertaking"), by or on behalf of such indemnitee, to repay all amounts so advanced if it shall ultimately be determined by final judicial decision from which there is no further right to appeal (hereinafter a "final adjudication") that such indemnitee is not entitled to be indemnified for such expenses under this Article X or otherwise.

C. Claims . The rights to indemnification and to the advancement of expenses conferred in Sections A and B of this Article X shall be contract rights. If a claim under Section A or B of this Article X is not paid in full by the Corporation within 60 days after a written claim has been received by the Corporation, except in the case of a claim for an advancement of expenses, in which case the applicable period shall be 20 days, the indemnitee may at any time thereafter bring suit against the Corporation to recover the unpaid amount of the claim. If successful in whole or in part in any such suit, or in a suit brought by the Corporation to recover an advancement of expenses pursuant to the terms of an undertaking, the indemnitee shall be entitled to be paid also the expense of prosecuting or defending such suit. In (i) any suit brought by the indemnitee to enforce a right to indemnification hereunder (but not in a suit brought by an indemnitee to enforce a right to an advancement of expenses), it shall be a defense that the indemnitee has not met any applicable standard for indemnification set forth in the DGCL, and (ii) any suit by the Corporation to recover an advancement of expenses pursuant to the terms of an undertaking, the Corporation shall be entitled to recover such expenses upon a final adjudication that the indemnitee has not met any applicable standard for indemnification set forth in the DGCL. Neither the failure of the Corporation (including the Board, its independent legal counsel or its stockholders) to have made a determination prior to the commencement of such suit that indemnification of the indemnitee is proper in the circumstances because the indemnitee has met the applicable standard of conduct set forth in the DGCL, nor an actual determination by the Corporation (including the Board, its independent legal counsel, or its stockholders) that the indemnitee has not met such applicable standard of conduct, shall create a presumption that the indemnitee has not met the applicable standard of conduct or, in the case of such a suit brought by the indemnitee, be a defense to such suit. In any suit brought by the indemnitee to enforce a right to indemnification or to an advancement of expenses hereunder, or by the Corporation to recover an advancement of expenses pursuant to the terms of an undertaking, the burden of proving that the indemnitee is not entitled to be indemnified, or to such advancement of expenses under this Article X or otherwise, shall be on the Corporation.

D. Nonexclusive Rights . The rights to indemnification and to the advancement of expenses conferred in this Article X shall not be exclusive of any other right that any person may

have or hereafter acquire under the Certificate, any statutes, by-law, agreement, vote of stockholders or disinterested directors, or otherwise.

E. Insurance . The Corporation may maintain insurance, at its expense, to protect itself and any director, officer, employee or agent of the Corporation or another corporation, partnership, joint venture, trust or other enterprise against any expense, liability or loss, whether or not the Corporation would have the power to indemnify such person against such expense, liability or loss under the DGCL.

F. Other Services . The Corporation's obligation, if any, to indemnify any person who was or is serving as a director, officer, employee or agent of any direct or indirect subsidiary of the Corporation or, at the request of the Corporation, of any other corporation or of a partnership, joint venture, trust or other enterprise shall be reduced by any amount such person may collect as indemnification from such other corporation, partnership, joint venture, trust or other enterprise.

G. Amendment or Repeal . Any amendment, repeal or modification of the foregoing provision of this Article X shall not adversely affect any right or protection of a director or officer existing at the time of, or increase the liability of any director of the Corporation with respect to any acts or omissions of such director or officer or occurring prior to, such amendment, repeal, modification or adoption.

ARTICLE XI

The Corporation shall have perpetual existence.

ARTICLE XII

The name and mailing address of the incorporator is as follows:

Ann Marie Bruski
c/o Duane Morris LLP
30 South 17th Street
Philadelphia, PA 19103-4196

I, the undersigned, for the purpose of forming a corporation under the laws of the State of Delaware, do make, file and record this Certificate of Incorporation, and, accordingly, have hereunto set my hand this 29th day of April, 2008.

/s/ Ann Marie Bruski
Ann Marie Bruski

CERTIFICATE OF AMENDMENT

OF

CERTIFICATE OF INCORPORATION

OF

QR PHARMA, INC.

QR Pharma, Inc., a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the "DGCL"),

DOES HEREBY CERTIFY THAT:

FIRST: The Board of Directors (the "Board") of QR Pharma, Inc. (the "Corporation"), at a meeting duly called and held on December 16, 2014, duly adopted the following resolution setting forth a proposed amendment of the Certificate of Incorporation of the Corporation, declaring such amendment to be advisable and calling for consideration thereof by the stockholders of the Corporation. The resolution setting forth the proposed amendment is as follows:

RESOLVED, that Article IV of the Certificate of Incorporation of the Corporation shall be amended and restated in its entirety to provide as set forth on Exhibit A hereto.

SECOND: Thereafter, in accordance with a resolution of the Board, the holders of a majority of the outstanding shares of all capital stock of the Corporation voted in favor of the amendment.

THIRD: The amendment was duly adopted in accordance with the provisions of Section 242 of the DGCL. With respect to such adoption, written consent has been given by the stockholders of the Corporation in accordance with the provisions of Section 228 of the DGCL, and written notice has been given as provided in Section 228.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the Corporation has caused this Certificate of Amendment to be executed this 19th day of December, 2014.

QR PHARMA, INC.

By: /s/ Maria L. Maccecchini
Name: Maria L. Maccecchini
Title: President and CEO

EXHIBIT A

ARTICLE IV

The total number of shares of all classes of stock that the Corporation shall have authority to issue is Thirteen Million (13,000,000) shares, divided into Eight Million (8,000,000) shares of Common Stock, par value $.0001 per share (the "Common Stock") and Five Million (5,000,000) shares of Preferred Stock, par value $.0001 per share (the "Preferred Stock").

Upon the time that this Certificate of Amendment becomes effective pursuant to the DGCL (the "Effective Time"), without any further action on the part of the Corporation or its stockholders, all shares of the Corporation's Common Stock that were authorized and issued and outstanding immediately prior to the Effective Time (the "Old Common Stock") shall be combined into shares of Common Stock at the rate of one share of Common Stock for each 5.5387 shares of Old Common Stock. At the Effective Time, the certificates representing shares of the Old Common Stock shall be deemed cancelled and shall not be recognized as outstanding on the books of the Corporation for any purpose. Thereupon, there shall be issued to each holder of Old Common Stock in such holder's name and at the address as shown on the records of the Corporation, a certificate for the number of shares of Common Stock into which the shares of Old Common Stock were combined; provided, however, that the Corporation shall not issue any fractional shares of Common Stock but shall round the number of shares of Common Stock to which each holder of Old Common Stock would otherwise be entitled so that any portion of a share equal to less than one whole share is rounded up. Whether or not fractional shares would be issuable shall be determined on the basis of the total number of shares of Old Common Stock owned by the applicable holder and the aggregate number of shares of Common Stock issuable upon the foregoing combination. All of the outstanding share amounts, amounts per share and per share numbers for the Common Stock set forth in the Corporation's Certificate of Incorporation shall be appropriately adjusted to give effect to the foregoing combination.

Subject to the foregoing, the following is a statement of the designations and the powers, privileges and rights, and the qualifications, limitations or restrictions thereof in respect of each class of capital stock of the Corporation.

A. COMMON STOCK

1. Dividend Rights . Subject to the rights of holders of Preferred Stock as to dividends, the holders of the Common Stock shall be entitled to receive, when and as declared by the Board, out of any assets of the Corporation legally available therefor, such dividends as may be declared from time to time by the Board.

2. Liquidation Rights . Subject to the rights of holders of Preferred Stock as to liquidation, upon the liquidation, dissolution or winding up of the Corporation, the assets of the Corporation shall be distributed to the holders of Common Stock.

3. Voting . The holders of the Common Stock are entitled to one vote for each share of Common Stock held at all meetings of stockholders (and written actions in lieu of meetings); provided, however, that, except as otherwise required by law, holders of Common Stock, as such, shall not be entitled to vote on any amendment to the Certificate of Incorporation (as

amended from time to time, the "Certificate of Incorporation") that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together with the holders of one or more other such series, to vote thereon pursuant to the Certificate of Incorporation or pursuant to the DGCL. There shall be no cumulative voting. The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by (in addition to any vote of the holders of one or more series of Preferred Stock that may be required by the terms of the Certificate of Incorporation) the affirmative vote of the holders of shares of capital stock of the Corporation representing a majority of the votes represented by all outstanding shares of capital stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the DGCL.

B. PREFERRED STOCK

The Board shall have the authority to the fullest extent permitted under the DGCL to adopt by resolution from time to time one or more certificates of designation providing for the designation of one or more classes or series of Preferred Stock and the voting powers, whether full or limited or no voting powers, and such designations, preferences and relative, participating, optional or other special rights and qualifications, limitations or restrictions thereof, and to fix or alter the number of shares comprising any such class or series, subject to any requirements of the DGCL and this Certificate of Incorporation. Subject to compliance with applicable protective voting rights that may be granted to the Preferred Stock or a series thereof in certificates of designation or this Certificate of Incorporation, but notwithstanding any other rights of the Preferred Stock or of a series thereof, the rights, preferences, privileges and restrictions of any such additional series or classes of Preferred Stock may be subordinated to, pari passu with (including, without limitation, in provisions regarding dividend, liquidation and acquisition preferences and/or approval of matters by vote or written consent) or senior to any of those of any present or future class or series of the Preferred Stock or the Common Stock.

Four Million (4,000,000) shares of the authorized and unissued Preferred Stock of the Corporation are hereby designated "Series A Preferred Stock" with the following rights, preferences, powers, privileges and restrictions, qualifications and limitations. The Series A Preferred Stock shall rank (a) senior to the Common Stock and any other class or series of capital stock of the Corporation either specifically ranking by its terms junior to the Series A Preferred Stock or not specifically ranking by its terms senior to or on parity with the Series A Preferred Stock, (b) on parity with any class or series of capital stock of the Corporation specifically ranking by its terms on parity with the Series A Preferred Stock and (c) junior to any class or series of capital stock of the Corporation specifically ranking by its terms senior to the Series A Preferred Stock, in each case, as to payment of dividends, distributions of assets upon a Liquidation or Liquidity Event or otherwise (each as defined herein or in any certificate of designation adopted as provided above and filed in accordance with the requirements of the DGCL and then in effect). Unless otherwise indicated, references to "Sections" or "Subsections" in this Part B of this Article IV refer to sections and subsections of Part B of this Article IV.

1. Dividend Rights . The holders of the outstanding shares of the Series A Preferred Stock (each, a "Series A Holder" and, collectively, the "Series A Holders") shall be entitled to

receive, when and as declared by the Board, out of any assets of the Corporation legally available therefor, such dividends as may be declared from time to time by the Board.

2. Liquidation, Dissolution or Winding Up; Certain Mergers, Consolidations and Asset Sales .

2.1 Treatment at Liquidation, Dissolution or Winding Up .

2.1.1 Liquidation Preference . In the event of any liquidation, dissolution or winding up of the Corporation (each such event, a "Liquidation"), the Series A Holders shall be entitled to be paid out of the assets of the Corporation available for distribution to holders of the Corporation's capital stock of all classes, whether such assets are capital, surplus or earnings ("Available Assets"), before any distribution or payment is made to any holders of Common Stock, an amount per share of Series A Preferred Stock equal to the Series A Original Issue Price plus an amount equal to all declared but unpaid dividends on such share of Series A Preferred Stock, whether or not declared (as it may be adjusted in the event of any stock dividend, split, combination, reclassification, recapitalization or other similar event with respect to such share) (the "Series A Liquidation Preference"). If, upon Liquidation, the Available Assets shall be insufficient to pay the full amount of the Series A Liquidation Preference, the Series A Holders shall share in any distribution of Available Assets pro rata in proportion to the respective Series A Liquidation Preference that would otherwise be payable upon a Liquidation with respect to the outstanding shares of the Series A Preferred Stock if the Series A Liquidation Preference payable with respect to such shares were paid in full.

2.1.2 Distribution of Remaining Available Assets . After the payment in full of the Series A Liquidation Preference pursuant to Subsection 2.1.1 , the remaining Available Assets, if any, shall be distributed among the holders of Common Stock in proportion to the number of shares of Common Stock then held by such holders of Common Stock, and the Series A Holders shall have no further rights thereto in respect of the shares of Series A Preferred Stock owned by them.

2.2 Treatment of a Liquidity Event . Unless the holders of at least of majority of the outstanding shares of Series A Preferred Stock elect otherwise by written notice to the Corporation at least ten days prior to the occurrence of a Liquidity Event stating that such Liquidity Event shall not be treated as a Liquidation, a Liquidity Event shall be treated as a Liquidation. As used herein, "Liquidity Event" means any sale, license or other transfer, in a single transaction or series of related transactions, of all or substantially all of the assets of the Corporation, or transaction or series of transactions involving the Corporation, or its securities, whether by consolidation, merger, purchase of shares of capital stock or other reorganization or combination or otherwise, in which the holders of the Corporation's outstanding shares of capital stock immediately prior to such transaction own, immediately after such transaction, securities representing less than 50% of the voting power of the entity surviving such transaction, except to the extent resulting from the issuance and sale of Series A Preferred Stock. For purposes of this Section 2 , the amount of Available Assets shall be determined as follows:

(a) insofar as Available Assets consist of cash, they shall be computed at the aggregate amount of cash held by the Corporation at the time of the liquidation, dissolution or winding up; and

(b) insofar as Available Assets consist of property other than cash, they shall be computed at the fair market value thereof at the time of the liquidation, dissolution or winding up, as determined in good faith by the Board.

3. Voting .

3.1 General . Except as otherwise stated herein, on any matter presented to the stockholders of the Corporation for their action or consideration at any meeting of stockholders of the Corporation (or by written consent of stockholders in lieu of meeting), each holder of outstanding shares of Series A Preferred Stock shall be entitled to cast the number of votes equal to the number of whole shares of Common Stock into which the shares of Series A Preferred Stock held by such holder are convertible as of the record date for determining stockholders entitled to vote on such matter. Except as provided by law or by the other provisions of the Certificate of Incorporation, Series A Holders shall vote together with the holders of Common Stock and all other series and classes of stock permitted to vote with the Common Stock on all matters submitted to a vote of the holders of the Common Stock as a single class.

3.2 Election of Directors .

3.2.1 Preferred Directors . The holders of record of Series A Preferred Stock, voting as a separate class, shall be entitled to elect three directors of the Corporation (the "Preferred Directors"). The Preferred Directors may be removed by, and only by, the affirmative vote of the holders of a majority of the Series A Preferred Stock, voting as a separate class, given either at a special meeting of such stockholders duly called for that purpose or pursuant to a written consent of such stockholders.

3.2.2 Common Directors . The holders of record of Common Stock, voting as a separate class, shall be entitled to elect one director of the Corporation (the "Common Director"). The Common Director may be removed by, and only by, the affirmative vote of the holders of a majority of the Common Stock, voting as a separate class, given either at a special meeting of such stockholders duly called for that purpose or pursuant to a written consent of such stockholders.

3.2.3 Remaining Directors . The holders of record of Common Stock and Preferred Stock, voting together as a single class and on an as-converted basis, shall be entitled to elect the remaining directors of the Corporation (the "Remaining Directors"). The Remaining Directors may be removed by, and only by, the affirmative vote of the holders of a majority of the Preferred Stock and Common Stock, voting together as a single class, given either at a special meeting of such stockholders duly called for that purpose or pursuant to a written consent of such stockholders.

3.2.4 Quorum . At any meeting held for the purpose of electing a director, the presence in person or by proxy of the holders of at least a majority of the outstanding shares of the class or series entitled to elect such director shall constitute a quorum

for the purpose of electing such director. A vacancy in any directorship filled by the holders of any class or series shall be filled only by vote or written consent in lieu of a meeting of the holders of such class or series.

3.3 Series A Preferred Stock Protective Provisions. At any time when at least One Million (1,000,000) shares of Series A Preferred Stock (as adjusted in the event of any stock dividend, split, combination, reclassification, recapitalization or other similar event with respect to such shares) are issued and outstanding, the Corporation shall not, either directly or indirectly by amendment, merger, consolidation or otherwise, take any of the following actions, without (in addition to any other vote required by law or the Certificate of Incorporation) the consent of the holders of at least a majority of the then outstanding shares of Series A Preferred Stock:

3.3.1 amend the Certificate of Incorporation in a manner that would alter or change the rights, preferences or privileges of the Series A Preferred Stock so as to adversely affect such series, or increase or decrease the number of authorized shares thereof;

3.3.2 create any new series or class of shares having a preference or priority as to dividends or assets superior to or on a parity with the Series A Preferred Stock;

3.3.3 apply any of its assets to the redemption or acquisition of any shares of Common Stock, except from employees, advisors, officers, directors, consultants and service providers of the Corporation on terms approved by the Board; or

3.3.4 authorize or effect the payment of any dividend to any holders of any class or series of capital stock (other than a stock dividend payable solely in Common Stock).

4. Optional Conversion.

The Series A Holders shall have conversion rights as follows (the "Conversion Rights"):

4.1 Right to Convert.

4.1.1 Conversion Ratio. Each share of Series A Preferred Stock shall be convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, into such number of fully paid and nonassessable shares of Common Stock as is determined by dividing the Series A Original Issue Price by the Series A Conversion Price (as defined below) in effect at the time of conversion. The "Series A Conversion Price" shall initially be equal to $0.50. Such initial Series A Conversion Price, and the rate at which shares of Series A Preferred Stock may be converted into shares of Common Stock, shall be subject to adjustment as provided below.

4.1.2 Termination of Conversion Rights. In the event of a liquidation, dissolution or winding up of the Corporation or a Liquidity Event, the Conversion Rights shall terminate at the close of business on the last full day preceding the date fixed for the payment of any such amounts distributable on such event to the Series A Holders.

4.2 Fractional Shares . No fractional shares of Common Stock shall be issued upon conversion of the Series A Preferred Stock. In lieu of any fractional shares to which the holder would otherwise be entitled, the Corporation shall round the number of shares of Common Stock to which such holder would otherwise be entitled so that any portion of a share that is equal to less than one whole share is rounded up. Whether or not fractional shares would be issuable upon such conversion shall be determined on the basis of the total number of shares of Series A Preferred Stock the holder is at the time converting into Common Stock and the aggregate number of shares of Common Stock issuable upon such conversion.

4.3 Mechanics of Conversion .

4.3.1 Notice of Conversion . In order for a registered Series A Holder to voluntarily convert shares of Series A Preferred Stock into shares of Common Stock, such holder shall surrender the certificate or certificates for such shares of Series A Preferred Stock (or, if such holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate), at the office of the transfer agent for the Series A Preferred Stock (or at the principal office of the Corporation if the Corporation serves as its own transfer agent), together with written notice that such holder elects to convert all or any number of the shares of the Series A Preferred Stock represented by such certificate or certificates and, if applicable, any event on which such conversion is contingent. Such notice shall state such holder's name or the names of the nominees in which such holder wishes the certificate or certificates for shares of Common Stock to be issued. If required by the Corporation, certificates surrendered for conversion shall be endorsed or accompanied by a written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or his, her or its attorney duly authorized in writing. The close of business on the date of receipt by the transfer agent (or by the Corporation if the Corporation serves as its own transfer agent) of such certificates (or lost certificate affidavit and agreement) and notice shall be the time of conversion (the "Conversion Time"), and the shares of Common Stock issuable upon conversion of the shares represented by such certificate shall be deemed to be outstanding of record as of such date. The Corporation shall, as soon as practicable after the Conversion Time: (i) issue and deliver to such Series A Holder, or to such holder's nominees, a certificate or certificates for the number of full shares of Common Stock issuable upon such conversion in accordance with the provisions hereof and a certificate for the number (if any) of the shares of Series A Preferred Stock represented by the surrendered certificate that were not converted into Common Stock, (ii) pay in cash such amount as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and (iii) pay all declared but unpaid dividends on the shares of Series A Preferred Stock converted.

4.3.2 Reservation of Shares . The Corporation shall at all times when the Series A Preferred Stock shall be outstanding, reserve and keep available out of its authorized but unissued capital stock, for the purpose of effecting the conversion of the Series A Preferred Stock, such number of its duly authorized shares of Common Stock as shall from time to time be sufficient to effect the conversion of all outstanding Series A Preferred Stock; and if at any time the number of authorized but unissued shares of Common Stock shall not be sufficient to effect the conversion of all then outstanding shares of the Series A Preferred Stock, the Corporation

shall take such corporate action as may be necessary to increase its authorized but unissued shares of Common Stock to such number of shares as shall be sufficient for such purposes, including, without limitation, seeking to obtain the requisite stockholder approval of any necessary amendment to the Certificate of Incorporation. Before taking any action that would cause an adjustment reducing the Series A Conversion Price below the then par value of the shares of Common Stock issuable upon conversion of the Series A Preferred Stock, the Corporation shall take any corporate action that may, in the opinion of its counsel, be necessary in order that the Corporation may validly and legally issue fully paid and nonassessable shares of Common Stock at such adjusted Series A Conversion Price.

4.3.3 Effect of Conversion . All shares of Series A Preferred Stock that shall have been surrendered for conversion as herein provided shall no longer be deemed to be outstanding and all rights with respect to such shares shall immediately cease and terminate at the Conversion Time, except only the right of the holders thereof to receive shares of Common Stock in exchange therefor, to receive payment in lieu of any fraction of a share otherwise issuable upon such conversion as provided in Subsection 4.2 and to receive payment of any declared dividends that remain unpaid thereon. Any shares of Series A Preferred Stock so converted shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Series A Preferred Stock accordingly.

4.3.4 No Further Adjustment . Upon any such conversion, no adjustment to the Series A Conversion Price shall be made for any declared but unpaid dividends on the Series A Preferred Stock surrendered for conversion or on the Common Stock delivered upon conversion.

4.4 Adjustments to Series A Conversion Price for Diluting Issues .

4.4.1 Special Definitions . For purposes of this Article IV, the following definitions shall apply:

(a) "Option" shall mean rights, options or warrants to subscribe for, purchase or otherwise acquire Common Stock or Convertible Securities.

(b) "Series A Original Issue Date" shall mean the date on which the first share of Series A Preferred Stock was issued.

(c) "Convertible Securities" shall mean any evidences of indebtedness, shares or other securities directly or indirectly convertible into or exchangeable for Common Stock, but excluding Options.

(d) "Additional Shares of Common Stock" shall mean all shares of Common Stock issued (or, pursuant to Subsection 4.4.3 below, deemed to be issued) by the Corporation after the Series A Original Issue Date, other than (1) the following shares of Common Stock and (2) shares of Common Stock deemed issued pursuant to the following (collectively, "Exempted Securities"):

(i) shares of Common Stock, Options or Convertible Securities issued as a dividend or distribution on, or upon conversion of, Series A Preferred Stock;

(ii) shares of Common Stock, Options or Convertible Securities issued by reason of a dividend, stock split, split-up or other distribution on shares of Common Stock that is covered by Subsection 4.5, 4.6, 4.7 or 4.8;

(iii) shares of Common Stock or Options issued to employees, officers or directors of, or consultants or advisors to, and other service providers of, the Corporation or any of its subsidiaries pursuant to any equity incentive plan, option plan or other compensatory plan, program or agreement approved by the Board;

(iv) shares of Common Stock or Convertible Securities actually issued upon the exercise of Options or shares of Common Stock actually issued upon the conversion or exchange of Convertible Securities;

(v) shares of Common Stock, Options or Convertible Securities issued to banks, equipment lessors or other financial institutions, or to real property lessors, pursuant to a debt financing, equipment leasing or real property leasing transaction approved by the Board;

(vi) shares of Common Stock, Options or Convertible Securities issued pursuant to the acquisition of another entity by the Corporation by merger, purchase of substantially all of the assets or other reorganization or pursuant to a joint venture, partnership, marketing, technology transfer or license or development arrangement or other strategic transaction, provided that the respective issuance is approved by the Board;

(vii) shares of Series A Preferred Stock issued under the Series A Preferred Stock Purchase Agreement and the Conversion Agreement and Amendment, each entered into among the Corporation and the investors parties thereto as of December 19, 2014, as amended, and

(viii) shares of Common Stock, Options or Convertible Securities issued in connection with the closing of the sale of shares of the Corporation's capital stock in an underwritten public offering by the Corporation under the Securities Exchange Act of 1934.

4.4.2 No Adjustment of Series A Conversion Price . No adjustment in the Series A Conversion Price shall be made as the result of the issuance or deemed issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of at least a majority of the then outstanding shares of Series A Preferred Stock agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock.

4.4.3 Deemed Issue of Additional Shares of Common Stock .

(a) If the Corporation at any time or from time to time after the Series A Original Issue Date shall issue any Options or Convertible Securities (excluding Options or Convertible Securities that are themselves Exempted Securities (as defined in Subsection 4.4.1) or shall fix a record date for the determination of holders of any class of securities entitled to receive any such Options or Convertible Securities, then the maximum number of shares of Common Stock (as set forth in the instrument relating thereto, assuming the satisfaction of any conditions to exercisability, convertibility or exchangeability but without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or, in the case of Convertible Securities and Options therefor, the conversion or exchange of such Convertible Securities, shall be deemed to be Additional Shares of Common Stock issued as of the time of such issue or, in case such a record date shall have been fixed, as of the close of business on such record date.

(b) If the terms of any Option or Convertible Security, the issuance of which resulted in an adjustment to the Series A Conversion Price pursuant to the terms of Subsection 4.4.4, are revised as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase or decrease in the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any such Option or Convertible Security or (2) any increase or decrease in the consideration payable to the Corporation upon such exercise, conversion and/or exchange, then, effective upon such increase or decrease becoming effective, the Series A Conversion Price computed upon the original issue of such Option or Convertible Security (or upon the occurrence of a record date with respect thereto) shall be readjusted to such Series A Conversion Price as would have been obtained had such revised terms been in effect upon the original date of issuance of such Option or Convertible Security. Notwithstanding the foregoing, no readjustment pursuant to this clause (b) shall have the effect of increasing the Series A Conversion Price to an amount that exceeds the lower of (i) the Series A Conversion Price in effect immediately prior to the original adjustment made as a result of the issuance of such Option or Convertible Security, or (ii) the Series A Conversion Price that would have resulted from any issuances of Additional Shares of Common Stock (other than deemed issuances of Additional Shares of Common Stock as a result of the issuance of such Option or Convertible Security) between the original adjustment date and such readjustment date.

(c) If the terms of any Option or Convertible Security (excluding Options or Convertible Securities that are themselves Exempted Securities), the issuance of which did not result in an adjustment to the Series A Conversion Price pursuant to the terms of Subsection 4.4.4 (either because the consideration per share (determined pursuant to Subsection 4.4.5) of the Additional Shares of Common Stock subject thereto was equal to or greater than the Series A Conversion Price then in effect, or because such Option or Convertible Security was issued before the Series A Original Issue Date), are revised after the Series A Original Issue Date as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security)

to provide for either (1) any increase in the number of shares of Common Stock issuable upon the exercise, conversion or exchange of any such Option or Convertible Security or (2) any decrease in the consideration payable to the Corporation upon such exercise, conversion or exchange, then such Option or Convertible Security, as so amended or adjusted, and the Additional Shares of Common Stock subject thereto (determined in the manner provided in Subsection 4.4.3(a)) shall be deemed to have been issued effective upon such increase or decrease becoming effective.

(d) Upon the expiration or termination of any unexercised Option or unconverted or unexchanged Convertible Security (or portion thereof) that resulted (either upon its original issuance or upon a revision of its terms) in an adjustment to the Series A Conversion Price pursuant to the terms of Subsection 4.4.4, the Series A Conversion Price shall be readjusted to such Series A Conversion Price as would have obtained had such Option or Convertible Security (or portion thereof) never been issued.

(e) If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, is calculable at the time such Option or Convertible Security is issued or amended but is subject to adjustment based upon subsequent events, any adjustment to the Series A Conversion Price provided for in this Subsection 4.4.3 shall be effected at the time of such issuance or amendment based on such number of shares or amount of consideration without regard to any provisions for subsequent adjustments (and any subsequent adjustments shall be treated as provided in clauses (b) and (c) of this Subsection 4.4.3). If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, cannot be calculated at all at the time such Option or Convertible Security is issued or amended, any adjustment to the Series A Conversion Price that would result under the terms of this Subsection 4.4.3 at the time of such issuance or amendment shall instead be effected at the time such number of shares and/or amount of consideration is first calculable (even if subject to subsequent adjustments), assuming for purposes of calculating such adjustment to the Series A Conversion Price that such issuance or amendment took place at the time such calculation can first be made.

4.4.4 Adjustment of Series A Conversion Price upon Issuance of Additional Shares of Common Stock . In the event the Corporation shall at any time after the Series A Original Issue Date issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Subsection 4.4.3), without consideration or for a consideration per share less than the Series A Conversion Price in effect immediately prior to such issue, then the Series A Conversion Price shall be reduced, concurrently with such issue, to a price (calculated to the nearest one-hundredth of a cent) as follows:

(a) Until December 19, 2015 (the “Full Ratchet Termination Date”), equal to the consideration per share received or deemed to have been received by the Corporation in such issuance; and

(b) after the Full Ratchet Termination Date, in accordance with the following formula:

$$CP_2 = CP_1 * ((A + B) \div (A + C)).$$

For purposes of the foregoing formula, the following definitions shall apply:

(i) "CP_2" shall mean the Series A Conversion Price in effect immediately after such issue of Additional Shares of Common Stock;

(ii) "CP_1" shall mean the Series A Conversion Price in effect immediately prior to such issue of Additional Shares of Common Stock;

(iii) "A" shall mean the number of shares of Common Stock outstanding immediately prior to such issue of Additional Shares of Common Stock (treating for this purpose as outstanding all shares of Common Stock issuable upon exercise of Options outstanding immediately prior to such issue or upon conversion or exchange of Convertible Securities (including the Series A Preferred Stock) outstanding (assuming exercise of any outstanding Options therefor) immediately prior to such issue);

(iv) "B" shall mean the number of shares of Common Stock that would have been issued if such Additional Shares of Common Stock had been issued at a price per share equal to CP_1 (determined by dividing the aggregate consideration received by the Corporation in respect of such issue by CP_1); and

(v) "C" shall mean the number of such Additional Shares of Common Stock issued in such transaction.

4.4.5 Determination of Consideration. For purposes of this Subsection 4.4, the consideration received by the Corporation for the issue of any Additional Shares of Common Stock shall be computed as follows:

(a) Cash and Property: Such consideration shall:

(i) insofar as it consists of cash, be computed at the aggregate amount of cash received by the Corporation, excluding amounts paid or payable for accrued interest;

(ii) insofar as it consists of property other than cash, be computed at the fair market value thereof at the time of such issue, as determined in good faith by the Board; and

(iii) in the event Additional Shares of Common Stock are issued together with other shares or securities or other assets of the Corporation for consideration that covers both, be the proportion of such consideration so received, computed as provided in clauses (i) and (ii) above, as determined in good faith by the Board.

(b) Options and Convertible Securities . The consideration per share received by the Corporation for Additional Shares of Common Stock deemed to have been issued pursuant to Subsection 4.4.3, relating to Options and Convertible Securities, shall be determined by dividing:

(i) the total amount, if any, received or receivable by the Corporation as consideration for the issue of such Options or Convertible Securities, plus the minimum aggregate amount of additional consideration (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such consideration) payable to the Corporation upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities, by

(ii) the maximum number of shares of Common Stock (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities.

4.4.6 Multiple Closing Dates . In the event the Corporation shall issue on more than one date Additional Shares of Common Stock that are a part of one transaction or a series of related transactions and that would result in an adjustment to the Series A Conversion Price pursuant to the terms of Subsection 4.4.4, then, upon the final such issuance, the Series A Conversion Price shall be readjusted to give effect to all such issuances as if they occurred on the date of the first such issuance (and without giving effect to any additional adjustments as a result of any such subsequent issuances within such period).

4.5 Adjustment for Stock Splits and Combinations . If the Corporation shall at any time or from time to time after the Series A Original Issue Date effect a subdivision of the outstanding Common Stock, the Series A Conversion Price in effect immediately before that subdivision shall be proportionately decreased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be increased in proportion to such increase in the aggregate number of shares of Common Stock outstanding. If the Corporation shall at any time or from time to time after the Series A Original Issue Date combine the outstanding shares of Common Stock, the Series A Conversion Price in effect immediately before the combination shall be proportionately increased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be decreased in proportion to such decrease in the aggregate number of shares of Common Stock outstanding. Any adjustment under this subsection shall become effective at the close of business on the date the subdivision or combination becomes effective.

4.6 Adjustment for Certain Dividends and Distributions . In the event the Corporation at any time or from time to time after the Series A Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable on the Common Stock in additional shares of Common

Stock, then and in each such event the Series A Conversion Price in effect immediately before such event shall be decreased as of the time of such issuance or, in the event such a record date shall have been fixed, as of the close of business on such record date, by multiplying the Series A Conversion Price then in effect by a fraction:

(1) the numerator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date, and

(2) the denominator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date plus the number of shares of Common Stock issuable in payment of such dividend or distribution.

Notwithstanding the foregoing, (a) if such record date shall have been fixed and such dividend is not fully paid or if such distribution is not fully made on the date fixed therefor, the Series A Conversion Price shall be recomputed accordingly as of the close of business on such record date and thereafter the Series A Conversion Price shall be adjusted pursuant to this subsection as of the time of actual payment of such dividends or distributions; and (b) that no such adjustment shall be made if the Series A Holders simultaneously receive a dividend or other distribution of shares of Common Stock in a number equal to the number of shares of Common Stock as they would have received if all outstanding shares of Series A Preferred Stock had been converted into Common Stock on the date of such event.

4.7 Adjustments for Other Dividends and Distributions . In the event the Corporation at any time or from time to time after the Series A Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable in securities of the Corporation (other than a distribution of shares of Common Stock in respect of outstanding shares of Common Stock) or in other property and the provisions of Section 1 do not apply to such dividend or distribution, then and in each such event the Series A Holders shall receive, simultaneously with the distribution to the holders of Common Stock, a dividend or other distribution of such securities or other property in an amount equal to the amount of such securities or other property as they would have received if all outstanding shares of Series A Preferred Stock had been converted into Common Stock on the date of such event.

4.8 Adjustment for Merger or Reorganization, etc . Subject to the provisions of Subsection 2.2, if there shall occur any reorganization, recapitalization, reclassification, consolidation or merger involving the Corporation in which the Common Stock (but not the Series A Preferred Stock) is converted into or exchanged for securities, cash or other property (other than a transaction covered by Subsections 4.4, 4.6 or 4.7), then, following any such reorganization, recapitalization, reclassification, consolidation or merger, each share of Series A Preferred Stock shall thereafter be convertible in lieu of the Common Stock into which it was convertible prior to such event into the kind and amount of securities, cash or other property that a holder of the number of shares of Common Stock of the Corporation issuable upon conversion of one share of Series A Preferred Stock immediately prior to such reorganization, recapitalization, reclassification, consolidation or merger would have been entitled to receive

pursuant to such transaction; and, in such case, appropriate adjustment (as determined in good faith by the Board) shall be made in the application of the provisions in this Section 4 with respect to the rights and interests thereafter of the holders of the Series A Preferred Stock, to the end that the provisions set forth in this Section 4 (including provisions with respect to changes in and other adjustments of the Series A Conversion Price) shall thereafter be applicable, as nearly as reasonably may be, in relation to any securities or other property thereafter deliverable upon the conversion of the Series A Preferred Stock.

4.9 Certificate as to Adjustments. Upon the occurrence of each adjustment or readjustment of the Series A Conversion Price pursuant to this Section 4, the Corporation at its expense shall, as promptly as reasonably practicable but in any event not later than 10 days thereafter, compute such adjustment or readjustment in accordance with the terms hereof and furnish to each holder of Series A Preferred Stock a certificate setting forth such adjustment or readjustment (including the kind and amount of securities, cash or other property into which the Series A Preferred Stock is convertible) and showing in detail the facts upon which such adjustment or readjustment is based. The Corporation shall, promptly after the written request at any time of any holder of Series A Preferred Stock, furnish or cause to be furnished to such holder a certificate setting forth (i) the Series A Conversion Price then in effect, and (ii) the number of shares of Common Stock and the amount, if any, of other securities, cash or property that then would be received upon the conversion of Series A Preferred Stock.

4.10 Notice of Record Date. In the event:

(a) the Corporation shall take a record of the holders of its Common Stock (or other capital stock or securities at the time issuable upon conversion of the Series A Preferred Stock) for the purpose of entitling or enabling them to receive any dividend or other distribution, or to receive any right to subscribe for or purchase any shares of capital stock of any class or any other securities, or to receive any other security; or

(b) of any capital reorganization of the Corporation, any reclassification of the Common Stock of the Corporation, or any Liquidity Event; or

(c) of the voluntary or involuntary dissolution, liquidation or winding-up of the Corporation, then, and in each such case, the Corporation will send or cause to be sent to the holders of the Series A Preferred Stock a notice specifying, as the case may be, (i) the record date for such dividend, distribution or right, and the amount and character of such dividend, distribution or right, or (ii) the effective date on which such reorganization, reclassification, consolidation, merger, transfer, dissolution, liquidation or winding-up is proposed to take place, and the time, if any is to be fixed, as of which the holders of record of Common Stock (or such other capital stock or securities at the time issuable upon the conversion of the Series A Preferred Stock) shall be entitled to exchange their shares of Common Stock (or such other capital stock or securities) for securities or other property deliverable upon such reorganization, reclassification, consolidation, merger, transfer, dissolution, liquidation or winding-up, and the amount per share and character of such exchange applicable to the Series A Preferred Stock and the Common Stock. Such notice shall be sent at least 10 days prior to the record date or effective date for the event specified in such notice.

5. Mandatory Conversion .

5.1 Trigger Events . Upon the earlier of (a) the closing of a sale of Common Stock pursuant to an underwritten public offering by the Corporation or the registration of the Common Stock under the Securities Exchange Act of 1934 yielding gross proceeds to the Corporation of at least $20,000,000 or (b) the date and time, or the occurrence of an event, specified by consent of the holders of at least a majority of the Series A Preferred Stock (the time of such closing or the date and time specified or the time of the event specified in such consent is referred to herein as the "Mandatory Conversion Time"), all outstanding shares of Series A Preferred Stock shall automatically be converted into shares of Common Stock, at the then effective conversion rate

5.2 Procedural Requirements . All holders of record of shares of Series A Preferred Stock shall be sent written notice of the Mandatory Conversion Time and the place designated for mandatory conversion of all such shares of Series A Preferred Stock pursuant to this Section 5. Such notice need not be sent in advance of the occurrence of the Mandatory Conversion Time. Upon receipt of such notice, each holder of shares of Series A Preferred Stock shall surrender his, her or its certificate or certificates for all such shares (or, if such holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation at the place designated in such notice. If so required by the Corporation, certificates surrendered for conversion shall be endorsed or accompanied by written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or by his, her or its attorney duly authorized in writing. All rights with respect to the Series A Preferred Stock converted pursuant to Section 5.1, including the rights, if any, to receive notices and vote (other than as a holder of Common Stock), will terminate at the Mandatory Conversion Time (notwithstanding the failure of the holder or holders thereof to surrender the certificates at or prior to such time), except only the rights of the holders thereof, upon surrender of their certificate or certificates (or lost certificate affidavit and agreement) therefor, to receive the items provided for in the next sentence of this Subsection 5.2. As soon as practicable after the Mandatory Conversion Time and the surrender of the certificate or certificates (or lost certificate affidavit and agreement) for Series A Preferred Stock, the Corporation shall issue and deliver to such holder, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable on such conversion in accordance with the provisions hereof, together with cash as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and the payment of any dividends declared but unpaid on the shares of Series A Preferred Stock converted. Such converted Series A Preferred Stock shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Series A Preferred Stock accordingly

5.3 Effect of Mandatory Conversion . All shares of Series A Preferred Stock shall, from and after the Mandatory Conversion Time, no longer be deemed to be outstanding and, notwithstanding the failure of the holder or holders thereof to surrender the certificates for such shares on or prior to such time, all rights with respect to such shares shall immediately

cease and terminate at the Mandatory Conversion Time, except only the right of the holders thereof to receive shares of Common Stock in exchange therefor and to receive payment of any dividends declared but unpaid thereon. Such converted Series A Preferred Stock shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Series A Preferred Stock accordingly.

6. Redemption . The Series A Preferred Stock is not redeemable.

7. Waiver . Any of the rights, powers, preferences and other terms of the Series A Preferred Stock set forth herein may be waived on behalf of all Series A Holders by the affirmative written consent or vote of the holders of at least a majority of the shares of Series A Preferred Stock then outstanding.

8. Notices . Any notice required or permitted by the provisions of this Article IV to be given to a holder of shares of Series A Preferred Stock shall be mailed, postage prepaid, to the post office address last shown on the records of the Corporation, or given by electronic communication in compliance with the provisions of the DGCL, and shall be deemed sent upon such mailing or electronic transmission.

CERTIFICATE OF
QR PHARMA, INC.
AMENDING NUMBER OF SHARES OF PREFERRED STOCK
DESIGNATED AS
SERIES A PREFERRED STOCK

Pursuant to Section 151 of the
General Corporation Law of the State of Delaware

QR Pharma, Inc., a Delaware corporation, does hereby certify as follows:

1. The name of the corporation (the "Corporation") is QR Pharma, Inc.

2. On April 29, 2008, the Corporation filed a Certificate of Incorporation (the "Certificate of Incorporation") with the Secretary of State of the State of Delaware. The Certificate of Incorporation was amended pursuant to a Certificate of Amendment filed with the Secretary of State of the State of Delaware on December 19, 2014 (the Certificate of Incorporation, as so amended, the "Amended Certificate"). Out of the 5,000,000 shares of Preferred Stock that the Corporation is authorized to issue pursuant to the Amended Certificate, an aggregate of 4,000,000 shares of Preferred Stock were designated therein as "Series A Preferred Stock."

3. Pursuant to the authority contained in Article IV of the Amended Certificate, and in accordance with the provisions of Section 151 of the Delaware General Corporation Law, the Board of Directors of the Corporation has duly adopted the following resolution:

RESOLVED , that, pursuant to authority conferred upon the Board of Directors by Article IV of the Amended Certificate, the Board of Directors does hereby amend the designation providing for the issuance of a series of Preferred Stock designated as "Series A Preferred Stock" so as to increase the number of shares so designated from 4,000,000 shares to 5,000,000 shares, with the relative rights, powers and preferences thereof remaining unchanged.

4. As a result of the adoption of the foregoing resolution, the number of shares of Preferred Stock of the Corporation designated as Series A Preferred Stock has been increased from 4,000,000 shares to 5,000,000 shares.

(Signature page follows.)

IN WITNESS WHEREOF, the Corporation has caused this Certificate to be executed by its duly authorized officer on this 16th day of September, 2016.

QR PHARMA, INC.

By: /s/ Maria L. Maccecchini
Name: Maria L. Maccecchini
Title: Chief Executive Officer and President

CERTIFICATE OF AMENDMENT

OF

CERTIFICATE OF INCORPORATION

OF

QR PHARMA, INC.

QR Pharma, Inc., a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the "DGCL"),

DOES HEREBY CERTIFY THAT:

FIRST: The Board of Directors (the "Board") of QR Pharma, Inc. (the "Corporation"), at a meeting duly called and held on October 11, 2016, duly adopted the following resolution setting forth a proposed amendment of the Certificate of Incorporation of the Corporation, as amended, declaring such amendment to be advisable and calling for consideration thereof by the stockholders of the Corporation. The resolution setting forth the proposed amendment is as follows:

RESOLVED, that Article IV of the Certificate of Incorporation of the Corporation, as amended, shall be amended as set forth on Exhibit A hereto.

SECOND: Thereafter, in accordance with a resolution of the Board, the holders of a majority of the outstanding shares of all capital stock of the Corporation and a majority of the outstanding shares of Series A Preferred Stock of the Corporation voted in favor of the amendment.

THIRD: The amendment was duly adopted in accordance with the provisions of Section 242 of the DGCL. With respect to such adoption, written consent has been given by the stockholders of the Corporation in accordance with the provisions of Section 228 of the DGCL, and written notice has been given as provided in Section 228.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the Corporation has caused this Certificate of Amendment to be executed this 20th day of October, 2016.

QR PHARMA, INC.

By: /s/ Maria Maccecchini
Name: Maria Maccecchini
Title: President and CEO

EXHIBIT A

1. The first paragraph of Article IV of the Certificate of Incorporation of the Corporation, as amended, is hereby amended and restated in its entirety so as to read as follows:

ARTICLE IV

"The total number of shares of all classes of stock that the Corporation shall have authority to issue is Fourteen Million One Hundred Thirty-Four Thousand Seven Hundred Eighteen (14,134,718) shares, divided into Nine Million (9,000,000) shares of Common Stock, par value $.0001 per share (the "Common Stock") and Five Million One Hundred Thirty-Four Thousand Seven Hundred Eighteen (5,134,718) shares of Preferred Stock, par value $.0001 per share (the "Preferred Stock")."

2. The second paragraph of Part B of Article IV of the Certificate of Incorporation of the Corporation, as amended, is hereby amended and restated in its entirety so as to read as follows:

"Five Million One Hundred Thirty Four Thousand Seven Hundred Eighteen (5,134,718) shares of the authorized and unissued Preferred Stock of the Corporation are hereby designated "Series A Preferred Stock" with the following rights, preferences, powers, privileges and restrictions, qualifications and limitations. The Series A Preferred Stock shall rank (a) senior to the Common Stock and any other class or series of capital stock of the Corporation either specifically ranking by its terms junior to the Series A Preferred Stock or not specifically ranking by its terms senior to or on parity with the Series A Preferred Stock, (b) on parity with any class or series of capital stock of the Corporation specifically ranking by its terms on parity with the Series A Preferred Stock and (c) junior to any class or series of capital stock of the Corporation specifically ranking by its terms senior to the Series A Preferred Stock, in each case, as to payment of dividends, distributions of assets upon a Liquidation or Liquidity Event or otherwise (each as defined herein or in any certificate of designation adopted as provided above and filed in accordance with the requirements of the DGCL and then in effect). Unless otherwise indicated, references to "Sections" or "Subsections" in this Part B of this Article IV refer to sections and subsections of Part B of this Article IV."

CERTIFICATE OF AMENDMENT

OF

CERTIFICATE OF INCORPORATION

OF

QR PHARMA, INC.

QR Pharma, Inc., a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the "DGCL"),

DOES HEREBY CERTIFY THAT:

FIRST: The Board of Directors (the "Board") of QR Pharma, Inc. (the "Corporation"), at a meeting duly called and held on September 26, 2017, duly adopted the following resolution setting forth a proposed amendment of the Certificate of Incorporation of the Corporation, declaring such amendment to be advisable and calling for consideration thereof by the stockholders of the Corporation. The resolution setting forth the proposed amendment is as follows:

RESOLVED, that Article IV of the Certificate of Incorporation of the Corporation shall be amended and restated in its entirety to provide as set forth on Exhibit A hereto.

SECOND: Thereafter, in accordance with a resolution of the Board, the holders of a majority of the outstanding shares of all capital stock of the Corporation voted in favor of the amendment.

THIRD: The amendment was duly adopted in accordance with the provisions of Section 242 of the DGCL. With respect to such adoption, written consent has been given by the stockholders of the Corporation in accordance with the provisions of Section 228 of the DGCL, and written notice has been given as provided in Section 228.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the Corporation has caused this Certificate of Amendment to be executed this 14th day of December, 2017.

QR PHARMA, INC.

By: /s/ Maria L. Maccecchini
Maria L. Maccecchini
President and Chief Executive Officer

EXHIBIT A

ARTICLE IV

The total number of shares of all classes of stock that the Corporation shall have authority to issue is Sixteen Million Three Hundred Ninety-Four Thousand Two Hundred Seventy (16,394,270) shares, divided into Ten Million One Hundred Fifty Thousand (10,150,000) shares of Common Stock, par value $.0001 per share (the "Common Stock") and Six Million Two Hundred Forty-Four Thousand Two Hundred Seventy (6,244,270) shares of Preferred Stock, par value $.0001 per share (the "Preferred Stock").

Subject to the foregoing, the following is a statement of the designations and the powers, privileges and rights, and the qualifications, limitations or restrictions thereof in respect of each class of capital stock of the Corporation.

A. COMMON STOCK

1. Dividend Rights. Subject to the rights of holders of Preferred Stock as to dividends, the holders of the Common Stock shall be entitled to receive, when and as declared by the Board, out of any assets of the Corporation legally available therefor, such dividends as may be declared from time to time by the Board.

2. Liquidation Rights. Subject to the rights of holders of Preferred Stock as to liquidation, upon the liquidation, dissolution or winding up of the Corporation, the assets of the Corporation shall be distributed to the holders of Common Stock.

3. Voting. The holders of the Common Stock are entitled to one vote for each share of Common Stock held at all meetings of stockholders (and written actions in lieu of meetings); provided, however, that, except as otherwise required by law, holders of Common Stock, as such, shall not be entitled to vote on any amendment to the Certificate of Incorporation (as amended from time to time, the "Certificate of Incorporation") that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together with the holders of one or more other such series, to vote thereon pursuant to the Certificate of Incorporation or pursuant to the DGCL. There shall be no cumulative voting. The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by (in addition to any vote of the holders of one or more series of Preferred Stock that may be required by the terms of the Certificate of Incorporation) the affirmative vote of the holders of shares of capital stock of the Corporation representing a majority of the votes represented by all outstanding shares of capital stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the DGCL.

B. PREFERRED STOCK

The Board shall have the authority to the fullest extent permitted under the DGCL to adopt by resolution from time to time one or more certificates of designation providing for the

designation of one or more classes or series of Preferred Stock and the voting powers, whether full or limited or no voting powers, and such designations, preferences and relative, participating, optional or other special rights and qualifications, limitations or restrictions thereof, and to fix or alter the number of shares comprising any such class or series, subject to any requirements of the DGCL and this Certificate of Incorporation. Subject to compliance with applicable protective voting rights that may be granted to the Preferred Stock or a series thereof in certificates of designation or this Certificate of Incorporation, but notwithstanding any other rights of the Preferred Stock or of a series thereof, the rights, preferences, privileges and restrictions of any such additional series or classes of Preferred Stock may be subordinated to, pari passu with (including, without limitation, in provisions regarding dividend, liquidation and acquisition preferences and/or approval of matters by vote or written consent) or senior to any of those of any present or future class or series of the Preferred Stock or the Common Stock.

One Million One Hundred Eleven Thousand One Hundred Eleven (1,111,111) shares of the authorized and unissued Preferred Stock of the Corporation are hereby designated "Series A-1 Preferred Stock" with the following rights, preferences, powers, privileges and restrictions, qualifications and limitations. Five Million One Hundred Thirty-Three Thousand One Hundred Fifty-Nine (5,133,159) shares of the authorized and unissued Preferred Stock of the Corporation are hereby designated "Series A Preferred Stock" with the following rights, preferences, powers, privileges and restrictions, qualifications and limitations. The Series A-1 Preferred Stock shall rank pari passu with the Series A Preferred Stock, and each of the Series A-1 Preferred Stock and Series A Preferred Stock shall rank (a) senior to the Common Stock and any other class or series of capital stock of the Corporation either specifically ranking by its terms junior to the Series A Preferred Stock and Series A-1 Preferred Stock or not specifically ranking by its terms senior to or on parity with the Series A Preferred Stock and Series A-1 Preferred Stock, (b) on parity with any class or series of capital stock of the Corporation specifically ranking by its terms on parity with the Series A Preferred Stock and Series A-1 Preferred Stock and (c) junior to any class or series of capital stock of the Corporation specifically ranking by its terms senior to the Series A Preferred Stock and Series A-1 Preferred Stock, in each case, as to payment of dividends, distributions of assets upon a Liquidation or Liquidity Event or otherwise (each as defined herein or in any certificate of designation adopted as provided above and filed in accordance with the requirements of the DGCL and then in effect). Unless otherwise indicated, references to "Sections" or "Subsections" in this Part B of this Article IV refer to sections and subsections of Part B of this Article IV.

1. Dividend Rights . The holders of the outstanding shares of the Series A Preferred Stock and Series A-1 Preferred Stock (each, a "Preferred Holder" and, collectively, the "Preferred Holders") shall be entitled to receive, when and as declared by the Board, out of any assets of the Corporation legally available therefor, such dividends as may be declared from time to time by the Board.

2. Liquidation, Dissolution or Winding Up; Certain Mergers, Consolidations and Asset Sales .

2.1 Treatment at Liquidation, Dissolution or Winding Up .

2.1.1 Liquidation Preference . In the event of any liquidation, dissolution or winding up of the Corporation (each such event, a "Liquidation"), the Preferred Holders shall be entitled to be paid out of the assets of the Corporation available for distribution to holders of the Corporation's capital stock of all classes, whether such assets are capital, surplus or earnings ("Available Assets"), before any distribution or payment is made to any holders of Common Stock, as follows:

(a) The holders of the Series A-1 Preferred Stock shall be entitled to receive, on a par with the amounts the holders of the Series A Preferred Stock shall be entitled to receive pursuant to Section 2.1.1(b) hereof, an amount per share of Series A-1 Preferred Stock equal to the Series A-1 Original Issue Price plus an amount equal to all declared but unpaid dividends on such share of Series A-1 Preferred Stock, whether or not declared (as it may be adjusted in the event of any stock dividend, split, combination, reclassification, recapitalization or other similar event with respect to such share) (the "Series A-1 Liquidation Preference").

(b) The holders of the Series A Preferred Stock shall be entitled to receive, on a par with the amounts the holders of the Series A-1 Preferred Stock shall be entitled to receive pursuant to Section 2.1.1(b) hereof, an amount per share of Series A Preferred Stock equal to the Series A Original Issue Price plus an amount equal to all declared but unpaid dividends on such share of Series A Preferred Stock, whether or not declared (as it may be adjusted in the event of any stock dividend, split, combination, reclassification, recapitalization or other similar event with respect to such share) (together with the Series A-1 Liquidation Preference, the "Series A Liquidation Preference").

(c) If, upon Liquidation, the Available Assets shall be insufficient to pay the full amount of the Series A Liquidation Preference, the Preferred Holders shall share in any distribution of Available Assets pro rata in proportion to the respective Series A Liquidation Preference that would otherwise be payable upon a Liquidation with respect to the outstanding shares of the Series A Preferred Stock and Series A-1 Preferred Stock if the Series A Liquidation Preference payable with respect to such shares were paid in full.

2.1.2 Distribution of Remaining Available Assets . After the payment in full of the Series A Liquidation Preference pursuant to Subsection 2.1.1, the remaining Available Assets, if any, shall be distributed among the holders of Common Stock in proportion to the number of shares of Common Stock then held by such holders of Common Stock, and the Preferred Holders shall have no further rights thereto in respect of the shares of Series A Preferred Stock and/or Series A-1 Preferred Stock owned by them.

2.2 Treatment of a Liquidity Event . Unless the holders of at least of majority of the outstanding shares of Preferred Stock elect otherwise by written notice to the Corporation at least ten days prior to the occurrence of a Liquidity Event stating that such Liquidity Event shall not be treated as a Liquidation, a Liquidity Event shall be treated as a Liquidation. As used herein, "Liquidity Event" means any sale, license or other transfer, in a single transaction or series of related transactions, of all or substantially all of the assets of the Corporation, or

transaction or series of transactions involving the Corporation, or its securities, whether by consolidation, merger, purchase of shares of capital stock or other reorganization or combination or otherwise, in which the holders of the Corporation's outstanding shares of capital stock immediately prior to such transaction own, immediately after such transaction, securities representing less than 50% of the voting power of the entity surviving such transaction, except to the extent resulting from the issuance and sale of Series A-1 Preferred Stock. For purposes of this Section 2, the amount of Available Assets shall be determined as follows:

(a) insofar as Available Assets consist of cash, they shall be computed at the aggregate amount of cash held by the Corporation at the time of the liquidation, dissolution or winding up; and

(b) insofar as Available Assets consist of property other than cash, they shall be computed at the fair market value thereof at the time of the liquidation, dissolution or winding up, as determined in good faith by the Board.

3. Voting .

3.1 General . Except as otherwise stated herein, on any matter presented to the stockholders of the Corporation for their action or consideration at any meeting of stockholders of the Corporation (or by written consent of stockholders in lieu of meeting), each holder of outstanding shares of Series A Preferred Stock and Series A-1 Preferred Stock shall be entitled to cast the number of votes equal to the number of whole shares of Common Stock into which the shares of Series A Preferred Stock and/or Series A-1 Preferred Stock held by such holder are convertible as of the record date for determining stockholders entitled to vote on such matter. Except as provided by law or by the other provisions of the Certificate of Incorporation, Preferred Holders shall vote together with the holders of Common Stock and all other series and classes of stock permitted to vote with the Common Stock on all matters submitted to a vote of the holders of the Common Stock as a single class.

3.2 Election of Directors .

3.2.1 Preferred Directors . The Preferred Holders, voting as a separate class, shall be entitled to elect three directors of the Corporation (the "Preferred Directors"). The Preferred Directors may be removed by, and only by, the affirmative vote of the holders of a majority of the Preferred Stock, voting as a separate class, given either at a special meeting of such stockholders duly called for that purpose or pursuant to a written consent of such stockholders.

3.2.2 Common Directors . The holders of record of Common Stock, voting as a separate class, shall be entitled to elect one director of the Corporation (the "Common Director"). The Common Director may be removed by, and only by, the affirmative vote of the holders of a majority of the Common Stock, voting as a separate class, given either at a special meeting of such stockholders duly called for that purpose or pursuant to a written consent of such stockholders.

3.2.3 Remaining Directors . The holders of record of Common Stock and Preferred Stock, voting together as a single class and on an as-converted basis, shall be

entitled to elect the remaining directors of the Corporation (the "Remaining Directors"). The Remaining Directors may be removed by, and only by, the affirmative vote of the holders of a majority of the Preferred Stock and Common Stock, voting together as a single class, given either at a special meeting of such stockholders duly called for that purpose or pursuant to a written consent of such stockholders.

3.2.4 Quorum. At any meeting held for the purpose of electing a director, the presence in person or by proxy of the holders of at least a majority of the outstanding shares of the class or series entitled to elect such director shall constitute a quorum for the purpose of electing such director. A vacancy in any directorship filled by the holders of any class or series shall be filled only by vote or written consent in lieu of a meeting of the holders of such class or series.

3.3 Preferred Stock Protective Provisions. At any time when at least One Million (1,000,000) shares of Preferred Stock (as adjusted in the event of any stock dividend, split, combination, reclassification, recapitalization or other similar event with respect to such shares) are issued and outstanding, the Corporation shall not, either directly or indirectly by amendment, merger, consolidation or otherwise, take any of the following actions, without (in addition to any other vote required by law or the Certificate of Incorporation) the consent of the holders of at least a majority of the then outstanding shares of Preferred Stock:

3.3.1 amend the Certificate of Incorporation in a manner that would alter or change the rights, preferences or privileges of the Series A Preferred Stock or Series A-1 Preferred Stock so as to adversely affect such series, or increase or decrease the number of authorized shares thereof;

3.3.2 create any new series or class of shares having a preference or priority as to dividends or assets superior to or on a parity with the Series A Preferred Stock and Series A-1 Preferred Stock;

3.3.3 apply any of its assets to the redemption or acquisition of any shares of Common Stock, except from employees, advisors, officers, directors, consultants and service providers of the Corporation on terms approved by the Board; or

3.3.4 authorize or effect the payment of any dividend to any holders of any class or series of capital stock (other than a stock dividend payable solely in Common Stock).

4. Optional Conversion.

The Series A Holders shall have conversion rights as follows (the "Conversion Rights"):

4.1 Right to Convert.

4.1.1 Conversion Ratio. Each share of S Preferred Stock shall be convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, into such number of fully paid and nonassessable shares of Common Stock as is determined by dividing the Original Issue Price

applicable thereto by the applicable Conversion Price (as defined below) in effect at the time of conversion. The "Series A-1 Conversion Price" shall initially be equal to $0.90 and the "Series A Conversion Price" shall initially be equal to $0.50. The Series A-1 Conversion Price and the Series A Conversion Price may be referred to herein as a "Conversion Price." Each such initial Conversion Price, and the rate at which shares of Preferred Stock may be converted into shares of Common Stock, shall be subject to adjustment as provided below.

4.1.2 Termination of Conversion Rights. In the event of a liquidation, dissolution or winding up of the Corporation or a Liquidity Event, the Conversion Rights shall terminate at the close of business on the last full day preceding the date fixed for the payment of any such amounts distributable on such event to the Preferred Holders.

4.2 Fractional Shares. No fractional shares of Common Stock shall be issued upon conversion of the Preferred Stock. In lieu of any fractional shares to which the holder would otherwise be entitled, the Corporation shall round the number of shares of Common Stock to which such holder would otherwise be entitled so that any portion of a share that is equal to less than one whole share is rounded up. Whether or not fractional shares would be issuable upon such conversion shall be determined on the basis of the total number of shares of Preferred Stock the holder is at the time converting into Common Stock and the aggregate number of shares of Common Stock issuable upon such conversion.

4.3 Mechanics of Conversion.

4.3.1 Notice of Conversion. In order for a registered Preferred Holder to voluntarily convert shares Preferred Stock into shares of Common Stock, such holder shall surrender the certificate or certificates for such shares of Preferred Stock (or, if such holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate), at the office of the transfer agent for the Preferred Stock (or at the principal office of the Corporation if the Corporation serves as its own transfer agent), together with written notice that such holder elects to convert all or any number of the shares of the Preferred Stock represented by such certificate or certificates and, if applicable, any event on which such conversion is contingent. Such notice shall state such holder's name or the names of the nominees in which such holder wishes the certificate or certificates for shares of Common Stock to be issued. If required by the Corporation, certificates surrendered for conversion shall be endorsed or accompanied by a written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or his, her or its attorney duly authorized in writing. The close of business on the date of receipt by the transfer agent (or by the Corporation if the Corporation serves as its own transfer agent) of such certificates (or lost certificate affidavit and agreement) and notice shall be the time of conversion (the "Conversion Time"), and the shares of Common Stock issuable upon conversion of the shares represented by such certificate shall be deemed to be outstanding of record as of such date. The Corporation shall, as soon as practicable after the Conversion Time: (i) issue and deliver to such Preferred Holder, or to such holder's nominees, a certificate or certificates for the number of full shares of Common Stock issuable upon such conversion in accordance with the provisions hereof and a certificate for the number (if any) of the shares of Preferred Stock represented by the surrendered

certificate that were not converted into Common Stock, (ii) pay in cash such amount as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and (iii) pay all declared but unpaid dividends on the shares of Preferred Stock converted.

4.3.2 Reservation of Shares. The Corporation shall at all times when the Preferred Stock shall be outstanding, reserve and keep available out of its authorized but unissued capital stock, for the purpose of effecting the conversion of the Preferred Stock, such number of its duly authorized shares of Common Stock as shall from time to time be sufficient to effect the conversion of all outstanding Preferred Stock; and if at any time the number of authorized but unissued shares of Common Stock shall not be sufficient to effect the conversion of all then outstanding shares of the Preferred Stock, the Corporation shall take such corporate action as may be necessary to increase its authorized but unissued shares of Common Stock to such number of shares as shall be sufficient for such purposes, including, without limitation, seeking to obtain the requisite stockholder approval of any necessary amendment to the Certificate of Incorporation. Before taking any action that would cause an adjustment reducing any Conversion Price below the then par value of the shares of Common Stock issuable upon conversion of the Preferred Stock, the Corporation shall take any corporate action that may, in the opinion of its counsel, be necessary in order that the Corporation may validly and legally issue fully paid and nonassessable shares of Common Stock at such adjusted Conversion Price.

4.3.3 Effect of Conversion. All shares of Preferred Stock that shall have been surrendered for conversion as herein provided shall no longer be deemed to be outstanding and all rights with respect to such shares shall immediately cease and terminate at the Conversion Time, except only the right of the holders thereof to receive shares of Common Stock in exchange therefor, to receive payment in lieu of any fraction of a share otherwise issuable upon such conversion as provided in Subsection 4.2 and to receive payment of any declared dividends that remain unpaid thereon. Any shares of Preferred Stock so converted shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Preferred Stock accordingly.

4.3.4 No Further Adjustment. Upon any such conversion, no adjustment to a Conversion Price shall be made for any declared but unpaid dividends on the Preferred Stock surrendered for conversion or on the Common Stock delivered upon conversion.

4.4 Adjustments to Series A Conversion Price for Diluting Issues.

4.4.1 Special Definitions. For purposes of this Article IV, the following definitions shall apply:

(a) "Option" shall mean rights, options or warrants to subscribe for, purchase or otherwise acquire Common Stock or Convertible Securities.

(b) "Series A-1 Original Issue Date" shall mean the date on which the first share of Series A-1 Preferred Stock was issued.

(c) "Convertible Securities" shall mean any evidences of indebtedness, shares or other securities directly or indirectly convertible into or exchangeable for Common Stock, but excluding Options.

(d) "Additional Shares of Common Stock" shall mean all shares of Common Stock issued (or, pursuant to Subsection 4.4.3 below, deemed to be issued) by the Corporation after the Series A-1 Original Issue Date, other than (1) the following shares of Common Stock and (2) shares of Common Stock deemed issued pursuant to the following (collectively, "Exempted Securities"):

(i) shares of Common Stock, Options or Convertible Securities issued as a dividend or distribution on, or upon conversion of, Preferred Stock;

(ii) shares of Common Stock, Options or Convertible Securities issued by reason of a dividend, stock split, split-up or other distribution on shares of Common Stock that is covered by Subsection 4.5, 4.6, 4.7 or 4.8;

(iii) shares of Common Stock or Options issued to employees, officers or directors of, or consultants or advisors to, and other service providers of, the Corporation or any of its subsidiaries pursuant to any equity incentive plan, option plan or other compensatory plan, program or agreement approved by the Board;

(iv) shares of Common Stock or Convertible Securities actually issued upon the exercise of Options or shares of Common Stock actually issued upon the conversion or exchange of Convertible Securities;

(v) shares of Common Stock, Options or Convertible Securities issued to banks, equipment lessors or other financial institutions, or to real property lessors, pursuant to a debt financing, equipment leasing or real property leasing transaction approved by the Board;

(vi) shares of Common Stock, Options or Convertible Securities issued pursuant to the acquisition of another entity by the Corporation by merger, purchase of substantially all of the assets or other reorganization or pursuant to a joint venture, partnership, marketing, technology transfer or license or development arrangement or other strategic transaction, provided that the respective issuance is approved by the Board;

(vii) shares of Series A-1 Preferred Stock issued under the Series A-1 Preferred Stock Purchase Agreement entered into among the Corporation and the investors parties thereto as of December 15, 2017, and

(viii) shares of Common Stock, Options or Convertible Securities issued in connection with the closing of the sale of shares of the Corporation's capital stock in an underwritten public offering by the Corporation under the Securities Exchange Act of 1934.

4.4.2 No Adjustment of Conversion Price . No adjustment in any Conversion Price shall be made as the result of the issuance or deemed issuance of Additional

Shares of Common Stock if the Corporation receives written notice from the holders of at least a majority of the then outstanding shares of Preferred Stock agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock. In addition, no adjustment to a Conversion Price for any particular series of Preferred Stock shall be made as a result of the issuance or deemed issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of at least a majority of the then outstanding shares of such series of Preferred Stock agreeing that no such adjustment shall be made as a result of the issuance or deemed issuance of such Additional Shares of Common Stock.

4.4.3 Deemed Issue of Additional Shares of Common Stock .

(a) If the Corporation at any time or from time to time after the Series A-1 Original Issue Date shall issue any Options or Convertible Securities (excluding Options or Convertible Securities that are themselves Exempted Securities (as defined in Subsection 4.4.1) or shall fix a record date for the determination of holders of any class of securities entitled to receive any such Options or Convertible Securities, then the maximum number of shares of Common Stock (as set forth in the instrument relating thereto, assuming the satisfaction of any conditions to exercisability, convertibility or exchangeability but without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or, in the case of Convertible Securities and Options therefor, the conversion or exchange of such Convertible Securities, shall be deemed to be Additional Shares of Common Stock issued as of the time of such issue or, in case such a record date shall have been fixed, as of the close of business on such record date.

(b) If the terms of any Option or Convertible Security, the issuance of which resulted in an adjustment to any Conversion Price pursuant to the terms of Subsection 4.4.4, are revised as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase or decrease in the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any such Option or Convertible Security or (2) any increase or decrease in the consideration payable to the Corporation upon such exercise, conversion and/or exchange, then, effective upon such increase or decrease becoming effective, any Conversion Price computed upon the original issue of such Option or Convertible Security (or upon the occurrence of a record date with respect thereto) shall be readjusted to such Conversion Price as would have been obtained had such revised terms been in effect upon the original date of issuance of such Option or Convertible Security. Notwithstanding the foregoing, no readjustment pursuant to this clause (b) shall have the effect of increasing a Conversion Price to an amount that exceeds the lower of (i) the Conversion Price in effect immediately prior to the original adjustment made as a result of the issuance of such Option or Convertible Security, or (ii) the Conversion Price that would have resulted from any issuances of Additional Shares of Common Stock (other than deemed issuances of Additional Shares of Common Stock as a result of the issuance of such Option or Convertible Security) between the original adjustment date and such readjustment date.

(c) If the terms of any Option or Convertible Security (excluding Options or Convertible Securities that are themselves Exempted Securities), the issuance of which did not result in an adjustment to a Conversion Price pursuant to the terms of Subsection 4.4.4 (either because the consideration per share (determined pursuant to Subsection 4.4.5) of the Additional Shares of Common Stock subject thereto was equal to or greater than the Conversion Price then in effect, or because such Option or Convertible Security was issued before the Series A-1 Original Issue Date), are revised after the Series A-1 Original Issue Date as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase in the number of shares of Common Stock issuable upon the exercise, conversion or exchange of any such Option or Convertible Security or (2) any decrease in the consideration payable to the Corporation upon such exercise, conversion or exchange, then such Option or Convertible Security, as so amended or adjusted, and the Additional Shares of Common Stock subject thereto (determined in the manner provided in Subsection 4.4.3(a)) shall be deemed to have been issued effective upon such increase or decrease becoming effective.

(d) Upon the expiration or termination of any unexercised Option or unconverted or unexchanged Convertible Security (or portion thereof) that resulted (either upon its original issuance or upon a revision of its terms) in an adjustment to a Conversion Price pursuant to the terms of Subsection 4.4.4, such Conversion Price shall be readjusted to the Conversion Price as would have obtained had such Option or Convertible Security (or portion thereof) never been issued.

(e) If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, is calculable at the time such Option or Convertible Security is issued or amended but is subject to adjustment based upon subsequent events, any adjustment to a Conversion Price provided for in this Subsection 4.4.3 shall be effected at the time of such issuance or amendment based on such number of shares or amount of consideration without regard to any provisions for subsequent adjustments (and any subsequent adjustments shall be treated as provided in clauses (b) and (c) of this Subsection 4.4.3). If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, cannot be calculated at all at the time such Option or Convertible Security is issued or amended, any adjustment to a Conversion Price that would result under the terms of this Subsection 4.4.3 at the time of such issuance or amendment shall instead be effected at the time such number of shares and/or amount of consideration is first calculable (even if subject to subsequent adjustments), assuming for purposes of calculating such adjustment to such Conversion Price that such issuance or amendment took place at the time such calculation can first be made.

4.4.4 Adjustment of Conversion Price upon Issuance of Additional Shares of Common Stock . In the event the Corporation shall at any time after the Series A-1 Original Issue Date issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Subsection 4.4.3), without consideration or for a consideration per share less than a Conversion Price in effect immediately prior to such issue,

then such Conversion Price shall be reduced, concurrently with such issue, to a price (calculated to the nearest one-hundredth of a cent) as follows:

(a) Until December 15, 2018 (the "Full Ratchet Termination Date"), equal to the consideration per share received or deemed to have been received by the Corporation in such issuance; and

(b) after the Full Ratchet Termination Date, in accordance with the following formula:

$$CP_2 = CP_1 * ((A + B) \div (A + C)).$$

For purposes of the foregoing formula, the following definitions shall apply:

(i) "CP_2" shall mean the Conversion Price in effect immediately after such issue of Additional Shares of Common Stock;

(ii) "CP_1" shall mean the Conversion Price in effect immediately prior to such issue of Additional Shares of Common Stock;

(iii) "A" shall mean the number of shares of Common Stock outstanding immediately prior to such issue of Additional Shares of Common Stock (treating for this purpose as outstanding all shares of Common Stock issuable upon exercise of Options outstanding immediately prior to such issue or upon conversion or exchange of Convertible Securities (including the Preferred Stock) outstanding (assuming exercise of any outstanding Options therefor) immediately prior to such issue);

(iv) "B" shall mean the number of shares of Common Stock that would have been issued if such Additional Shares of Common Stock had been issued at a price per share equal to CP1 (determined by dividing the aggregate consideration received by the Corporation in respect of such issue by CP1); and

(v) "C" shall mean the number of such Additional Shares of Common Stock issued in such transaction.

4.4.5 Determination of Consideration . For purposes of this Subsection 4.4, the consideration received by the Corporation for the issue of any Additional Shares of Common Stock shall be computed as follows:

(a) Cash and Property: Such consideration shall:

(i) insofar as it consists of cash, be computed at the aggregate amount of cash received by the Corporation, excluding amounts paid or payable for accrued interest;

(ii) insofar as it consists of property other than cash, be computed at the fair market value thereof at the time of such issue, as determined in good faith by the Board; and

(iii) in the event Additional Shares of Common Stock are issued together with other shares or securities or other assets of the Corporation for consideration that covers both, be the proportion of such consideration so received, computed as provided in clauses (i) and (ii) above, as determined in good faith by the Board.

(b) Options and Convertible Securities. The consideration per share received by the Corporation for Additional Shares of Common Stock deemed to have been issued pursuant to Subsection 4.4.3, relating to Options and Convertible Securities, shall be determined by dividing:

(i) the total amount, if any, received or receivable by the Corporation as consideration for the issue of such Options or Convertible Securities, plus the minimum aggregate amount of additional consideration (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such consideration) payable to the Corporation upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities, by

(ii) the maximum number of shares of Common Stock (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities.

4.4.6 Multiple Closing Dates. In the event the Corporation shall issue on more than one date Additional Shares of Common Stock that are a part of one transaction or a series of related transactions and that would result in an adjustment to a Conversion Price pursuant to the terms of Subsection 4.4.4, then, upon the final such issuance, such Conversion Price shall be readjusted to give effect to all such issuances as if they occurred on the date of the first such issuance (and without giving effect to any additional adjustments as a result of any such subsequent issuances within such period).

4.5 Adjustment for Stock Splits and Combinations. If the Corporation shall at any time or from time to time after the Series A-1 Original Issue Date effect a subdivision of the outstanding Common Stock, the Conversion Prices in effect immediately before that subdivision shall be proportionately decreased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be increased in proportion to such increase in the aggregate number of shares of Common Stock outstanding. If the Corporation shall at any time or from time to time after the Series A-1 Original Issue Date combine the outstanding shares of Common Stock, the Conversion Prices in effect immediately before the combination shall be proportionately increased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be decreased in proportion to such decrease in the aggregate number of shares of Common Stock outstanding. Any adjustment under this subsection shall become effective at the close of business on the date the subdivision or combination becomes effective.

4.6 Adjustment for Certain Dividends and Distributions . In the event the Corporation at any time or from time to time after the Series A-1 Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable on the Common Stock in additional shares of Common Stock, then and in each such event the Conversion Prices in effect immediately before such event shall be decreased as of the time of such issuance or, in the event such a record date shall have been fixed, as of the close of business on such record date, by multiplying the Conversion Prices then in effect by a fraction:

(1) the numerator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date, and

(2) the denominator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date plus the number of shares of Common Stock issuable in payment of such dividend or distribution.

Notwithstanding the foregoing, (a) if such record date shall have been fixed and such dividend is not fully paid or if such distribution is not fully made on the date fixed therefor, the Conversion Prices shall be recomputed accordingly as of the close of business on such record date and thereafter the Conversion Prices shall be adjusted pursuant to this subsection as of the time of actual payment of such dividends or distributions; and (b) that no such adjustment shall be made if the Preferred Holders simultaneously receive a dividend or other distribution of shares of Common Stock in a number equal to the number of shares of Common Stock as they would have received if all outstanding shares of Preferred Stock had been converted into Common Stock on the date of such event.

4.7 Adjustments for Other Dividends and Distributions . In the event the Corporation at any time or from time to time after the Series A-1 Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable in securities of the Corporation (other than a distribution of shares of Common Stock in respect of outstanding shares of Common Stock) or in other property and the provisions of Section 1 do not apply to such dividend or distribution, then and in each such event the Preferred Holders shall receive, simultaneously with the distribution to the holders of Common Stock, a dividend or other distribution of such securities or other property in an amount equal to the amount of such securities or other property as they would have received if all outstanding shares of Preferred Stock had been converted into Common Stock on the date of such event.

4.8 Adjustment for Merger or Reorganization, etc . Subject to the provisions of Subsection 2.2, if there shall occur any reorganization, recapitalization, reclassification, consolidation or merger involving the Corporation in which the Common Stock (but not the Preferred Stock) is converted into or exchanged for securities, cash or other property (other than a transaction covered by Subsections 4.4, 4.6 or 4.7), then, following any such reorganization, recapitalization, reclassification, consolidation or merger, each share of Preferred Stock shall thereafter be convertible in lieu of the Common Stock into which it was convertible prior to such

event into the kind and amount of securities, cash or other property that a holder of the number of shares of Common Stock of the Corporation issuable upon conversion of one share of Series A Preferred Stock or Series A-1 Preferred Stock, as applicable, immediately prior to such reorganization, recapitalization, reclassification, consolidation or merger would have been entitled to receive pursuant to such transaction; and, in such case, appropriate adjustment (as determined in good faith by the Board) shall be made in the application of the provisions in this Section 4 with respect to the rights and interests thereafter of the holders of the Preferred Stock, to the end that the provisions set forth in this Section 4 (including provisions with respect to changes in and other adjustments of the Conversion Prices) shall thereafter be applicable, as nearly as reasonably may be, in relation to any securities or other property thereafter deliverable upon the conversion of Preferred Stock.

4.9 Certificate as to Adjustments. Upon the occurrence of each adjustment or readjustment of the Conversion Prices pursuant to this Section 4, the Corporation at its expense shall, as promptly as reasonably practicable but in any event not later than 10 days thereafter, compute such adjustment or readjustment in accordance with the terms hereof and furnish to each holder of Preferred Stock a certificate setting forth such adjustment or readjustment (including the kind and amount of securities, cash or other property into which the Preferred Stock is convertible) and showing in detail the facts upon which such adjustment or readjustment is based. The Corporation shall, promptly after the written request at any time of any holder of Preferred Stock, furnish or cause to be furnished to such holder a certificate setting forth (i) the Conversion Prices then in effect, and (ii) the number of shares of Common Stock and the amount, if any, of other securities, cash or property that then would be received upon the conversion of Preferred Stock.

4.10 Notice of Record Date. In the event:

(a) the Corporation shall take a record of the holders of its Common Stock (or other capital stock or securities at the time issuable upon conversion of the Preferred Stock) for the purpose of entitling or enabling them to receive any dividend or other distribution, or to receive any right to subscribe for or purchase any shares of capital stock of any class or any other securities, or to receive any other security; or

(b) of any capital reorganization of the Corporation, any reclassification of the Common Stock of the Corporation, or any Liquidity Event; or

(c) of the voluntary or involuntary dissolution, liquidation or winding-up of the Corporation,

then, and in each such case, the Corporation will send or cause to be sent to the holders of the Preferred Stock a notice specifying, as the case may be, (i) the record date for such dividend, distribution or right, and the amount and character of such dividend, distribution or right, or (ii) the effective date on which such reorganization, reclassification, consolidation, merger, transfer, dissolution, liquidation or winding-up is proposed to take place, and the time, if any is to be fixed, as of which the holders of record of Common Stock (or such other capital stock or securities at the time issuable upon the conversion of the Preferred Stock) shall be entitled to exchange their shares of Common Stock (or such other capital stock or securities) for securities

or other property deliverable upon such reorganization, reclassification, consolidation, merger, transfer, dissolution, liquidation or winding-up, and the amount per share and character of such exchange applicable to the Preferred Stock and the Common Stock. Such notice shall be sent at least 10 days prior to the record date or effective date for the event specified in such notice.

5. Mandatory Conversion .

5.1 Trigger Events . Upon the earlier of (a) the closing of a sale of Common Stock pursuant to an underwritten public offering by the Corporation or the registration of the Common Stock under the Securities Exchange Act of 1934 yielding gross proceeds to the Corporation of at least $20,000,000 or (b) the date and time, or the occurrence of an event, specified by consent of the holders of at least a majority of the Preferred Stock (the time of such closing or the date and time specified or the time of the event specified in such consent is referred to herein as the "Mandatory Conversion Time"), all outstanding shares of Preferred Stock shall automatically be converted into shares of Common Stock, at the then effective conversion rate.

5.2 Procedural Requirements . All holders of record of shares of Preferred Stock shall be sent written notice of the Mandatory Conversion Time and the place designated for mandatory conversion of all such shares of Preferred Stock pursuant to this Section 5. Such notice need not be sent in advance of the occurrence of the Mandatory Conversion Time. Upon receipt of such notice, each holder of shares of Preferred Stock shall surrender his, her or its certificate or certificates for all such shares (or, if such holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation at the place designated in such notice. If so required by the Corporation, certificates surrendered for conversion shall be endorsed or accompanied by written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or by his, her or its attorney duly authorized in writing. All rights with respect to the Preferred Stock converted pursuant to Section 5.1, including the rights, if any, to receive notices and vote (other than as a holder of Common Stock), will terminate at the Mandatory Conversion Time (notwithstanding the failure of the holder or holders thereof to surrender the certificates at or prior to such time), except only the rights of the holders thereof, upon surrender of their certificate or certificates (or lost certificate affidavit and agreement) therefor, to receive the items provided for in the next sentence of this Subsection 5.2. As soon as practicable after the Mandatory Conversion Time and the surrender of the certificate or certificates (or lost certificate affidavit and agreement) for Preferred Stock, the Corporation shall issue and deliver to such holder, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable on such conversion in accordance with the provisions hereof, together with cash as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and the payment of any dividends declared but unpaid on the shares of Preferred Stock converted. Such converted Preferred Stock shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Preferred Stock accordingly.

5.3 Effect of Mandatory Conversion . All shares of Preferred Stock shall, from and after the Mandatory Conversion Time, no longer be deemed to be outstanding and, notwithstanding the failure of the holder or holders thereof to surrender the certificates for such shares on or prior to such time, all rights with respect to such shares shall immediately cease and terminate at the Mandatory Conversion Time, except only the right of the holders thereof to receive shares of Common Stock in exchange therefor and to receive payment of any dividends declared but unpaid thereon. Such converted Preferred Stock shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Preferred Stock accordingly.

6. Redemption . The Preferred Stock is not redeemable.

7. Waiver . Any of the rights, powers, preferences and other terms of the Preferred Stock set forth herein may be waived on behalf of all holders of Preferred Stock by the affirmative written consent or vote of the holders of at least a majority of the shares of Preferred Stock then outstanding. In addition, any of the rights, powers, preferences and other terms of a particular series of Preferred Stock set forth herein may be waived on behalf of all holders of such series of Preferred Stock by the affirmative written consent or vote of the holders of at least a majority of the shares of such series of Preferred Stock then outstanding.

8. Notices . Any notice required or permitted by the provisions of this Article IV to be given to a holder of shares of Preferred Stock shall be mailed, postage prepaid, to the post office address last shown on the records of the Corporation, or given by electronic communication in compliance with the provisions of the DGCL, and shall be deemed sent upon such mailing or electronic transmission.

CERTIFICATE OF AMENDMENT

OF

CERTIFICATE OF INCORPORATION

OF

QR PHARMA, INC.

QR Pharma, Inc., a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the "DGCL"),

DOES HEREBY CERTIFY THAT:

FIRST: The Board of Directors (the "Board") of QR Pharma, Inc. (the "Corporation") duly adopted the following resolution setting forth a proposed amendment to the Certificate of Incorporation of the Corporation, as amended, declaring such amendment to be advisable. The resolution setting forth the proposed amendment is as follows:

RESOLVED, that Article I of the Corporation's Certificate of Incorporation, as amended (the "Charter"), is hereby amended and restated to provide as follows (the "Charter Amendment"):

"ARTICLE I

The name of the corporation is Annovis Bio, Inc. (the "Corporation")."

SECOND: The Charter Amendment was duly adopted in accordance with the provisions of Section 242 of the DGCL.

IN WITNESS WHEREOF, the Corporation has caused this Certificate of Amendment to be executed this 9th day of April, 2019.

QR PHARMA, INC.

By: /s/ Maria L. Maccecchini
Maria L. Maccecchini
President and Chief Executive Officer

Exhibit 3. 3

BY-LAWS

OF

ANNOVIS BIO, INC.

(a Delaware corporation)

Adopted on April 29, 2008

BY-LAWS
OF
ANNOVIS BIO, INC.

ARTICLE I
OFFICES

Section 1.1 Offices. The registered office of the Corporation shall be in the State of Delaware. The Corporation may have offices at such other places, both within and without the State of Delaware, as the Board of Directors may from time to time determine or as may be necessary or convenient to the business of the Corporation.

ARTICLE II
MEETINGS OF STOCKHOLDERS

Section 2.1 Annual Meeting. The annual meeting of stockholders shall be held on such date, at such time and at such place (if any), either within or without the State of Delaware, as shall be designated from time to time by the Board of Directors by resolution and stated in the notice of the meeting. At such annual meeting, the stockholders shall elect a Board of Directors and transact such other business as may properly be brought before the meeting. In lieu of holding an annual meeting of stockholders at a designated place, the Board of Directors may, in its sole discretion, determine that any annual meeting of stockholders may be held solely by means of remote communication.

Section 2.2 Special Meetings. Special meetings of stockholders shall be held on such date, at such time and at such place (if any), either within or without the State of Delaware, as shall be designated from time to time by the Board of Directors by resolution and stated in the notice of the meeting. Special meetings of stockholders, for any purpose or purposes, unless otherwise prescribed by statute or by the Certificate of Incorporation, may be called by the Chairman of the Board, if any, or the President and shall be called by the President or Secretary at the request in writing of a majority of the members of the Board of Directors, or at the request in writing of the stockholders entitled to cast at least a majority of the votes that all stockholders are entitled to cast at the particular meeting. Any such request shall state the purpose or purposes of the proposed meeting. In lieu of holding a special meeting of stockholders at a designated place, the Board of Directors may, in its sole discretion, determine that any special meeting of stockholders may be held solely by means of remote communication.

Section 2.3 Notice of Meetings and Record Date.

(a) The Corporation shall give notice of any annual or special meeting of stockholders. Notices of meetings of the stockholders shall state the place, if any, date and time thereof, and the means of remote communication, if any, by which each stockholder and proxyholder may be deemed to be present in person and vote at such meeting. In the case of a special meeting, the notice shall state the purpose or purposes for which the meeting is called. No business other than that specified in the notice thereof shall be transacted at any special meeting. Unless otherwise provided by applicable law or the Certificate of Incorporation, notice shall be given to each stockholder entitled to vote at such meeting not less than 10 days nor more than 60 days prior to the meeting.

(b) Notice to stockholders may be given by personal delivery, mail, or, with the consent of the stockholder entitled to receive notice, by facsimile or other means of electronic transmission. If mailed, such notice shall be delivered by postage prepaid envelope directed to each stockholder at such stockholder's address as it appears in the records of the Corporation and shall be deemed given when deposited in the United States mail. Notice given pursuant to this subsection shall be deemed given: (1) if by facsimile telecommunication, when directed to a facsimile telecommunication number at which the stockholder has consented to receive notice; (2) if by electronic mail, when directed to an electronic mail address at which the stockholder has consented to receive notice; (3) if by posting on an electronic network together with separate notice to the stockholder of such specific posting, upon the later of (A) such posting and (B) the giving of such separate notice; and (4) if by any other form of electronic transmission, when directed to the stockholder. An affidavit of the Secretary or an Assistant Secretary or of the transfer agent or other agent of the Corporation that the notice has been given by personal delivery, by mail, or by a form of electronic transmission shall, in the absence of fraud, be prima facie evidence of the facts stated therein.

(c) Without limiting the manner by which notice otherwise may be given effectively to stockholders, any notice to stockholders given by the Corporation shall be effective if given by a single written notice to stockholders who share an address if consented to by the stockholders at that address to whom such notice is given. Any such consent shall be revocable by the stockholder by written notice to the Corporation. Any stockholder who fails to object in writing to the Corporation, within 60 days of having been given written notice by the Corporation of its intention to send the single notice, shall be deemed to have consented to receiving such single written notice.

(d) Notice of any meeting of stockholders need not be given to any stockholder if waived by such stockholder either in a writing signed by such stockholder or by electronic transmission, whether such waiver is given before or after such meeting is held. If such a waiver is given by electronic transmission, the electronic transmission must either set forth or be submitted with information from which it can be determined that the electronic transmission was authorized by the stockholder.

(e) In order that the Corporation may determine the stockholders entitled to notice of or to vote at any meeting of stockholders or any adjournment thereof, the Board of Directors may fix a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors, and which record date shall not be more than 60 or fewer than 10 days before the date of such meeting. If no record date is fixed by the Board of Directors, the record date for determining stockholders entitled to notice of or to vote at any meeting of stockholders or any adjournment thereof shall be at the close of business on the day next preceding the day on which notice is given, or, if notice is waived, at the close of business on the day next preceding the day on which the meeting is held.

Section 2.4 Presiding Officer. Meetings of stockholders shall be presided over by the Chairman of the Board, if any, or, if the Chairman of the Board is not present (or, if there is none), by the President, or, if the President is not present, by a Vice President, or, if no Vice President is present (or, if there is none), by such person who may have been chosen by the Board of Directors, or, if none of such persons is present, by a chairman to be chosen by the

holders of a majority of the voting power of the shares of capital stock of the Corporation issued and outstanding and entitled to vote at the meeting and who are present in person or represented by proxy. The Secretary of the Corporation, or, if the Secretary is not present, an Assistant Secretary, or, if the Assistant Secretary is not present (or, if there is none), such person as may be chosen by the Board of Directors, shall act as secretary of meetings of stockholders, or, if none of such persons is present, the holders of a majority of the voting power of the shares of capital stock of the Corporation issued and outstanding and entitled to vote at the meeting and who are present in person or represented by proxy shall choose any person present to act as secretary of the meeting.

Section 2.5 Quorum; Adjournments. The holders of a majority of the aggregate voting power of the shares of capital stock of the Corporation issued and outstanding and entitled to vote thereat, present in person or represented by proxy, shall be necessary to, and shall constitute a quorum for, the transaction of business at all meetings of the stockholders, except as otherwise provided by law, by the Certificate of Incorporation or these By-Laws. If, however, a quorum shall not be present or represented at any meeting of the stockholders, the stockholders entitled to vote thereat, present in person or represented by proxy, shall have the power to adjourn the meeting from time to time, without notice of the adjourned meeting if the time and place thereof are announced at the meeting at which the adjournment is taken, until a quorum shall be present or represented. Even if a quorum shall be present or represented at any meeting of the stockholders, the stockholders entitled to vote thereat, present in person or represented by proxy, shall have the power to adjourn the meeting from time to time for good cause, without notice of the adjourned meeting if the time and place thereof are announced at the meeting at which the adjournment is taken, until a date which is not more than 30 days after the date of the original meeting. At any such adjourned meeting, at which a quorum shall be present in person or represented by proxy, any business may be transacted which might have been transacted at the meeting as originally called. A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of such meeting; provided, however, that the Board of Directors may fix a new record date for the adjourned meeting. If the adjournment is for more than 30 days, or if after the adjournment a new record date is fixed for the adjourned meeting, a notice of the adjourned meeting shall be given to each stockholder of record entitled to vote thereat.

Section 2.6 Voting.

(a) At any meeting of stockholders, every stockholder having the right to vote shall be entitled to vote in person or by proxy. Except as otherwise provided by law or the Certificate of Incorporation, each stockholder of record shall be entitled to one vote for each share of capital stock having voting power and registered in such stockholder's name on the books of the Corporation.

(b) Each person entitled to vote at a meeting of stockholders or to express consent or dissent to corporate action in writing without a meeting may authorize another person or persons to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. A proxy shall be irrevocable if it states that it is irrevocable and if, and only so long as, it is coupled with an interest sufficient in

law to support an irrevocable power. Proxies need not be filed with the Secretary of the Corporation until the meeting is called to order, but shall be filed before being voted.

(c) All elections shall be determined by a plurality vote, and, except as otherwise provided by law or the Certificate of Incorporation, all other matters shall be determined by the vote of the holders of a majority of the voting power of the shares present in person or represented by proxy and voting on such other matters.

Section 2.7 Remote Communication. For the purposes of these By-Laws, if authorized by the Board of Directors in its sole discretion, and subject to such guidelines and procedures as the Board of Directors may adopt, stockholders and proxyholders may, by means of remote communication:

(a) participate in a meeting of stockholders; and

(b) be deemed present in person and vote at a meeting of stockholders whether such meeting is to be held at a designated place or solely by means of remote communication, provided that (i) the Corporation shall implement reasonable measures to verify that each person deemed present and permitted to vote at the meeting by means of remote communication is a stockholder or proxyholder, (ii) the Corporation shall implement reasonable measures to provide such stockholders and proxyholders a reasonable opportunity to participate in the meeting and to vote on matters submitted to the stockholders, including an opportunity to read or hear the proceedings of the meeting substantially concurrently with such proceedings, and (iii) if any stockholder or proxyholder votes or takes other action at the meeting by means of remote communication, a record of such vote or other action shall be maintained by the Corporation.

Section 2.8 Action by Consent. Any action required or permitted by law or the Certificate of Incorporation to be taken at any meeting of stockholders may be taken without a meeting, without prior notice and without a vote, if a written consent, setting forth the action so taken, shall be signed by the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares entitled to vote thereon were present or represented by proxy and voted. A telegram, facsimile or other electronic transmission consenting to an action to be taken and transmitted by a stockholder or proxyholder, or by a person or persons authorized to act for a stockholder or proxyholder, shall be deemed to be written, signed and dated for the purposes of this section, provided that any such telegram, facsimile or other electronic transmission sets forth or is delivered with information from which the Corporation can determine that the telegram, facsimile or other electronic transmission was transmitted by the stockholder or proxyholder or by a person or persons authorized to act for the stockholder or proxyholder and the date on which such stockholder or proxyholder or authorized person or persons transmitted such telegram, cablegram or electronic transmission. The date on which such telegram, facsimile or electronic transmission is transmitted shall be deemed to be the date on which such consent was signed. No consent given by telegram, facsimile or other electronic transmission shall be deemed to have been delivered until such consent is reproduced in paper form and until such paper shall be delivered to the Corporation by delivery to its principal place of business or an officer or agent of the Corporation having custody of the book in which the proceedings of meetings of stockholders are recorded, to the extent and in the manner provided by resolution of the Board of

Directors of the Corporation. Any copy, facsimile or other reliable reproduction of a consent in writing may be substituted or used in lieu of the original writing for any and all purposes for which the original writing could be used, provided that such copy, facsimile or other reproduction shall be a complete reproduction of the entire original writing. Prompt notice of the taking of the corporate action without a meeting by less than unanimous written consent shall be given to those stockholders who have not consented in writing.

ARTICLE III
DIRECTORS

Section 3.1 General Powers; Number; Tenure. The business of the Corporation shall be managed by its Board of Directors, which may exercise all powers of the Corporation and perform all lawful acts and things that are not by law, the Certificate of Incorporation or these By-Laws directed or required to be exercised or performed by the stockholders or any class or classes or series thereof. The initial number of directors shall be one. Thereafter, except as may otherwise be provided in the Certificate of Incorporation, the number of directors shall be determined by the Board of Directors. The directors shall be elected at the annual meeting of the stockholders, except as provided in Section 3.2 hereof, and each director elected shall hold office until such director's successor is elected and shall qualify. Directors need not be stockholders. Meetings of the Board of Directors shall be presided over by the Chairman of the Board, if any, or in his or her absence by the Chief Executive Officer, if any, or in his or her absence by a presiding person chosen at the meeting. The Secretary shall act as secretary of the meeting, but in his or her absence the presiding person at the meeting may appoint any person to act as secretary of the meeting. The Chairman of the Board shall serve for such term and shall exercise such powers and perform such duties as shall be determined from time to time by the Board of Directors.

Section 3.2 Vacancies. Unless otherwise provided in the Certificate of Incorporation or these By-Laws, if any vacancies occur in the Board of Directors, or if any new directorships are created, they may be filled by vote of a majority of the directors then in office, although less than a quorum, or by a sole remaining director. Unless otherwise provided in the Certificate of Incorporation or these By-Laws, when one or more directors shall resign from the Board, effective at a future date, a majority of directors then in office, including those who have resigned, shall have the power to fill such vacancy or vacancies, the vote thereon to take effect when such resignation or resignations shall become effective. Each director so chosen shall hold office until the next annual meeting of stockholders and until his or her successor is duly elected and shall qualify. If there are no directors in office, any officer or stockholder may call a special meeting of stockholders in accordance with the provisions of the Certificate of Incorporation or these By-Laws, at which meeting such vacancies shall be filled.

Section 3.3 Removal; Resignation.

(a) Except as otherwise provided by law or the Certificate of Incorporation, any director, directors or the entire Board of Directors may be removed, with or without cause, by the holders of a majority of the voting power of the shares then entitled to vote at an election of directors.

(b) Any director may resign at any time by giving written notice to the Board of Directors, the Chairman of the Board, the President or the Secretary of the Corporation; provided, however, that if such notice is given by electronic transmission, such electronic transmission must either set forth or be submitted with information from which it can be determined that the electronic transmission was authorized by the director. Unless otherwise specified in such written notice, a resignation shall take effect upon delivery thereof to the Board of Directors or the designated officer. It shall not be necessary for a resignation to be accepted before it becomes effective.

Section 3.4 Annual Meeting. The annual meeting of each newly elected Board of Directors shall be held immediately following the annual meeting of stockholders, at the place where such meeting of stockholders has been held, or at such other place as shall be fixed by the person presiding over the meeting of the stockholders, for the purpose of election of officers and consideration of such other business as the Board of Directors considers relevant to the management of the Corporation, and no notice of such meeting shall be necessary to the newly elected directors in order legally to constitute the meeting, provided a quorum shall be present. In the event that in any year directors are elected by written consent in lieu of an annual meeting of stockholders, the Board of Directors shall meet in such year as soon as practicable after receipt of such written consent by the Corporation at such time and place as shall be fixed by the Chairman of the Board, for the purpose of election of officers and consideration of such other business as the Board of Directors considers relevant to the management of the Corporation.

Section 3.5 Regular Meetings. Regular meetings of the Board of Directors shall be held on such dates and at such times and places, within or without the State of Delaware, as shall from time to time be determined by the Board of Directors, such determination to constitute the only notice of such regular meetings to which any director shall be entitled. In the absence of any such determination, such meetings shall be held, upon notice to each director in accordance with Section 3.7 of this Article III, at such times and places, within or without the State of Delaware, as shall be designated by the Chairman of the Board.

Section 3.6 Special Meetings. Special meetings of the Board of Directors shall be held at the call of the Chairman of the Board at such times and places, within or without the State of Delaware, as he or she shall designate, upon notice to each director in accordance with Section 3.7 of this Article III. Special meetings shall be called by the Secretary on like notice at the written request of a majority of the directors then in office.

Section 3.7 Notice; Waiver of Notice.

(a) Notice of any regular (if required) or special meeting of the Board of Directors may be given by personal delivery, mail, telegram, courier service (including, without limitation, Federal Express), facsimile transmission (directed to the facsimile transmission number at which the director has consented to receive notice), electronic mail (directed to the electronic mail address at which the director has consented to receive notice), or other form of electronic transmission pursuant to which the director has consented to receive notice. If notice is given by personal delivery, by facsimile transmission, by telegram, by electronic mail, or by other form of electronic transmission pursuant to which the director has consented to receive notice, then such notice shall be given on not less than twenty-four hours' notice to each director. If written notice

is delivered by mail or courier service, then it shall be given on not less than three (3) calendar days' notice to each director. Notice of special meetings of the Board of Directors need not state the purpose thereof, except as otherwise expressly provided by law, the Certificate of Incorporation or these By-Laws. Any and all business may be transacted at a special meeting, unless otherwise indicated in the notice thereof or provided by law, the Certificate of Incorporation or these By-Laws.

(b) Notice of any meeting of the Board of Directors, or any committee thereof, need not be given to any member if waived by him or her in writing or by electronic transmission, whether before or after such meeting is held, or if he or she shall sign the minutes of such meeting or attend the meeting, except that if such director attends a meeting for the express purpose of objecting at the beginning of the meeting to the transaction of any business because the meeting is not lawfully called or convened, then such director shall not be deemed to have waived notice of such meeting. If waiver of notice is given by electronic transmission, such electronic transmission must either set forth or be submitted with information from which it can be determined that the electronic transmission was authorized by the director.

Section 3.8 Quorum; Adjournments. At all meetings of the Board of Directors and of each committee thereof, a majority of the total number of directors constituting the whole board or such committee shall be necessary and sufficient to constitute a quorum for the transaction of business. The act of a majority of the members present at any meeting of the Board of Directors or a committee thereof at which a quorum is present shall be the act of the Board of Directors or such committee, unless by express provision of applicable law, the Certificate of Incorporation, or these By-Laws, a different vote is required, in which case such express provision shall govern and control. In the absence of a quorum, a majority of the members present at any meeting may, without notice other than announcement at the meeting, adjourn such meeting from time to time until a quorum is present.

Section 3.9 Committees. The Board of Directors, by a vote of a majority of the whole Board of Directors, may from time to time designate one or more committees, each committee to consist of one or more directors, with such lawfully delegable powers and duties as it thereby confers (including the power and authority to designate other committees of the Board of Directors); provided, however, that no such committee shall have the power or authority in reference to the following matters: (i) approving or adopting, or recommending to the stockholders, any action or matter expressly required by the General Corporation Law of the State of Delaware to be submitted to stockholders for approval or (ii) adopting, amending, or repealing any By-Law of the Corporation. The Board of Directors may designate one or more directors as alternate members of any committee to replace any absent or disqualified member of the committee. In the absence or disqualification of a member of a committee, the member or members present at any meeting of such committee and not disqualified from voting, whether or not such member or members constitute a quorum, may unanimously appoint another member of the Board of Directors to act at the meeting in place of such absent or disqualified director.

Section 3.10 Committee Procedure.

(a) Except as otherwise determined by the Board of Directors or provided by these By-Laws, each committee shall adopt its own rules governing the time, place, and method of

holding its meetings and the conduct of its proceedings and shall meet as provided by such rules or by resolution of the Board of Directors. Unless otherwise provided by these By-Laws or any such rules or resolutions, notice of the time and place of each meeting of a committee shall be given to each member of such committee as provided in Section 3.7 of this Article III with respect to notices of meetings of the Board of Directors.

(b) Each committee shall keep regular minutes of its proceedings and report the same to the Board of Directors when required.

(c) Any member of any committee may be removed from such committee either with or without cause, at any time, by the Board of Directors at any meeting thereof. Any vacancy in any committee may be filled by the Board of Directors in the manner prescribed by the Certificate of Incorporation or these By-Laws for the original appointment of the members of such committee.

Section 3.11 Compensation. Directors shall be entitled to such compensation for their services as a director and to such reimbursement for any reasonable expenses incurred with respect to duties as a member of the Board of Directors or any committee thereof. The compensation of directors may be on such basis as is determined by the Board of Directors. Any director may waive compensation for any meeting. Any director receiving compensation under these provisions shall not be barred from serving the Corporation in any other capacity and receiving compensation and reimbursement for reasonable expenses for such other services.

Section 3.12 Action by Consent. Any action required or permitted to be taken at any meeting of the Board of Directors or any committee thereof may be taken without a meeting if all members of the Board of Directors or such committee, as the case may be, consent thereto in writing or by electronic transmission, and the writing or writings or electronic transmission or transmissions are filed with the minutes of proceedings of the Board of Directors or such committee; provided, however, that such electronic transmission or transmissions must either set forth or be submitted with information from which it can be determined that the electronic transmission or transmissions were authorized by the director. Such filing shall be in paper form if the minutes are maintained in paper form and shall be in electronic form if the minutes are maintained in electronic form.

Section 3.13 Meetings by Telephone or Similar Communications. Members of the Board of Directors, or any committee thereof, may participate in any meeting of the Board of Directors or such committee by means of conference telephone or other communications equipment by means of which all persons participating therein can hear each other, and participation in a meeting by such means shall constitute presence in person at such meeting.

ARTICLE IV
OFFICERS

Section 4.1 Designations. The officers of the Corporation shall be chosen by the Board of Directors. The Board of Directors may choose a Chief Executive Officer, a President, a Vice President or Vice Presidents, a Secretary, a Treasurer, one or more Assistant Secretaries and/or Assistant Treasurers and other officers and agents as it shall deem necessary or appropriate. All officers of the Corporation shall exercise such powers and perform such duties

as shall from time to time be determined by the Board of Directors. None of the officers of the Corporation needs to be a director of the Corporation. Any two or more offices may be held by the same person to the extent permitted by the General Corporation Law of the State of Delaware and other applicable law, unless the Certificate of Incorporation or these By-Laws otherwise provide.

Section 4.2 Term of Office; Removal. The Board of Directors at its annual meeting after each annual meeting of stockholders shall elect a President, a Secretary and a Treasurer. The Board of Directors may also elect a Chief Executive Officer, a Chief Operating Officer, a Chief Financial Officer, a Vice President or Vice Presidents, one or more Assistant Secretaries and/or Assistant Treasurers, and such other officers and agents as it shall deem necessary or appropriate. Each officer of the Corporation shall hold office at the pleasure of the Board of Directors, except as may otherwise be expressly provided in a contract of employment duly authorized by the Board of Directors. Any officer elected by the Board of Directors may be removed, with or without cause, at any time by the affirmative vote of a majority of the directors then in office. Such removal shall not prejudice the contract rights, if any, of the person so removed. Any vacancy occurring in any office of the Corporation may be filled for the unexpired portion of the term by the Board of Directors.

Section 4.3 Compensation. The salaries of all officers of the Corporation shall be fixed from time to time by the Board of Directors and no officer shall be prevented from receiving such salary by reason of the fact that such officer is also a director of the Corporation.

Section 4.4 The Chief Executive Officer. The Chief Executive Officer shall have general management, direction and control of the business and affairs of the Corporation, subject to the direction of the Board of Directors. The Chief Executive Officer shall preside, if no Chairman of the Board shall be designated, at all meetings of the Board of Directors. Unless otherwise directed by the Board of Directors from time to time, the Chief Executive Officer shall have the power to vote and otherwise act on behalf of the Corporation, in person or by proxy, at any meeting of stockholders of or with respect to any action of stockholders of any other corporation in which the Corporation may hold securities and otherwise to exercise any and all rights and powers which the Corporation may possess by reason of its ownership of securities in such other corporation.

Section 4.5 The President. The President shall be the chief operating officer of the Corporation and shall have such powers and perform such duties as may from time to time be assigned to the President by the Chief Executive Officer or the Board of Directors. If no Chief Executive Officer shall be designated and then be serving, the President shall be the chief executive officer of the Corporation, and, as such, shall have the functions, authority and duties provided for the Chief Executive Officer.

Section 4.6 The Vice Presidents. The Vice President, if any (or in the event there be more than one, the Vice Presidents in the order designated, or in the absence of any designation, in the order of their election), shall, in the absence of the President or in the event of his or her disability, perform the duties and exercise the powers of the President and shall generally assist the Chief Executive Officer and the President and perform such other duties and have such other

powers as may from time to time be assigned by the Chief Executive Officer or the Board of Directors.

Section 4.7 The Secretary. The Secretary shall attend meetings of the Board of Directors and of stockholders and record all votes and the proceedings of the meetings in a book to be kept for that purpose and shall perform like duties for the committees, if requested by the Board of Directors or any such committee. The Secretary shall give, or cause to be given, notice of all meetings of stockholders and special meetings of the Board of Directors, and shall perform such other duties as may from time to time be prescribed by the Board of Directors or the President, under whose supervision the Secretary shall act. The Secretary shall have custody of the seal of the Corporation, and the Secretary, or an Assistant Secretary, shall have authority to affix the same to any instrument requiring it, and, when so affixed, the seal may be attested by the signature of the Secretary or of an Assistant Secretary. The Board of Directors may give general authority to any other officer to affix the seal of the Corporation and to attest the affixing thereof by such officer's signature.

Section 4.8 The Assistant Secretary. The Assistant Secretary, if any (or in the event there be more than one, the Assistant Secretaries in the order designated, or in the absence of any designation, in the order of their election), shall, in the absence of the Secretary or in the event of his or her disability, perform the duties and exercise the powers of the Secretary and shall perform such other duties and have such other powers as may from time to time be prescribed by the Board of Directors.

Section 4.9 The Treasurer. The Treasurer shall have the custody of the corporate funds and other valuable effects, including securities, and shall keep full and accurate accounts of receipts and disbursements in books belonging to the Corporation and shall deposit all moneys and other valuable effects in the name and to the credit of the Corporation in such depositories as may from time to time be designated by the Board of Directors. The Treasurer shall disburse the funds of the Corporation as may be ordered by the Board of Directors, taking proper vouchers for such disbursements, and shall render to the Chief Executive Officer and the Board of Directors, at regular meetings of the Board, or whenever they may require it, an account of all his or her transactions as Treasurer and of the financial condition of the Corporation.

Section 4.10 The Assistant Treasurer. The Assistant Treasurer, if any (or in the event there shall be more than one, the Assistant Treasurers in the order designated, or in the absence of any designation, in the order of their election), shall, in the absence of the Treasurer or in the event of his or her disability, perform the duties and exercise the powers of the Treasurer and shall perform such other duties and have such other powers as may from time to time be prescribed by the Board of Directors.

ARTICLE V
INDEMNIFICATION OF DIRECTORS, OFFICERS, EMPLOYEES AND AGENTS

Section 5.1 Indemnification.

(a) Subject to Section 5.3 of this Article V, the Corporation shall indemnify, to the full extent that it shall have power under applicable law to do so and in a manner permitted by such law, any person who is made or threatened to be made a party to or is otherwise involved

(as a witness or otherwise) in any threatened, pending, or completed action, suit, or proceeding, whether civil, criminal, administrative, or investigative (hereinafter, a "Proceeding"), by reason of the fact that such person is or was a director or officer of the Corporation, or, while serving as a director or officer of the Corporation, is or was serving at the request of Corporation as a director, officer, employee, or agent of another corporation, partnership, joint venture, trust, or other enterprise, including service with respect to an employee benefit plan (collectively, "Another Enterprise") (such person hereinafter, a "Mandatory Indemnitee").

(b) The Corporation may indemnify, to the full extent that it shall have power under applicable law to do so and in a manner permitted by such law, any person who is made or threatened to be made a party to or is otherwise involved (as a witness or otherwise) in any Proceeding, by reason of the fact that such person is or was an employee or agent of the Corporation, or, while serving as an employee or agent of the Corporation, is or was serving at the request of the Corporation as a director, officer, employee, or agent of Another Enterprise (such person hereinafter, a "Permissive Indemnitee").

Section 5.2 Advancement of Expenses.

(a) Subject to Section 5.3 of this Article V, with respect to any Mandatory Indemnitee, the Corporation shall pay the expenses (including attorneys' fees) incurred by such person in defending any such Proceeding in advance of its final disposition (hereinafter an "advancement of expenses"); provided, however, that any advancement of expenses shall be made only upon receipt of an undertaking (hereinafter an "undertaking") by such person to repay all amounts advanced if it shall ultimately be determined by final judicial decision from which there is no further right to appeal that such person is not entitled to be indemnified for such expenses under this Article V or otherwise.

(b) With respect to any Permissive Indemnitee, the Corporation may, in its discretion and upon such terms and conditions, if any, as the Corporation deems appropriate, pay the expenses (including attorneys' fees) incurred by such person in defending any such Proceeding in advance of its final disposition.

Section 5.3 Actions Initiated Against the Corporation. Anything in Section 5.1(a) or Section 5.2(a) of this Article V to the contrary notwithstanding, except as provided in Section 5.5(b) of this Article V, with respect to a Proceeding initiated against the Corporation by a director or officer of the Corporation (whether initiated by such person in such capacity or in any other capacity, including as a director, officer, employee or agent of Another Enterprise), the Corporation shall not be required to indemnify or to advance expenses (including attorneys' fees) to such person in connection with prosecuting such Proceeding (or part thereof) or in defending any counterclaim, cross-claim, affirmative defense, or like claim of the Corporation in such Proceeding (or part thereof) unless such Proceeding was authorized by the Board of Directors of the Corporation.

Section 5.4 Contract Rights. With respect to any Mandatory Indemnitee, the rights to indemnification and to the advancement of expenses conferred in Sections 5.1(a) and 5.2(a) of this Article V shall be contract rights. Any amendment, repeal, or modification of, or adoption of any provision inconsistent with, this Article V (or any provision hereof) shall not adversely

affect any right to indemnification or advancement of expenses granted to any person pursuant hereto with respect to any act or omission of such person occurring prior to the time of such amendment, repeal, modification, or adoption (regardless of whether the Proceeding relating to such acts or omissions is commenced before or after the time of such amendment, repeal, modification, or adoption).

Section 5.5 Claims.

(a) If (i) a claim under Section 5.1(a) of this Article V with respect to any right to indemnification is not paid in full by the Corporation (following the final disposition of the Proceeding) within 60 days after a written demand has been received by the Corporation or (ii) a claim under Section 5.2(a) of this Article V with respect to any right to the advancement of expenses is not paid in full by the Corporation within 20 days after a written demand has been received by the Corporation, then the person seeking to enforce a right to indemnification or to an advancement of expenses, as the case may be, may at any time thereafter bring suit against the Corporation to recover the unpaid amount of the claim.

(b) If successful in whole or in part in any suit brought pursuant to Section 5.5(a) of this Article V, or in a suit brought by the Corporation to recover an advancement of expenses (whether pursuant to the terms of an undertaking or otherwise), the person seeking to enforce a right to indemnification or an advancement of expenses hereunder or the person from whom the Corporation sought to recover an advancement of expenses, as the case may be, shall be entitled to be paid by the Corporation the reasonable expenses (including attorneys' fees) of prosecuting or defending such suit.

(c) In any suit brought by a person seeking to enforce a right to indemnification hereunder (but not a suit brought by a person seeking to enforce a right to an advancement of expenses hereunder), it shall be a defense that the person seeking to enforce a right to indemnification has not met any applicable standard for indemnification under applicable law. With respect to any suit brought by a person seeking to enforce a right to indemnification or right to advancement of expenses hereunder or any suit brought by the Corporation to recover an advancement of expenses (whether pursuant to the terms of an undertaking or otherwise), neither (i) the failure of the Corporation to have made a determination prior to commencement of such suit that indemnification of such person is proper in the circumstances because such person has met the applicable standards of conduct under applicable law, nor (ii) an actual determination by the Corporation that such person has not met such applicable standards of conduct, shall create a presumption that such person has not met the applicable standards of conduct or, in a case brought by such person seeking to enforce a right to indemnification, be a defense to such suit.

(d) In any suit brought by a person seeking to enforce a right to indemnification or to an advancement of expenses hereunder, or by the Corporation to recover an advancement of expenses (whether pursuant to the terms of an undertaking or otherwise), the burden shall be on the Corporation to prove that the person seeking to enforce a right to indemnification or to an advancement of expenses or the person from whom the Corporation seeks to recover an advancement of expenses is not entitled to be indemnified, or to such an advancement of expenses, under this Article V or otherwise.

Section 5.6 Determination of Entitlement to Indemnification. Any indemnification required or permitted under this Article V (unless ordered by a court) shall be made by the Corporation only as authorized in the specific case upon a determination that indemnification of the present or former director, officer, employee or agent is proper in the circumstances because he or she has met all applicable standards of conduct set forth in this Article V and Section 145 of the General Corporation Law of the State of Delaware. Such determination shall be made, with respect to a person who is a director or officer of the Corporation at the time of such determination, (i) by a majority vote of the directors who are not parties to such action, suit or proceeding, even though less than a quorum; (ii) by a committee of such directors designated by majority vote of such directors, even though less than a quorum; (iii) if there are no such directors, or if such directors so direct, by independent legal counsel in a written opinion; or (iv) by the stockholders. Such determination shall be made, with respect to any person who is not a director or officer of the Corporation at the time of such determination, in the manner determined by the Board of Directors (including in such manner as may be set forth in any general or specific action of the Board of Directors applicable to indemnification claims by such person) or in the manner set forth in any agreement to which such person and the Corporation are parties.

Section 5.7 Non-Exclusive Rights. The indemnification and advancement of expenses provided in this Article V shall not be deemed exclusive of any other rights to which any person may be entitled under any by-law, agreement, vote of stockholders or disinterested directors, or otherwise, both as to action in such person's official capacity and as to action in another capacity while holding such office, and shall continue as to a person who has ceased to be such director, officer, employee, or agent and shall inure to the benefit of the heirs, executors, and administrators of such person.

Section 5.8 Insurance. The Corporation may purchase and maintain insurance on behalf of any person who is or was a director, officer, employee, or agent of the Corporation, or is or was serving at the request of the Corporation as a director, officer, employee, or agent of Another Enterprise against any liability asserted against such person and incurred by such person in any such capacity, or arising out of such person's status as such, whether or not the Corporation would have the power to indemnify such person against such liability under the provisions of this Article V or otherwise.

Section 5.9 Severability. If any provision or provisions of this Article V shall be held to be invalid, illegal, or unenforceable for any reason whatsoever: (a) the validity, legality, and enforceability of the remaining provisions of this Article V (including, without limitation, each portion of any paragraph or clause containing any such provision held to be invalid, illegal, or unenforceable, that is not itself held to be invalid, illegal, or unenforceable) shall not in any way be affected or impaired thereby; and (b) to the fullest extent possible, the provisions of this Article V (including, without limitation, each such portion of any paragraph or clause containing any such provision held to be invalid, illegal, or unenforceable) shall be construed so as to give effect to the intent manifested by the provision held invalid, illegal, or unenforceable.

Section 5.10 Miscellaneous. For purposes of this Article V: (a) references to serving at the request of the Corporation as a director or officer of Another Enterprise shall include any service as a director or officer of the Corporation that imposes duties on, or involves services by, such director or officer with respect to an employee benefit plan; (b) references to serving at the

request of the Corporation as a employee or agent of Another Enterprise shall include any service as an employee or agent of the Corporation that imposes duties on, or involves services by, such employee or agent with respect to an employee benefit plan; (c) a person who acted in good faith and in a manner such person reasonably believed to be in the interest of the participants and beneficiaries of an employee benefit plan shall be deemed to have acted in a manner not opposed to the best interests of the Corporation; and (d) references to a director of Another Enterprise shall include, in the case of any entity that is not managed by a board of directors, such other position, such as manager or trustee or member of the governing body of such entity, that entails responsibility for the management and direction of such entity's affairs, including, without limitation, general partner of any partnership (general or limited) and manager or managing member of any limited liability company .

ARTICLE VI
AFFILIATED TRANSACTIONS AND INTERESTED DIRECTORS

Section 6.1 Affiliated Transactions. No contract or transaction between the Corporation and one or more of its directors or officers, or between the Corporation and any other corporation, partnership, association or other organization in which one or more of its directors or officers are directors or officers, or have a financial interest, shall be void or voidable solely for this reason, or solely because the director or officer is present at or participates in the meeting of the Board of Directors or committee thereof which authorizes the contract or transaction or solely because his, her or their votes are counted for such purpose, if:

(a) The material facts as to his or her relationship or interest and as to the contract or transaction are disclosed or are known to the Board of Directors or the committee, and the Board of Directors or committee in good faith authorizes the contract or transaction by the affirmative vote of a majority of the disinterested directors, even though the disinterested directors be less than a quorum; or

(b) The material facts as to his or her relationship or interest and as to the contract or transaction are disclosed or are known to the stockholders entitled to vote thereon, and the contract or transaction is specifically approved in good faith by vote of the stockholders; or

(c) The contract or transaction is fair as to the Corporation as of the time it is authorized, approved or ratified by the Board of Directors, a committee thereof, or the stockholders.

Section 6.2 Determining Quorum. Common or interested directors may be counted in determining the presence of a quorum at a meeting of the Board of Directors or of a committee thereof which authorizes the contract or transaction.

ARTICLE VII
STOCK CERTIFICATES

Section 7.1 Form; Signatures.

(a) Shares of any or all of the Corporation's classes or series of capital stock may be evidenced by certificates for shares of stock, in such form as the Board of Directors may from

time to time prescribe, or may be issued in uncertificated form. The issuance of shares in uncertificated form shall not affect shares already represented by a certificate until the certificate is surrendered to the Corporation. Except as expressly provided by law, there shall be no differences in the rights and obligations of stockholders based on whether or not their shares are represented by certificates. The Corporation shall issue to any holder who so requests a share certificate representing shares registered in the holder's name, signed by the Chairman of the Board or the President and the Treasurer or an Assistant Treasurer or the Secretary or an Assistant Secretary of the Corporation, exhibiting the number and class (and series, if any) of shares owned by such stockholder, and bearing the seal of the Corporation. Such signatures and seal may be facsimiles. In case any officer who has signed, or whose facsimile signature was placed on, a certificate shall have ceased to be such officer before such certificate is issued, it may nevertheless be issued by the Corporation with the same effect as if he or she were such officer at the date of its issue.

(b) All stock certificates representing shares of capital stock that are subject to restrictions on transfer or to other restrictions may have imprinted thereon such notation to such effect as may be determined by the Board of Directors.

Section 7.2 Transfers. Transfers of stock of the Corporation shall be made on the books of the Corporation only upon surrender to the Corporation of a certificate (if any) for the shares duly endorsed or accompanied by proper evidence of succession, assignment, or authority to transfer; provided, however, that such succession, assignment, or transfer is not prohibited by the Certificate of Incorporation, these By-Laws, applicable law, or contract. Thereupon, the Corporation shall issue a new certificate (if requested) to the person entitled thereto, cancel the old certificate (if any), and record the transaction upon its books.

Section 7.3 Registered Stockholders.

(a) Except as otherwise provided by law, the Corporation shall be entitled to recognize the exclusive right of a person who is registered on its books as the owner of shares of its capital stock to receive dividends or other distributions, to vote as such owner, and to hold liable for calls and assessments any person who is registered on its books as the owner of shares of its capital stock. The Corporation shall not be bound to recognize any equitable or legal claim to or interest in such shares on the part of any other person.

(b) If a stockholder desires that notices and/or dividends shall be sent to a name or address other than the name or address appearing on the stock ledger maintained by the Corporation (or by the transfer agent or registrar, if any), such stockholder shall have the duty to notify the Corporation (or the transfer agent or registrar, if any) in writing, of such desire. Such written notice shall specify the alternate name or address to be used.

Section 7.4 Lost, Stolen or Destroyed Certificates. The Board of Directors may direct a new certificate to be issued in place of any certificate theretofore issued by the Corporation which is claimed to have been lost, stolen or destroyed, upon the making of an affidavit of that fact by the person claiming the certificate of stock to be lost, stolen or destroyed. When authorizing such issue of a new certificate, the Board of Directors may, in its discretion and as a condition precedent to the issuance thereof, require the owner of such lost, stolen or

destroyed certificate, or his or her legal representative, to advertise the same in such manner as it shall require and/or to give the Corporation a bond in such sum, or other security in such form, as it may direct as indemnity against any claim that may be made against the Corporation with respect to the certificate claimed to have been lost, stolen or destroyed.

ARTICLE VIII
GENERAL PROVISIONS

Section 8.1 Books and Records .

(a) Any books or records maintained by the Corporation in the regular course of its business, including its stock ledger, books of account, and minute books, may be kept on, or by means of, or be in the form of, any information storage device or method; provided, however, that the books and records so kept can be converted into clearly legible paper form within a reasonable time. The Corporation shall so convert any books or records so kept upon the request of any person entitled to inspect such records pursuant to the Certificate of Incorporation, these By-Laws, or the provisions of the General Corporation Law of the State of Delaware.

(b) It shall be the duty of the Secretary or other officer of the Corporation who shall have charge of the stock ledger to prepare and make, at least 10 days before every meeting of the stockholders, a complete list of the stockholders entitled to vote thereat, arranged in alphabetical order, and showing the address of each stockholder and the number of shares registered in the stockholder's name. Nothing contained in this subsection (b) shall require the Corporation to include electronic mail addresses or other electronic contact information on such list. Such list shall be open to the examination of any stockholder, for any purpose germane to the meeting for a period of at least 10 days prior to the meeting: (i) on a reasonably accessible electronic network, provided that the information required to gain access to such list is provided with the notice of the meeting, or (ii) during ordinary business hours, at the principal place of business of the Corporation. In the event that the Corporation determines to make the list available on an electronic network, the Corporation may take reasonable steps to ensure that such information is available only to stockholders of the Corporation. If the meeting is to be held at a place, then the list shall be produced and kept at the time and place of the meeting during the whole time thereof, and may be inspected by any stockholder who is present. If the meeting is to be held solely by means of remote communication, then the list shall also be open to the examination of any stockholder during the whole time of the meeting on a reasonably accessible network, and the information required to access such list shall be provided with the notice of the meeting. The stock ledger shall be the only evidence of the identity of the stockholders entitled to examine such list.

(c) Except to the extent otherwise required by law, the Certificate of Incorporation or these By-Laws, the Board of Directors shall determine from time to time whether and, if allowed, when and under what conditions and regulations the stock ledger, books, records, and accounts of the Corporation, or any of them, shall be open to inspection by the stockholders and the stockholders' rights, if any, in respect thereof. The stock ledger shall be the only evidence of the identity of the stockholders entitled to examine the stock ledger, the books, records, or accounts of the Corporation.

Section 8.2 Voting Shares in Other Business Entities. The Chief Executive Officer or any other officer of the Corporation designated by the Board of Directors may vote any and all shares of stock or other equity interest held by the Corporation in any other corporation or other business entity, and may exercise on behalf of the Corporation any and all rights and powers incident to the ownership of such stock or other equity interest.

Section 8.3 Record Date for Distributions and Other Actions. In order that the Corporation may determine the stockholders entitled to receive payment of any dividend or other distribution, or allotment of any rights, or the stockholders entitled to exercise any rights in respect of any change, conversion, or exchange of capital stock, or for the purpose of any other lawful action, except as may otherwise be provided in these By-Laws, the Board of Directors may fix a record date. Such record date shall not precede the date upon which the resolution fixing such record date is adopted, and shall not be more than 60 days prior to such action. If no record date is fixed, the record date for determining stockholders for any such purpose shall be the close of business on the day on which the Board of Directors adopts the resolution relating thereto.

Section 8.4 Fiscal Year. The fiscal year of the Corporation shall be such fiscal year as the Board of Directors from time to time by resolution shall determine.

Section 8.5 Gender/Number. As used in these By-Laws, the masculine, feminine, or neuter gender, and the singular and plural number, shall each include the other whenever the context so indicates.

Section 8.6 Section Titles. The titles of the sections and subsections have been inserted as a matter of reference only and shall not control or affect the meaning or construction of any of the terms and provisions hereof.

Section 8.7 Electronic Transmission. For purposes of these By-Laws, “electronic transmission” means any form of communication, not directly involving the physical transmission of paper, that creates a record that may be retained, retrieved, and reviewed by a recipient thereof, and that may be directly reproduced in paper form by such a recipient through an automated process.

Section 8.8 Amendment. These By-Laws may be altered, amended, or repealed at any annual or regular meeting of the Board of Directors or at any special meeting of the Board of Directors if notice of the proposed alteration, amendment, or repeal be contained in written notice of such special meeting, or at any meeting of the stockholders of the Corporation.

Section 8.9 Certificate of Incorporation. Notwithstanding anything to the contrary contained herein, if any provision contained in these By-Laws is inconsistent with or conflicts with a provision of the Certificate of Incorporation, such provision of these By-Laws shall be superseded by the inconsistent provision in the Certificate of Incorporation to the extent necessary to give effect to such provision in the Certificate of Incorporation.

EXHIBIT 10.1

AMENDED AND RESTATED
EMPLOYMENT AGREEMENT

EMPLOYMENT AGREEMENT effective as of May 10, 2019 between Annovis Bio, Inc. (the "Employer"), a Delaware corporation, and Maria L. Maccecchini (the "Employee").

Recital:

The Employer and the Employee are parties to an Amended and Restated Employment Agreement dated as of April 12, 2010 and subsequently amended on January 1, 2011, (collectively, the "2010 Employment Agreement"), which provides for the employment of the Employee by the Employer. The parties wish to amend and restate the 2010 Employment Agreement, as provided in this Agreement, to provide for the continuing employment of the Employee by the Employer and for certain other matters in connection with such employment, all as set forth more fully in this Agreement.

NOW, THEREFORE, in consideration of the premises and covenants set forth herein, and intending to be legally bound hereby, the parties to this Agreement hereby agree as follows:

1. Duties. The Employer agrees that the Employee shall be employed by the Employer to serve as President and Chief Executive Officer of the Employer. The Employee shall report to the Board of Directors of the Employer (the "Board"). The Employee agrees to be so employed by the Employer and to devote her best efforts and substantially all of her business time to advance the interests of the Employer and to perform such executive, managerial, administrative and financial functions as are required to develop the Employer's business and to perform other duties assigned to the Employee by the Board that are consistent with the Employee's position as President and Chief Executive Officer. Nothing set forth herein shall prohibit the Employee from engaging in personal investing activities or serving on the boards of directors of other entities whose businesses are not competitive with the Employer, provided that such activities do not interfere in any material respect with the services to be provided by the Employee under this Agreement.

2. Term. Except for earlier termination as provided in Section 4 hereof, the Employee's employment under this Agreement shall continue in effect until either party shall give to the other party at least ten business days' prior written notice of the termination of this Agreement, which notice shall specify the date of termination.

3. Compensation.

(a) Salary. From and after December 31, 2010, the Employee shall be paid an annual salary at the rate of not less than $120,000 (the "Base Salary"). The Base Salary shall be paid in accordance with the Employer's regular payroll practices. The Base Salary may be increased from time to time by the Board. The Board shall review the Base Salary at least annually at the end of each fiscal year of the Employer. After the closing of an Initial Public Offering (as such term is defined below), the annual Base Salary shall be increased on a prospective basis to an amount to be determined by the Compensation Committee of the Board

of Directors of the Employer (the "Committee") in consultation with a compensation consultant hired by the Committee. As used herein: an "Initial Public Offering" mean the first closing of a firm commitment underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended.

(b) Bonuses. At the end of each fiscal year of the Employer that ends during the term of this Agreement, the Board shall consider the award of a performance bonus to the Employee for such fiscal year in an amount of up to 50% of the Employee's Base Salary as in effect at the end of such fiscal year based upon the achievement of performance objectives established annually by the Board or its Compensation Committee. Whether the performance objectives for any year have been achieved by the Employee shall be determined by the Board or its Compensation Committee. The Employee shall also be eligible for the award of an additional discretionary bonus each year for exceptional performance. Notwithstanding the foregoing, all bonuses shall be paid within two and one-half months after the close of each year.

(c) Equity Incentive Programs. The Employee shall be eligible to participate in equity incentive programs established by the Employer from time to time to provide stock options and other equity-based incentives to key employees of the Employer in accordance with the terms of those programs. All stock options and restricted stock awards granted to the Employee will vest in full upon a change of control of the Employer (as defined in the stock option agreements covering such grants).

(d) Fringe Benefits. The Employee shall be entitled to participate in all insurance, vacation and other fringe benefit programs of the Employer to the extent and on the same terms and conditions as are accorded to other officers and key employees of the Employer.

(e) Reimbursement of Expenses. The Employee shall be reimbursed for all normal items of travel, entertainment and miscellaneous business expenses reasonably incurred by the Employee on behalf of the Employer, provided that such expenses are documented and submitted in accordance with the reimbursement policies of the Employer as in effect from time to time.

(f) Entire Compensation. The compensation provided for in this Agreement shall constitute full payment for the services to be rendered by the Employee to the Employer hereunder.

4. Termination.

(a) Death. This Agreement shall automatically terminate effective as of the date of the Employee's death, in which event the Employer shall not have any further obligation or liability under this Agreement except that the Employer shall pay to the Employee's estate: (i) any portion of the Employee's Base Salary for the period up to the Employee's date of death that has been earned but remains unpaid; and (ii) any benefits that have accrued to the Employee under the terms of the employee benefit plans of the Employer, which benefits shall be paid in accordance with the terms of those plans.

(b) Total Disability. The Employer may terminate the employment of the Employee immediately upon written notice to the Employee in the event of the Disability (as that

term is hereinafter defined) of the Employee for a period of 60 consecutive days, in which event, the Employer shall not have any further obligation or liability under this Agreement except that the Employer shall pay to the Employee: (i) any portion of the Employee's Base Salary for the period up to the date of termination that has been earned but remains unpaid; and (ii) any benefits that have accrued to the Employee under the terms of the employee benefit plans of the Employer, which benefits shall be paid in accordance with the terms of those plans. The term "Disability," when used herein, shall mean an illness, incapacity or a mental or physical condition that renders the Employee unable or incompetent to carry out the job responsibilities that the Employee held or the tasks that she was assigned at the time the disability commenced, as determined by the Board and supported by the opinion of a physician. The Employee shall fully cooperate with the physician retained to furnish such opinion, including submitting to such examinations and tests as may be requested by the physician.

(c) Termination by the Employer for Cause. The Employer may terminate the Employee's employment hereunder upon written notice to the Employee for any of the following reasons: (i) habitual intoxication; (ii) abuse of a controlled substance; (iii) conviction of a felony involving moral turpitude; (iv) adjudication as an incompetent; (v) a breach by the Employee of any material term of this Agreement, including the Employee's failure to faithfully, diligently and adequately perform her duties under this Agreement that is not corrected within ten days after written notice from the Employer, which notice shall set forth the nature of the breach; (vi) violation in any material respect of any of the Employer's rules, regulations or policies; (vii) gross insubordination by the Employee in the performance of her duties under this Agreement; (viii) engaging in any conduct, action or behavior that, in the reasonable opinion of the Board, has had a material adverse effect on the reputation of the Employer or the Employee; (ix) any continued or repeated absence from the Employer, unless the absence is approved or excused by the Board or the result of the Employee's illness, disability or incapacity (in which event the provisions of Section 4(b) hereof shall control); or (x) misappropriation of any funds or property of the Employer, theft, embezzlement or fraud. In the event that the Employer shall discharge the Employee pursuant to this Section 4(c), the Employer shall not have any further obligation or liability under this Agreement, except that the Employer shall pay to the Employee: (i) any portion of the Employee's Base Salary for the period up to the date of termination that has been earned but remains unpaid; and (ii) any benefits that have accrued to the Employee under the terms of the employee benefit plans of the Employer, which benefits shall be paid in accordance with the terms of those plans.

(d) Other Termination by the Employer. The Employer may terminate the employment of the Employee for any reason other than one specified in Section 4(b) or 4(c) hereof immediately upon written notice to the Employee, in which event the Employer shall pay to the Employee: (i) any portion of the Employee's Base Salary for the period up to the date of termination that has been earned but remains unpaid; (ii) any benefits that have accrued to the Employee under the terms of any employee benefit plans of the Employer, which benefits shall be paid in accordance with the terms of those plans; and (iii) subject to the execution by the Employee of a release satisfactory to the Employer and the compliance by the Employee with all terms and provisions of this Agreement that survive the termination of the Employee's employment by the Employer, the Employee's Base Salary for a period of twelve months after the effective date of the release, payable in accordance with the Employer's regular payroll practices.

(e) Termination by the Employee for Good Reason. The Employee may terminate her employment by providing written notice to the Employer of a breach constituting Good Reason, which notice shall be provided within 90 days of the initial existence of the breach, provided such breach is not cured in all material respects to the reasonable satisfaction of the Employee within 30 days after such notice. "Good Reason" shall be deemed to exist with respect to any termination of employment by the Employee for any of the following reasons: (i) a reassignment of the Employee to a location outside the Greater Philadelphia area; (ii) any material failure by the Employer to comply with any material term of this Agreement; or (iii) the demotion of the Employee to a lesser position than described in Section 1 hereof or a substantial diminution of the Employee's authority, duties or responsibilities as in effect on the date of this Agreement or as hereafter increased; provided, however, that Good Reason shall not include a termination of the Employee's employment pursuant to Section 4(b) or 4(c) hereof or, following a change of control of the Employer, a reduction in title, position, responsibilities or duties solely by virtue of the Employer being acquired and made part of a larger entity or operated as a subsidiary. If the Employee shall terminate her employment hereunder for Good Reason, the Employee shall be entitled to be paid: (i) any portion of the Employee's Base Salary for the period up to the date of termination that has been earned but remains unpaid; (ii) any benefits that have accrued to the Employee under the terms of any employee benefit plans of the Employer, which benefits shall be paid in accordance with the terms of those plans; and (iii) subject to the execution by the Employee of a release satisfactory to the Employer and the compliance by the Employee with all terms and provisions of this Agreement that survive the termination of the Employee's employment by the Employer, the Employee's Base Salary for a period of twelve months after the effective date of the release, payable in accordance with the Employer's regular payroll practices.

(f) Determination of Accrued Bonus. For purposes of this Section 4, upon the termination of the Employee's employment, the Board or its Compensation Committee shall consider whether all or any portion of the Employee's bonus has accrued based upon a review and determination of the Employee's progress toward achieving the performance objectives on which her bonus is based. All decisions regarding the achievement of the performance objectives and the accrual of all or any portion of the bonus shall be in the absolute discretion of the Board or Compensation Committee, as the case may be.

(g) Base Salary Continuation. The Base Salary continuation set forth in Sections 4(d) and (e) above shall be intended either (i) to satisfy the safe harbor set forth in the regulations issued under section 409A of the Internal Revenue Code of 1986, as amended (the "Code") (Treas. Regs. 1.409A-1(n)(2)(ii)) or (ii) be treated as a Short-term Deferral as that term is defined under Code section 409A (Treas. Regs. 1.409A-1(b)(4)). To the extent such continuation payments exceed the applicable safe harbor amount or do not constitute a Short-term Deferral, the excess amount shall be treated as deferred compensation under Code section 409A and as such shall be payable pursuant to the following schedule: such excess amount shall be paid via standard payroll in periodic installments in accordance with the Employer's usual practice for its senior executives. Notwithstanding any provision in this Agreement to the contrary, in the event that the Employee is a "specified employee" as defined in Section 409A, any continuation payment, continuation benefits or other amounts payable under this Agreement that would be subject to the special rule regarding payments to "specified employees" under Section 409A(a)(2)(B) of the Code shall not be paid before the expiration of a period of six

months following the date of the Employee's termination of employment or before the date of the Employee's death, if earlier.

5. Non-Disclosure and Non-Competition.

(a) Non-Disclosure. The Employee acknowledges that in the course of performing services for the Employer, the Employee will obtain knowledge of the Employer's business plans, products, processes, software, know-how, trade secrets, formulas, methods, models, prototypes, discoveries, inventions, improvements, disclosures, names and positions of employees and/or other proprietary and/or confidential information (collectively the "Confidential Information"). The Employee agrees to keep the Confidential Information secret and confidential and not to publish, disclose or divulge to any other party, and the Employee agrees not to use any of the Confidential Information for the Employee's own benefit or to the detriment of the Employer without the prior written consent of the Employer, whether or not such Confidential Information was discovered or developed by the Employee. The Employee also agrees not to divulge, publish or use any proprietary and/or confidential information of others that the Employer is obligated to maintain in confidence.

(b) Non-Competition. The Employee agrees that, during her employment by the Employer hereunder and for an additional period of one year after the termination of the Employee's employment hereunder, neither the Employee nor any corporation or other entity in which the Employee may be interested as a partner, trustee, director, officer, employee, agent, shareholder, lender of money or guarantor, or for which she performs services in any capacity (including as a consultant or independent contractor) shall at any time during such period (i) be engaged, directly or indirectly, in any Competitive Business (as that term is hereinafter defined) or (ii) solicit, hire, contract for services or otherwise employ, directly or indirectly, any of the employees of the Employer. For purposes of this Section 5(b) the term "Competitive Business" shall mean any firm or business organization that engages in the research, development, manufacturing, distribution, licensing or sale of any product that (i) relates to the prevention or treatment of Alzheimer's Disease or (ii) otherwise relates to any line of business, activity or field of interest or investigation engaged in by the Employer, or as to which the Employee has substantive oversight or other responsibilities in the performance of her duties on behalf of the Employer, during the term of the Employee's employment by the Employer. The foregoing prohibition shall not prevent any employment or engagement of the Employee, after termination of employment with the Employer, by any company or business organization not substantially engaged in a Competitive Business as long as the activities of any such employment or engagement, in any capacity, do not involve work on matters related to any product or service being developed, manufactured, marketed, distributed or planned in writing by the Employer at the time of termination of Employee's employment with the Employer. The Employee's ownership of no more than 5% of the outstanding voting stock of a publicly traded company shall not constitute a violation of this Section 5(b). The parties acknowledge and agree that the provisions of this Section 5(b) are a continuation of those set forth in the 2008 Employment Agreement and are intended to continue in effect in accordance with this Agreement.

6. Inventions and Discoveries.

(a) Disclosure. The Employee shall promptly and fully disclose to the Employer, with all necessary detail, all developments, know-how, discoveries, inventions, improvements, concepts, ideas, formulae, processes and methods (whether copyrightable, patentable or otherwise) made, received, conceived, acquired or written by the Employee (whether or not at the request or upon the suggestion of the Employer, solely or jointly with others), during the period of her employment with the Employer that (i) result from, arise out of, or relate to any work, assignment or task performed by the Employee on behalf of the Employer, whether undertaken voluntarily or assigned to the Employee within the scope of her responsibilities to the Employer, or (ii) were developed using the Employer's facilities or other resources or in Employer time, or (iii) result from the Employee's use or knowledge of the Employer's Confidential Information, or (iv) relate to the Employer's business or any of the products or services being developed, manufactured or sold by the Employer or that may be used in relation therewith (collectively referred to as "Inventions"). The Employee hereby acknowledges that all original works of authorship that are made by the Employee (solely or jointly with others) within the above terms and that are protectable by copyright are "works made for hire," as that term is defined in the United States Copyright Act. The Employee understands and hereby agrees that the decision whether or not to commercialize or market any Invention developed by the Employee solely or jointly with others is within the Employer's sole discretion and for the Employer's sole benefit and that no royalty shall be due to the Employee as a result of the Employer's efforts to commercialize or market any such Invention.

(b) Assignment and Transfer. The Employee agrees to assign and transfer to the Employer all of the Employee's right, title and interest in and to the Inventions, and the Employee further agrees to deliver to the Employer any and all drawings, notes, specifications and data relating to the Inventions, and to sign, acknowledge and deliver all such further papers, including applications for and assignments of copyrights and patents, and all renewals thereof, as may be necessary to obtain copyrights and patents for any Inventions in any and all countries and to vest title thereto in the Employer and its successors and assigns and to otherwise protect the Employer's interests therein. The Employee shall not charge the Employer for time spent in complying with these obligations. If the Employer is unable because of the Employee's mental or physical incapacity or for any other reason to secure the Employee's signature to apply for or to pursue any application for any United States or foreign patents or copyright registrations covering Inventions or original works of authorship assigned to the Employer as above, then the Employee hereby irrevocably designates and appoints the Employer and its duly authorized officers and agents as the Employee's agent and attorney in fact, to act for and in the Employee's behalf and stead to execute and file any such applications and to do all other lawfully permitted acts to further the prosecution and issuance of letters patent or copyright registrations thereon with the same legal force and effect as if executed by the Employee.

(c) Records. The Employee agrees that in connection with any research, development or other services performed for the Employer, the Employee will maintain careful, adequate and contemporaneous written records of all Inventions, which records shall be the property of the Employer.

7. Employer Documentation. The Employee shall hold in a fiduciary capacity for the benefit of the Employer all documentation, disks, programs, data, records, drawings, manuals, reports, sketches, blueprints, letters, notes, notebooks and all other writings, electronic data, graphics and tangible information and materials of a secret, confidential or proprietary information nature relating to the Employer or the Employer's business that are in the possession or under the control of the Employee.

8. Injunctive Relief. The Employee acknowledges that her compliance with the agreements in Sections 5, 6 and 7 hereof is necessary to protect the good will and other proprietary interests of the Employer and that the Employee is one of the principal executives of the Employer and conversant with the Employer's affairs, its trade secrets and other proprietary information. The Employee acknowledges that a breach of any of her agreements in Sections 5, 6 and 7 hereof will result in irreparable and continuing damage to the Employer for which there will be no adequate remedy at law; and the Employee agrees that in the event of any breach of the aforesaid agreements, the Employer and its successors and assigns shall be entitled to injunctive relief and to such other and further relief as may be proper.

9. Full Agreement, Modification. This Agreement amends, restates and supersedes the 2008 Employment Agreement and all other employment arrangements between the Employee and the Employer, but shall not supersede any existing confidentiality or nondisclosure agreements between the Employee and the Employer. This Agreement constitutes the entire agreement of the parties concerning its subject matter and supersedes all other oral or written understandings, discussions, and agreements, and may be modified only in a writing signed by both parties.

10. Amendments. Any amendment to this Agreement shall be made in writing and signed by the parties hereto.

11. Enforceability. If any provision of this Agreement shall be invalid or unenforceable, in whole or in part, then such provision shall be deemed to be modified or restricted to the extent and in the manner necessary to render the same valid and enforceable, or shall be deemed excised from this Agreement, as the case may require, and this Agreement shall be construed and enforced to the maximum extent permitted by law as if such provision had been originally incorporated herein as so modified or restricted or as if such provision had not been originally incorporated herein, as the case may be.

12. Construction. This Agreement shall be construed and interpreted in accordance with the internal laws of the Commonwealth of Pennsylvania.

13. Assignment.

(a) By the Employer. The rights and obligations of the Employer under this Agreement shall inure to the benefit of, and shall be binding upon, the successors and assigns of the Employer. This Agreement may be assigned by the Employer without the consent of the Employee.

(b) By the Employee. This Agreement and the obligations created hereunder may not be assigned by the Employee, but all rights of the Employee hereunder shall inure to the

benefit of and be enforceable by her heirs, devisees, legatees, executors, administrators and personal representatives.

14. Notices. All notices required or permitted to be given hereunder shall be in writing and shall be deemed to have been given when mailed by certified mail, return receipt requested, or delivered by a national overnight delivery service addressed to the intended recipient as follows:

If to the Employer:

Annovis Bio, Inc.
1055 Westlakes Drive, Suite 300
Berwyn, PA 19312
Attention: Chairman of the Board

If to the Employee:

Maria L. Maccecchini
1223 Foxglove Lane
West Chester, PA 19380-5854

Any party may from time to time change its address for the purpose of notices to that party by a similar notice specifying a new address, but no such change shall be deemed to have been given until it is actually received by the party sought to be charged with its contents.

15. Waivers. No claim or right arising out of a breach or default under this Agreement shall be discharged in whole or in part by a waiver of that claim or right unless the waiver is supported by consideration and is in writing and executed by the aggrieved party hereto or her or its duly authorized agent. A waiver by any party hereto of a breach or default by the other party hereto of any provision of this Agreement shall not be deemed a waiver of future compliance therewith, and such provisions shall remain in full force and effect.

16. Section 409A. It is intended that this Agreement be drafted and administered in compliance with section 409A of the Code, including, but not limited to, any future amendments to Code section 409A, and any other Internal Revenue Service or other governmental rulings or interpretations (together, "Section 409A") issued pursuant to Section 409A so as not to subject the Employee to payment of interest or any additional tax under Code section 409A. The parties intend for any payments under this Agreement to either satisfy the requirements of Section 409A or to be exempt from the application of Section 409A, and this Agreement shall be construed and interpreted accordingly. In furtherance thereof, if payment or provision of any amount or benefit hereunder that is subject to Section 409A at the time specified herein would subject such amount or benefit to any additional tax under Section 409A, the payment or provision of such amount or benefit shall be postponed to the earliest commencement date on which the payment or provision of such amount or benefit could be made without incurring such additional tax. In addition, to the extent that any Internal Revenue Service guidance issued under Section 409A would result in the Employee being subject to the payment of interest or any additional tax under Section 409A, the parties agree, to the extent reasonably possible, to amend this Agreement in order to avoid

the imposition of any such interest or additional tax under Section 409A, which amendment shall have the minimum economic effect necessary and be reasonably determined in good faith by the Employer and the Employee.

17. Survival of Covenants. The provisions of Sections 5, 6, 7 and 8 hereof shall survive the termination of this Agreement. Furthermore, any other provision of this Agreement that, by its terms, is intended to continue beyond the termination of the Employee's employment shall continue in effect thereafter.

IN WITNESS WHEREOF, this Agreement has been executed by the parties as of the date first above written.

ANNOVIS BIO, INC.

By: /s/ Maria L. Maccecchini

Title: President & CEO

/s/ Maria L. Maccecchini
Maria L. Maccecchini

EXHIBIT 10.2

Effective Date: April 12, 2018

ANNOVIS BIO, INC.

2018 EQUITY INCENTIVE PLAN

The purpose of the Annovis Bio, Inc. (formerly QR Pharma, Inc.) 2018 Equity Incentive Plan (this "Plan") is to provide (i) designated employees of Annovis Bio, Inc. (the "Company") and its parents and subsidiaries, (ii) certain consultants and advisors who perform services for the Company or its parents or subsidiaries and (iii) non-employee members of the Board of Directors of the Company (the "Board") with the opportunity to receive grants of incentive stock options, nonqualified stock options and stock awards. The Company believes that this Plan will encourage the participants to contribute materially to the growth of the Company, thereby benefitting the Company's stockholders, and will align the economic interests of the participants with those of the stockholders.

This Plan is intended as the successor to the Company's Amended and Restated 2008 Equity Incentive Plan (the "Prior Plan"). Following the effective date of this Plan set forth above (the "Effective Date"), no additional grants of options or stock awards shall be granted under the Prior Plan. Any shares remaining available for issuance pursuant to the exercise of options or settlement of stock awards under the Prior Plan shall become available for issuance under this Plan pursuant to Grants (as defined in Section 2) granted hereunder, as provided in Section 3(a). Any shares subject to outstanding stock options or stock awards granted under the Prior Plan that expire or terminate or are repurchased by the Company for any reason prior to exercise, settlement or vesting shall become available for issuance under this Plan pursuant to stock options and stock awards granted hereunder. All outstanding stock options and stock awards granted under the Prior Plan shall remain subject to the terms of the Prior Plan with respect to which they were originally granted.

1. Administration.

(a) Committee. This Plan shall be administered and interpreted by the Board or by a committee consisting of members of the Board, which shall be appointed by the Board. After an initial public offering of the Company's stock as described in Section 17(b) (a "Public Offering"), this Plan shall be administered by a committee of Board members, which may consist of "non-employee directors" as defined under Rule 16b-3 under the Securities Exchange Act of 1934, as amended (the "Exchange Act"). However, the Board may ratify or approve any grants as it deems appropriate, and the Board shall approve and administer all grants made to non-employee directors. The committee may delegate authority to one or more subcommittees as it deems appropriate. To the extent that a committee or subcommittee administers this Plan, references in this Plan to the "Board" shall be deemed to refer to the committee or subcommittee; provided, however, that the Board of Directors itself may, at any time, exercise any and all rights and authority granted by it to a committee or subcommittee.

(b) Board Authority. The Board shall have the sole authority to (i) determine the individuals to whom grants shall be made under this Plan, (ii) determine the type, size and terms of the grants to be made to each such individual, (iii) determine the time when the grants will be made and the duration of any applicable exercise or restriction period, including the criteria for

exercisability and the acceleration of exercisability, (iv) amend the terms of any previously issued grant, and (v) deal with any other matters arising under this Plan.

(c) Board Determinations. The Board shall have full power and authority to administer and interpret this Plan, to make factual determinations and to adopt or amend such rules, regulations, agreements and instruments for implementing this Plan and for the conduct of its business as it deems necessary or advisable, in its sole discretion. The Board's interpretations of this Plan and all determinations made by the Board pursuant to the powers vested in it hereunder shall be conclusive and binding on all persons having any interest in this Plan or in any awards granted hereunder. All powers of the Board shall be executed in its sole discretion, in the best interest of the Company, not as a fiduciary, and in keeping with the objectives of this Plan and need not be uniform as to similarly situated individuals.

(d) Delegation to Officers. To the extent permitted by applicable law, the Board may delegate to one or more officers of the Company the power to grant Options and Stock Awards (as each such term is defined in Section 2) to employees or officers of the Company or any of its present or future subsidiary corporations and to exercise such other powers under this Plan as the Board may determine, provided that the Board shall fix the terms of the Options and Stock Awards to be granted by such officers (including the exercise price of such Options, and the consideration, if any, for the Stock Awards, which may include a formula by which the exercise price or purchase price, if any, will be determined) and the maximum number of shares subject to Options and Stock Awards that the officers may grant; provided further, however, that no officer shall be authorized to grant any Options or Stock Awards to himself or herself.

2. Grants. Awards under this Plan may consist of grants of incentive stock options as described in Section 5 ("Incentive Stock Options"), nonqualified stock options as described in Section 5 ("Nonqualified Stock Options") (Incentive Stock Options and Nonqualified Stock Options are collectively referred to as "Options") and stock awards as described in Section 6 ("Stock Awards") (hereinafter collectively referred to as "Grants"). All Grants shall be subject to the terms and conditions set forth herein and to such other terms and conditions consistent with this Plan as the Board deems appropriate and as are specified in writing by the Board to the individual in a grant instrument or an amendment to the grant instrument (the "Grant Instrument"). All Grants shall be made conditional upon the Grantee's acknowledgement, in writing or by acceptance of the Grant, that all decisions and determinations of the Board shall be final and binding on the Grantee, his or her beneficiaries and any other person having or claiming an interest under such Grant. The Board shall approve the form and provisions of each Grant Instrument. Grants under a particular Section of this Plan need not be uniform as among the grantees.

3. Shares Subject to This Plan.

(a) Shares Reserved. Subject to adjustment as described below, the aggregate number of shares of common stock of the Company ("Company Stock") that may be issued under this Plan is equal to (i) the 524,233 shares (being the 24,233 shares remaining available for issuance under the Prior Plan as of the Effective Date plus 500,000 additional shares), and (ii) the number of shares that may be added to this Plan pursuant to Section 3(b) (collectively the "Share Reserve"), each of which may be granted as an Incentive Stock Option, up to the maximum limit

set forth in Section 3(d) below. After a Public Offering, the maximum aggregate number of shares of Company Stock that shall be subject to Grants made under this Plan to (i) any employee during any calendar year shall be 600,000 shares and (ii) any non-employee member of the Board during any calendar year shall be 100,000 shares, subject to adjustment as described below. Shares issued under this Plan may be authorized but unissued shares of Company Stock or reacquired shares of Company Stock, including shares purchased by the Company on the open market for purposes of this Plan.

(b) Additions to the Share Reserve. The Share Reserve also shall be increased from time to time by a number of shares equal to the number of shares of Company Stock that (i) are issuable pursuant to options outstanding under the Prior Plan as of the Effective Date and (ii) but for the termination of the Prior Plan as of the Effective Date, would otherwise have reverted to the share reserve of the Prior Plan pursuant to the provisions thereof.

(c) Reversion of Shares to the Share Reserve. If and to the extent Options granted under this Plan terminate, expire, or are canceled, forfeited, exchanged or surrendered without having been exercised or if any Stock Awards (including restricted Stock Awards received upon the exercise of Options) are forfeited, the shares subject to such Grants shall again be available for purposes of this Plan.

(d) Incentive Stock Option Limit. Notwithstanding anything to the contrary in this Section 3, subject to the provisions of Section 3(e) relating to capitalization adjustments, the aggregate maximum number of shares of Company Stock that may be issued pursuant to the exercise of Incentive Stock Options shall be 524,233 shares of Company Stock plus the amount of any increase in the number of shares that may be available for issuance pursuant to Grants pursuant to Section 3(b), but in no event shall greater than 524,233 shares of Company Stock be issued as Incentive Stock Options (the "Maximum Incentive Stock Option Limit"). Any additional shares added to the Plan pursuant to the Share Reserve in excess of the Maximum Incentive Stock Option Limit shall not be issued as Incentive Stock Options but may be issued as Nonqualified Stock Options or Stock Awards.

(e) Adjustments. If there is any change in the number or kind of shares of Company Stock outstanding (i) by reason of a stock dividend, spinoff, recapitalization, stock split, or combination or exchange of shares, (ii) by reason of a merger, reorganization or consolidation, (iii) by reason of a reclassification or change in par value, or (iv) by reason of any other extraordinary or unusual event affecting the outstanding Company Stock as a class without the Company's receipt of consideration, or if the value of outstanding shares of Company Stock is substantially reduced as a result of a spinoff or the Company's payment of an extraordinary dividend or distribution, the maximum number of shares of Company Stock available for Grants, the maximum number of shares of Company Stock that any individual participating in this Plan may be granted in any year, the number of shares covered by outstanding Grants, the kind of shares issued under this Plan, and the price per share of such Grants shall be appropriately adjusted by the Board to reflect any increase or decrease in the number of, or change in the kind or value of, issued shares of Company Stock to preclude, to the extent practicable, the enlargement or dilution of rights and benefits under such Grants; provided, however, that any fractional shares resulting from such adjustment shall be eliminated. Any adjustments determined by the Board shall be final, binding and conclusive.

4. Eligibility for Participation .

(a) Eligible Persons . All employees of the Company and its parents or subsidiaries ("Employees"), including Employees who are officers or members of the Board, and members of the Board who are not Employees ("Non-Employee Directors") shall be eligible to participate in this Plan. Consultants and advisors who perform services for the Company or any of its parents or subsidiaries ("Key Advisors") shall be eligible to participate in this Plan if the Key Advisors render bona fide services to the Company or its parents or subsidiaries, the services are not in connection with the offer and sale of securities in a capital-raising transaction, and the Key Advisors do not directly or indirectly promote or maintain a market for the Company's securities.

(b) Selection of Grantees . The Board shall select the Employees, Non-Employee Directors and Key Advisors to receive Grants and shall determine the number of shares of Company Stock subject to a particular Grant in such manner as the Board determines. Employees, Key Advisors and Non-Employee Directors who receive Grants under this Plan shall hereinafter be referred to as "Grantees."

5. Granting of Options .

(a) Number of Shares . The Board shall determine the number of shares of Company Stock that will be subject to each Grant of Options to Employees, Non-Employee Directors and Key Advisors.

(b) Type of Option and Price .

(i) The Board may grant Incentive Stock Options that are intended to qualify as "incentive stock options" within the meaning of section 422 of the Code or Nonqualified Stock Options that are not intended so to qualify or any combination of Incentive Stock Options and Nonqualified Stock Options, all in accordance with the terms and conditions set forth herein. Incentive Stock Options may be granted only to employees of the Company or its parents or subsidiaries, as defined in section 424 of the Code. Nonqualified Stock Options may be granted to Employees, Non-Employee Directors and Key Advisors. The date of grant of an Option shall be the date on which the Board makes the determination to grant such Option unless a later date is otherwise specified by the Board.

(ii) The purchase price (the "Exercise Price") of Company Stock subject to an Option shall be determined by the Board and may be equal to or greater than the Fair Market Value (as defined below) of a share of Company Stock on the date the Option is granted; provided, however, that (x) the Exercise Price of an Incentive Stock Option shall be equal to, or greater than, the Fair Market Value of a share of Company Stock on the date the Incentive Stock Option is granted and (y) an Incentive Stock Option may not be granted to an Employee who, at the time of grant, owns stock possessing more than 10% of the total combined voting power of all classes of stock of the Company or any parent or subsidiary of the Company, unless the Exercise Price per share is not less than 110% of the Fair Market Value of Company Stock on the date of grant.

(iii) If the Company Stock is publicly traded, then the Fair Market Value per share shall be determined as follows: (x) if the principal trading market for the Company Stock is a national securities exchange, the last reported sale price thereof on the relevant date or (if there were no trades on that date) the latest preceding date upon which a sale was reported, or (y) if the Company Stock is not principally traded on such exchange or market, the mean between the last reported "bid" and "asked" prices of Company Stock on the relevant date, as reported by the National Daily Quotation Bureau, Inc. or as reported in a customary financial reporting service, as applicable and as the Board determines. If the Company Stock is not publicly traded or, if publicly traded, is not subject to reported transactions or "bid" or "asked" quotations as set forth above, the Fair Market Value per share shall be as determined by the Board.

(c) Option Term . The Board shall determine the term of each Option. The term of any Option shall not exceed ten years from the date of grant. However, an Incentive Stock Option that is granted to an Employee who, at the time of grant, owns stock possessing more than 10% of the total combined voting power of all classes of stock of the Company, or any parent or subsidiary of the Company, may not have a term that exceeds five years from the date of grant.

(d) Exercisability of Options .

(i) Options shall become exercisable in accordance with such terms and conditions, consistent with this Plan, as may be determined by the Board and specified in the Grant Instrument. The Board may accelerate the exercisability of any or all outstanding Options at any time for any reason.

(ii) The Board may provide in a Grant Instrument that the Grantee may elect to exercise part or all of an Option before it otherwise has become exercisable. Any shares so purchased shall be restricted shares and shall be subject to a repurchase right in favor of the Company during a specified restriction period, with the repurchase price equal to the lesser of (i) the Exercise Price or (ii) the Fair Market Value of such shares at the time of repurchase, or such other restrictions as the Board deems appropriate.

(e) Grants to Non-Exempt Employees . Notwithstanding the foregoing, Options granted to persons who are non-exempt employees under the Fair Labor Standards Act of 1938, as amended, shall have an Exercise Price not less than the Fair Market Value of the Company Stock on the date of grant, and may not be exercisable for at least six months after the date of grant (except that such Options may become exercisable, as determined by the Board, upon the Grantee's death, Disability or retirement, or upon a Change of Control or other circumstances permitted by applicable regulations).

(f) Termination of Employment, Disability or Death .

(i) Except as provided below, an Option may only be exercised while the Grantee is employed by, or providing service to, the Employer (as defined below) as an Employee, Key Advisor or member of the Board. In the event that a Grantee ceases to be employed by, or provide service to, the Employer for any reason other than Disability, death, or termination for Cause, any Option which is otherwise exercisable by the Grantee shall terminate unless exercised within three months after the date on which the Grantee ceases to be employed

by, or provide service to, the Employer (or within such other period of time as may be specified by the Board), but in any event no later than the date of expiration of the Option term. Except as otherwise provided by the Board, any of the Grantee's Options that are not otherwise exercisable as of the date on which the Grantee ceases to be employed by, or provide service to, the Employer shall terminate as of such date.

(ii) In the event the Grantee ceases to be employed by, or provide service to, the Employer on account of a termination for Cause by the Employer, any Option held by the Grantee shall terminate as of the date the Grantee ceases to be employed by, or provide service to, the Employer. In addition, notwithstanding any other provisions of this Section 5, if the Board determines that the Grantee has engaged in conduct that constitutes Cause at any time while the Grantee is employed by, or providing service to, the Employer or after the Grantee's termination of employment or service, any Option held by the Grantee shall immediately terminate, and the Grantee shall automatically forfeit all shares underlying any exercised portion of an Option for which the Company has not yet delivered the share certificates, upon refund by the Company of the Exercise Price paid by the Grantee for such shares. Upon any exercise of an Option, the Company may withhold delivery of share certificates pending resolution of an inquiry that could lead to a finding resulting in a forfeiture.

(iii) In the event the Grantee ceases to be employed by, or provide service to, the Employer because the Grantee is Disabled, any Option which is otherwise exercisable by the Grantee shall terminate unless exercised within one year after the date on which the Grantee ceases to be employed by, or provide service to, the Employer (or within such other period of time as may be specified by the Board), but in any event no later than the date of expiration of the Option term. Except as otherwise provided by the Board, any of the Grantee's Options which are not otherwise exercisable as of the date on which the Grantee ceases to be employed by, or provide service to, the Employer shall terminate as of such date.

(iv) If the Grantee dies while employed by, or providing service to, the Employer or within three months after the date on which the Grantee ceases to be employed or provide service on account of a termination specified in Section 5(f)(i) (or within such other period of time as may be specified by the Board), any Option that is otherwise exercisable by the Grantee shall terminate unless exercised within one year after the date on which the Grantee ceases to be employed by, or provide service to, the Employer (or within such other period of time as may be specified by the Board), but in any event no later than the date of expiration of the Option term. Except as otherwise provided by the Board, any of the Grantee's Options that are not otherwise exercisable as of the date on which the Grantee ceases to be employed by, or provide service to, the Employer shall terminate as of such date.

(v) For purposes of this Section 5(f) and Section 6:

(A) The term "Employer" shall include the Company and its parent and subsidiary corporations or other entities, as appropriate and as determined by the Board.

(B) "Employed by, or provide service to, the Employer" shall mean employment or service as an Employee, Key Advisor or member of the Board (so that, for purposes of exercising Options and satisfying conditions with respect to Stock Awards, a Grantee shall not be considered to have terminated employment or service

until the Grantee ceases to be an Employee, Key Advisor or member of the Board), unless the Board determines otherwise.

(C) "Disability" shall mean a Grantee's becoming disabled within the meaning of section 22(e)(3) of the Code, within the meaning of the Employer's long-term disability plan applicable to the Grantee, or as otherwise determined by the Board.

(D) "Cause" shall mean, except to the extent specified otherwise by the Board, a finding by the Board that the Grantee (i) has breached his or her employment or service contract with the Employer, (ii) has engaged in disloyalty to the Company, including, without limitation, fraud, embezzlement, theft, commission of a felony or proven dishonesty, (iii) has disclosed trade secrets or confidential information of the Employer to persons not entitled to receive such information, (iv) has breached any written noncompetition or nonsolicitation agreement between the Grantee and the Employer or (v) has engaged in such other behavior detrimental to the interests of the Employer as the Board determines.

(g) Exercise of Options . A Grantee may exercise an Option that has become exercisable, in whole or in part, by delivering a notice of exercise to the Company with payment of the Exercise Price; provided, however, that the Committee shall have the power to permit: (i) the exercise of unvested Options, or portions thereof, for the purchase of shares of restricted Common Stock subject to a repurchase right in favor of the Company, with the repurchase price being equal to the lesser of (x) the original purchase price or (y) the Fair Market Value of the shares on the date of repurchase, or to any other restrictions as the Committee deems to be appropriate, and (ii) the acceleration of previously established exercise terms, in each case upon such circumstances and subject to such terms and conditions as the Committee shall determine. The Grantee shall pay the Exercise Price for an Option as specified by the Board (I) in cash, (II) with the approval of the Board, by delivering shares of Company Stock owned by the Grantee (including Company Stock acquired in connection with the exercise of an Option, subject to such restrictions as the Board deems appropriate) and having a Fair Market Value on the date of exercise equal to the Exercise Price or by attestation (on a form prescribed by the Board) to ownership of shares of Company Stock having a Fair Market Value on the date of exercise equal to the Exercise Price, (III) after a Public Offering, payment through a broker in accordance with procedures permitted by Regulation T of the Federal Reserve Board, or (IV) by such other method as the Board may approve. The Board may authorize loans by the Company to Grantees in connection with the exercise of an Option, upon such terms and conditions as the Board, in its sole discretion, deems appropriate. Shares of Company Stock used to exercise an Option shall have been held by the Grantee for the requisite period of time to avoid adverse accounting consequences to the Company with respect to the Option. The Grantee shall pay the Exercise Price and the amount of any withholding tax due (pursuant to Section 7) at the time of exercise.

(h) Limits on Incentive Stock Options . Each Incentive Stock Option shall provide that, if the aggregate Fair Market Value of the stock on the date of the grant with respect to which Incentive Stock Options are exercisable for the first time by a Grantee during any calendar year, under this Plan or any other stock option plan of the Company or a parent or subsidiary, exceeds $100,000, then the Option, as to the excess, shall be treated as a Nonqualified Stock Option. An Incentive Stock Option shall not be granted to any person who is not an Employee

of the Company or a parent or subsidiary (within the meaning of section 424(f) of the Code) of the Company.

6. Stock Awards. The Board may issue shares of Company Stock to an Employee, Non-Employee Director or Key Advisor under a Stock Award, upon such terms as the Board deems appropriate. The following provisions are applicable to Stock Awards:

(a) General Requirements. Shares of Company Stock issued pursuant to Stock Awards may be issued for consideration or for no consideration, and subject to restrictions or no restrictions, as determined by the Board. The Board may establish conditions under which restrictions on Stock Awards shall lapse over a period of time or according to such other criteria as the Board deems appropriate. The period of time during which the Stock Award will remain subject to restrictions will be designated in the Grant Instrument as the "Restriction Period."

(b) Number of Shares. The Board shall determine the number of shares of Company Stock to be issued pursuant to a Stock Award and the restrictions applicable to such shares.

(c) Requirement of Employment or Service. If the Grantee ceases to be employed by, or provide service to, the Employer (as defined in Section 5(f)) during a period designated in the Grant Instrument as the Restriction Period, or if other specified conditions are not met, the Stock Award shall terminate as to all shares covered by the award as to which the restrictions have not lapsed, and those shares of Company Stock must be immediately returned to the Company. The Board may, however, provide for complete or partial exceptions to this requirement as it deems appropriate.

(d) Restrictions on Transfer and Legend on Stock Certificate. During the Restriction Period, a Grantee may not sell, assign, transfer, pledge or otherwise dispose of the shares of the Stock Award except to a successor under Section 8(a). Each certificate for Stock Awards shall contain a legend giving appropriate notice of the restrictions in the Grant. The Grantee shall be entitled to have the legend removed from the stock certificate covering the shares subject to restrictions when all restrictions on such shares have lapsed. The Board may determine that the Company will not issue certificates for Stock Awards until all restrictions on such shares have lapsed, or that the Company will retain possession of certificates for Stock Awards until all restrictions on such shares have lapsed.

(e) Right to Vote and to Receive Dividends. During the Restriction Period, the Grantee shall have the right to vote shares subject to Stock Awards and to receive any dividends or other distributions paid on such shares, subject to any restrictions deemed appropriate by the Board.

(f) Lapse of Restrictions. All restrictions imposed on Stock Awards shall lapse upon the expiration of the applicable Restriction Period and the satisfaction of all conditions imposed by the Board. The Board may determine, as to any or all Stock Awards, that the restrictions shall lapse without regard to any Restriction Period.

7. Withholding of Taxes.

(a) Required Withholding. All Grants under this Plan shall be subject to applicable federal (including FICA), state and local tax withholding requirements. The Employer may require that the Grantee or other person receiving or exercising Grants pay to the Employer the amount of any federal, state or local taxes that the Employer is required to withhold with respect to such Grants, or the Employer may deduct from other wages paid by the Employer the amount of any withholding taxes due with respect to such Grants.

(b) Election to Withhold Shares. If the Board so permits, a Grantee may elect to satisfy the Employer's income tax withholding obligation with respect to a Grant by having shares withheld up to an amount that does not exceed the Grantee's minimum applicable withholding tax rate for federal (including FICA), state and local tax liabilities. The election must be in a form and manner prescribed by the Board and may be subject to the prior approval of the Board.

8. Transferability of Grants.

(a) Nontransferability of Grants. Except as provided below, only the Grantee may exercise rights under a Grant during the Grantee's lifetime. A Grantee may not transfer those rights except (i) by will or by the laws of descent and distribution or (ii) with respect to Grants other than Incentive Stock Options, if permitted in any specific case by the Board, pursuant to a domestic relations order or otherwise as permitted by the Board. When a Grantee dies, the personal representative or other person entitled to succeed to the rights of the Grantee may exercise such rights. Any such successor must furnish proof satisfactory to the Company of his or her right to receive the Grant under the Grantee's will or under the applicable laws of descent and distribution.

(b) Transfer of Nonqualified Stock Options. Notwithstanding the foregoing, the Board may provide, in a Grant Instrument, that a Grantee may transfer Nonqualified Stock Options to family members, or one or more trusts or other entities for the benefit of or owned by family members, consistent with applicable securities laws, according to such terms as the Board may determine; provided that the Grantee receives no consideration for the transfer of an Option and the transferred Option shall continue to be subject to the same terms and conditions as were applicable to the Option immediately before the transfer.

9. Right of First Refusal; Repurchase Right.

(a) Offer. Prior to a Public Offering, if at any time an individual desires to sell, encumber, or otherwise dispose of shares of Company Stock that were distributed to him or her under this Plan and that are transferable, the individual may do so only pursuant to a bona fide written offer, and the individual shall first offer the shares to the Company by giving the Company written notice disclosing: (i) the name of the proposed transferee of the Company Stock; (ii) the certificate number and number of shares of Company Stock proposed to be transferred or encumbered; (iii) the proposed price; (iv) all other terms of the proposed transfer; and (v) a written copy of the proposed offer. Within 60 days after receipt of such notice, the Company shall have the option to purchase all or part of such Company Stock at the price and on

the terms described in the written notice; provided that the Company may pay such price in installments over a period not to exceed four years, at the discretion of the Board.

(b) Sale . In the event the Company (or a stockholder, as described below) does not exercise the option to purchase Company Stock, as provided above, the individual shall have the right to sell, encumber, or otherwise dispose of the shares of Company Stock described in Section 9(a) at the price and on the terms of the transfer set forth in the written notice to the Company, provided such transfer is effected within 15 days after the expiration of the option period. If the transfer is not effected within such period, the Company must again be given an option to purchase, as provided above.

(c) Assignment of Rights . The Board, in its sole discretion, may waive the Company's right of first refusal and repurchase right under this Section 9. If the Company's right of first refusal or repurchase right is so waived, the Board may, in its sole discretion, assign such right to the remaining stockholders of the Company in the same proportion that each stockholder's stock ownership bears to the stock ownership of all the stockholders of the Company, as determined by the Board. To the extent that a stockholder has been given such right and does not purchase his or her allotment, the other stockholders shall have the right to purchase such allotment on the same basis.

(d) Purchase by the Company . Prior to a Public Offering, if a Grantee ceases to be employed by, or provide service to, the Employer, the Company shall have the right to purchase all or part of any Company Stock distributed to him or her under this Plan at its then current Fair Market Value (as defined in Section 5(b)) (or at such other price as may be established in the Grant Instrument); provided, however, that such repurchase shall be made in accordance with applicable accounting rules to avoid adverse accounting treatment.

(e) Public Offering . On and after a Public Offering, the Company shall have no further right to purchase shares of Company Stock under this Section 9.

(f) Stockholders Agreement . Notwithstanding the provisions of this Section 9, if the Board requires that a Grantee execute a Stockholders Agreement (or other agreement containing first refusal or repurchase rights) with respect to any Company Stock distributed pursuant to this Plan, such Grantee shall execute such Stockholders Agreement (or other such agreement) as a condition to retaining his or her rights to such Company Stock. If such Stockholders Agreement (or other such agreement) contains a right of first refusal or repurchase right, the provisions of this Section 9 shall not apply to such Company Stock for as long as those provisions of the Stockholders Agreement (or other agreement) are in effect, unless the Board determines otherwise.

10. Change of Control of the Company .

(a) Definitions .

As used in this Plan, a "Change of Control" shall mean:

(i) any merger or consolidation in which voting securities of the Company possessing more than 50% of the total combined voting power of the Company's outstanding

securities are Transferred to a person or persons different from the person holding those securities immediately prior to such transaction and the composition of the Board following such transaction is such that the directors of the Company prior to the transaction constitute less than 50% of the Board membership following the transaction;

(ii) any acquisition, directly or indirectly, by a person or related group of persons (other than the Company or a person that directly or indirectly controls, is controlled by, or is under common control with, the Company) of beneficial ownership of voting securities of the Company possessing more than 50% of the total combined voting power of the Company's outstanding securities; provided, however, that, no Change of Control shall be deemed to occur by reason of the acquisition of shares of the Company's capital stock by an investor in the Company in a capital-raising transaction;

(iii) any acquisition, directly or indirectly, by a person or related group of persons of the right to appoint a majority of the directors of the Company or otherwise directly or indirectly control the management, affairs and business of the Company;

(iv) any sale, transfer or other disposition of all or substantially all of the assets of the Company; or

(v) a complete liquidation or dissolution of the Company.

As used in this Section 10, "Transfer" shall include any sale, exchange, assignment, gift, bequest, disposition, mortgage, charge, pledge, encumbrance, grant of a security interest or other arrangement by which possession, legal title or beneficial ownership passes from one Person to another, or to the same Person in a different capacity, whether or not voluntarily and whether or not for value, and including without limitation any merger or amalgamation and any agreement to effect any of the foregoing.

(b) Assumption of Grants . Upon a Change of Control where the Company is not the surviving corporation (or survives only as a subsidiary of another corporation), unless the Board determines otherwise, all outstanding Options that are not exercised shall be assumed by, or replaced with comparable options by the surviving corporation (or a parent or subsidiary of the surviving corporation), and outstanding Stock Awards shall be converted to Stock Awards of the surviving corporation (or a parent or subsidiary of the surviving corporation).

(c) Other Alternatives . Notwithstanding the foregoing, in the event of a Change of Control, the Board may take any of the following actions with respect to any or all outstanding Grants: the Board may (i) determine that outstanding Options shall accelerate and become exercisable, in whole or in part, upon the Change of Control or upon such other event as the Board determines, (ii) determine that the restrictions and conditions on outstanding Stock Awards shall lapse, in whole or in part, upon the Change of Control or upon such other event as the Board determines, (iii) require that Grantees surrender their outstanding Options in exchange for a payment by the Company, in cash or stock as determined by the Board, in an amount equal to the amount by which the then Fair Market Value of the shares of Company Stock subject to the Grantee's unexercised Options exceeds the Exercise Price of the Options or (iv) after giving Grantees an opportunity to exercise their outstanding Options, terminate any or all unexercised Options at such time as the Board deems appropriate. Such surrender or termination shall take

place as of the date of the Change of Control or such other date as the Board may specify. The Board shall have no obligation to take any of the foregoing actions, and, in the absence of any such actions, outstanding Options and Stock Awards shall continue in effect according to their terms (subject to any assumption pursuant to subsection (b)).

11. Requirements for Issuance of Shares.

(a) Stockholders Agreement/Voting Agreement. The Board may require that a Grantee execute a stockholders agreement and/or a voting agreement, in each case, with such terms as the Board deems appropriate, with respect to any Company Stock issued pursuant to this Plan.

(b) Limitations on Issuance of Shares. No Company Stock shall be issued in connection with any Grant hereunder unless and until all legal requirements applicable to the issuance of such Company Stock have been complied with to the satisfaction of the Board. The Board shall have the right to condition any Grant made to any Grantee hereunder on such Grantee's undertaking in writing to comply with such restrictions on his or her subsequent disposition of such shares of Company Stock as the Board shall deem necessary or advisable, and certificates representing such shares may be legended to reflect any such restrictions. Certificates representing shares of Company Stock issued under this Plan will be subject to such stop-transfer orders and other restrictions as may be required by applicable laws, regulations and interpretations, including any requirement that a legend be placed thereon.

(c) Lock-Up Period. If so requested by the Company or any representative of the underwriters (the "Managing Underwriter") in connection with any underwritten offering of securities of the Company under the Securities Act of 1933, as amended (the "Securities Act"), a Grantee (including any successor or assigns) shall not sell or otherwise transfer any shares or other securities of the Company during the 30-day period preceding and the 180-day period following the effective date of a registration statement of the Company filed under the Securities Act for such underwriting (or such shorter period as may be requested by the Managing Underwriter and agreed to by the Company) (the "Market Standoff Period"). If so requested, the Grantee shall enter into a separate written agreement to such effect in form and substance requested by the Company or the Managing Underwriter. The Company may impose stop-transfer instructions with respect to securities subject to the foregoing restrictions until the end of such Market Standoff Period. Notwithstanding the foregoing, the Company may require that a Grantee execute a Stockholders Agreement or other agreement containing lock-up provisions. If such Stockholders Agreement or other agreement contains any lock-up or market standoff provisions that differ from the provisions of this Section 11(c), for as long as the provisions of such other agreement are in effect, the provisions of this Section 11(c) shall not apply to such Company Stock, unless the Board determines otherwise.

12. Amendment and Termination of This Plan.

(a) Amendment. The Board may amend or terminate this Plan at any time; provided, however, that the Board shall not amend this Plan without stockholder approval if such approval is required in order to comply with the Code or other applicable laws, or, after a Public Offering, to comply with applicable stock exchange requirements.

(b) Termination of This Plan. This Plan shall terminate on the day immediately preceding the tenth anniversary of the Effective Date, unless this Plan is terminated earlier by the Board or is extended by the Board with the approval of the stockholders.

(c) Termination and Amendment of Outstanding Grants. A termination or amendment of this Plan that occurs after a Grant is made shall not materially impair the rights of a Grantee unless the Grantee consents or unless the Board acts under Section 18(b). The termination of this Plan shall not impair the power and authority of the Board with respect to an outstanding Grant. Whether or not this Plan has terminated, an outstanding Grant may be terminated or amended under Section 18(b) or may be amended by agreement of the Company and the Grantee consistent with this Plan.

(d) Governing Document. This Plan shall be the controlling document. No other statements, representations, explanatory materials or examples, oral or written, may amend this Plan in any manner. This Plan shall be binding upon and enforceable against the Company and its successors and assigns.

13. Funding of This Plan. This Plan shall be unfunded. The Company shall not be required to establish any special or separate fund or to make any other segregation of assets to assure the payment of any Grants under this Plan. In no event shall interest be paid or accrued on any Grant, including unpaid installments of Grants.

14. Rights of Participants. Nothing in this Plan shall entitle any Employee, Key Advisor, Non-Employee Director or other person to any claim or right to be granted a Grant under this Plan. Neither this Plan nor any action taken hereunder shall be construed as giving any individual any rights to be retained by or in the employ of the Employer or any other employment rights.

15. No Fractional Shares. No fractional shares of Company Stock shall be issued or delivered pursuant to this Plan or any Grant. The Board shall determine whether cash, other awards or other property shall be issued or paid in lieu of such fractional shares or whether such fractional shares or any rights thereto shall be forfeited or otherwise eliminated.

16. Headings. Section headings are for reference only. In the event of a conflict between a title and the content of a Section, the content of the Section shall control.

17. Effective Date of This Plan.

(a) Effective Date. This Plan shall be effective on the Effective Date set forth on the first page above.

(b) Public Offering. The provisions of this Plan that refer to a Public Offering, or that refer to, or are applicable to persons subject to, section 16 of the Exchange Act, shall be effective, if at all, upon the initial registration of the Company Stock under section 12(b) or 12(g) of the Exchange Act, and shall remain effective thereafter for as long as such stock is so registered.

18. Miscellaneous .

(a) Grants in Connection with Corporate Transactions and Otherwise . Nothing contained in this Plan shall be construed to (i) limit the right of the Board to make Grants under this Plan in connection with the acquisition, by purchase, lease, merger, consolidation or otherwise, of the business or assets of any corporation, firm or association, including Grants to employees thereof who become Employees, or for other proper corporate purposes, or (ii) limit the right of the Company to grant stock options or make other awards outside of this Plan. Without limiting the foregoing, the Board may make a Grant to an employee of another corporation who becomes an Employee by reason of a corporate merger, consolidation, acquisition of stock or property, reorganization or liquidation involving the Company, the Parent or any of their subsidiaries in substitution for a stock option or Stock Awards grant made by such corporation. The terms and conditions of the substitute grants may vary from the terms and conditions required by this Plan and from those of the substituted stock incentives. The Board shall prescribe the provisions of the substitute grants.

(b) Compliance with Law . This Plan, the exercise of Options and the obligations of the Company to issue shares of Company Stock under Grants shall be subject to all applicable laws and to approvals by any governmental or regulatory agency as may be required. With respect to persons subject to section 16 of the Exchange Act, after a Public Offering it is the intent of the Company that this Plan and all transactions under this Plan comply with all applicable provisions of Rule 16b-3 or its successors under the Exchange Act. In addition, it is the intent of the Company that this Plan and applicable Grants under this Plan comply with the applicable provisions of section 422 of the Code. To the extent that any legal requirement of section 16 of the Exchange Act or 422 of the Code as set forth in this Plan ceases to be required under section 16 of the Exchange Act or section 422 of the Code, that Plan provision shall cease to apply. The Board may revoke any Grant if it is contrary to law or modify a Grant to bring it into compliance with any valid and mandatory government regulation. The Board may also adopt rules regarding the withholding of taxes on payments to Grantees. The Board may, in its sole discretion, agree to limit its authority under this Section.

(c) Employees Subject to Taxation Outside the United States . With respect to Grantees who are subject to taxation in countries other than the United States, the Board may make Grants on such terms and conditions as the Board deems appropriate to comply with the laws of the applicable countries, and the Board may create such procedures, addenda and subplans and make such modifications as may be necessary or advisable to comply with such laws.

(d) Governing Law . The validity, construction, interpretation and effect of this Plan and Grant Instruments issued under this Plan shall be governed and construed by and determined in accordance with the laws of the State of Delaware, without giving effect to the conflict of laws provisions thereof.

EXHIBIT 10.3

LICENSE AGREEMENT

THIS LICENSE AGREEMENT (this " **Agreement** "), dated as of November 10, 2008, is by and between TORREYPINES THERAPEUTICS, INC., a Delaware corporation having its principal place of business at 11085 North Torrey Pines Road, Suite 300, La Jolla, CA 92037 (hereinafter referred to as " **Licensor** "); and QR Pharma, Inc., a Delaware corporation and having its principal place of business at 1223 Foxglove Lane, West Chester, PA 19380 (hereinafter referred to as " **Licensee** "). Licensor and Licensee are sometimes referred to herein individually as a " **Party** " and collectively as the " **Parties** ."

Recitals:

WHEREAS , Licensor has developed and possesses the right to certain chemical compounds and related know-how and associated intellectual property rights relating thereto that may be suitable for the development of human therapeutics; and

WHEREAS , Licensee desires to receive from Licensor, and Licensor desires to grant to Licensee, a worldwide, exclusive license under Licensor's intellectual property rights to such compounds and know-how, with the right to sublicense, to develop, make, have made, import, use, offer for sale and sell Licensed Products in the Field in the Territory (as such terms are defined below) on the terms and conditions set forth in this Agreement; and

WHEREAS , Licensee desires to obtain an option to purchase such intellectual property rights and know-how from Licensor, and Licensor wishes to provide such option to Licensee.

NOW, THEREFORE, in consideration of the foregoing premises and the mutual covenants set forth herein, the Parties, intending to be legally bound, hereby agree as follows:

ARTICLE 1 — DEFINITIONS

As used in this Agreement, the following capitalized terms, whether used in the singular or plural, shall have the respective meanings set forth below:

1.1 " **Affiliate** " shall mean any individual or entity directly or indirectly controlling, controlled by or under common control with a Party to this Agreement. For purposes of this Agreement, the direct or indirect ownership of 50% or more of the outstanding voting securities of an entity shall be deemed to constitute control.

1.2 " **Calendar Quarter** " shall mean the respective periods of three consecutive calendar months ending on March 31, June 30, September 30 and December 31, for as long as this Agreement is in effect.

1.3 " **Calendar Year** " shall mean each successive period of twelve months commencing on January 1 and ending on December 31, for as long as this Agreement is in effect.

1.4 " **Combination Product** " shall mean a product that is comprised of a (a) Licensed Product and (b) one or more other active ingredients or substances.

1.5 " **Commercialization** " or " **Commercialize** " shall mean, with respect to Licensed Products, any and all activities directed to the marketing, promotion, distribution, offering for sale and selling such Licensed Product, importing and exporting such Licensed Product for sale, and interacting with Regulatory Authorities regarding the foregoing in the Field.

1.6 " **Development** " or " **Develop** " shall mean all preclinical research and development activities and all clinical drug development activities with respect to Licensed Product in the Field, including, among other things: drug discovery, toxicology, formulation, statistical analysis and report writing, conducting clinical trials for the purpose of obtaining and maintaining Regulatory Approval (including without limitation, post-marketing studies), and regulatory affairs related to all of the foregoing. Development shall include all clinical studies (including Phase III-B) that are primarily intended to support or maintain a Regulatory Approval, maintain a label or obtain any label change.

1.7 " **Effective Date** " shall mean the date of this Agreement.

1.8 " **Enforcement Action** " shall mean any action reasonably related to the enforcement or protection of the Patent Rights or Licensed Trademarks in any dispute, disagreement, complaint or proceeding that could affect the enforcement, validity, scope, ownership or licensing of any of the Patent Rights or Licensed Trademarks in any country or jurisdiction. The term "Enforcement Action" shall include, without limitation, actions directed at third party infringement, oppositions, reexaminations, interferences and inventorship disputes.

1.9 " **Excluded Field** " shall mean human chemical and bioterrorism defense.

1.10 " **FDA** " shall mean the United Stated Food and Drug Administration.

1.11 " **Field** " shall mean all fields other than the Excluded Field.

1.12 " **First Commercial Sale** " shall mean, with respect to any Licensed Product, the first sale for end use of such Licensed Product in a country in the Territory after receipt of the requisite Regulatory Approval. Sales for test marketing, sampling and promotional uses, clinical trial purposes or compassionate or similar use shall not be considered to constitute a First Commercial Sale.

1.13 " **IND** " shall mean an investigational new drug application with respect to any Licensed Product filed with the FDA for beginning clinical trials in humans or animals, or any comparable application filed with the Regulatory Authorities (as defined below) of a country other than the United States prior to beginning clinical trials in humans or animals in that country, as well as all supplements or amendments filed with respect to such filings.

1.14 " **Know-How** " shall mean any and all Proprietary Information (as defined below) and materials (whether patentable or not), which are necessary or useful for the development, manufacture, use or sale of a Licensed Compound or a Licensed Product, or otherwise for the practice of the Patent Rights in the Field, including, without limitation, (a) ideas, discoveries, inventions, improvements, technology or trade secrets, (b) pharmaceutical, chemical and biological materials, products, components or compositions, (c) methods, procedures, formulas, processes, tests, assays, techniques, regulatory requirements and strategies, (d) biological,

chemical, pharmacological, toxicological, pharmaceutical, physical and analytical, clinical, safety, manufacturing and quality control data and information related thereto, (e) technical and non-technical data and other information related to the foregoing, (f) drawings, plans, designs, diagrams, sketches, specifications or other documents containing or relating to such information or materials and (g) all applications, registrations, licenses, authorizations, approvals and correspondence relating to the Licensed Compounds and/or Licensed Products in the Field submitted to Regulatory Authorities.

1.15 " **Licensed Compound** " shall mean each of those certain compounds currently known as Posiphen™ (+)-phenserine, phenserine (-)-phenserine and bisnorcymserine.

1.16 " **Licensed Product** " shall mean any product containing or incorporating a Licensed Compound, including, without limitation, a Combination Product.

1.17 " **Licensed Trademarks** " shall mean trademarks, trade names, brand names, copyrights, logo types, symbols, service marks and designs relating to Licensed Compounds and/or Licensed Products that are listed on Exhibit B attached hereto.

1.18 " **Licensor Know-How** " shall mean any and all Know-How owned or licensed (with the right to further sublicense) by Licensor as of the Effective Date.

1.19 " **Manufacture** " shall mean all activities related to the manufacturing of a Licensed Compound or Licensed Product, or any ingredient thereof, including but not limited to test method development and stability testing, formulation, process development, manufacturing scale-up, manufacturing quality assurance/quality control development, quality control testing (including in-process release and stability testing), packaging, release of product or any component or ingredient thereof, quality assurance activities related to manufacturing and release of product, and regulatory activities related to all of the foregoing.

1.20 " **NDA** " shall mean a New Drug Application or Product License Application filed with the FDA seeking approval to market and sell a Licensed Product in the United States.

1.21 " **Net Sales** " shall mean, with respect to each country in the Territory, the aggregate gross amount actually received by Licensee, its Affiliates or sublicensees on all sales of Licensed Products to an unaffiliated third party, less the following reasonable and customary deductions from such gross amounts: (a) normal and customary trade, cash and quantity discounts, allowances and credits; (b) credits or allowances actually granted for damaged goods, returns or rejections of Licensed Products and retroactive price reductions; (c) sales or similar taxes (including duties or other governmental charges levied on, absorbed or otherwise imposed on the sale of Licensed Products including, without limitation, value added taxes or other governmental charges otherwise measured by the billing amount, when included in billing); (d) freight, postage, shipping, customs duties and insurance charges; (e) charge back payments and rebates granted to managed health care organizations or their agencies, and purchasers and reimbursers or to trade customers, including but not limited to, wholesalers and chain and pharmacy buying groups; and (f) rebates (or equivalents thereof) granted to or charged by national, state or local governmental authorities in a country in the Territory. Each of the deductions set forth above shall be reasonable and customary, and shall be determined on an

accrual basis in accordance with United States Generally Accepted Accounting Principles. To the extent that any discounts or other similar deductions that are based on sales to the customer of multiple products are included in determining Net Sales of Licensed Products, such discounts or deductions shall be allocated to Licensed Products and the other relevant products on a pro rata basis based on the respective invoiced prices for such multiple products, which allocation in any event shall not disproportionately be applied to Licensed Products. Any transfer or disposal of Licensed Products for, or use of Licensed Products in, clinical or pre-clinical trials or distributed for indigent programs shall not be included in Net Sales.

The following provisions shall apply with respect to Combination Products:

In the event that a Licensed Product is sold in the form of a Combination Product, Net Sales for such Combination Product will be calculated by multiplying actual Net Sales of such Combination Product by the fraction A/(A+B) where: A is the invoice price of the Licensed Product if sold separately by Licensee, or its Affiliate or sublicensee; and B is the invoice price of any other active component or components in the Combination Product if sold separately by Licensee, or its Affiliate or sublicensee.

In the event that Licensee or its Affiliates or sublicensee sells a Licensed Product included in a Combination Product as a separate Licensed Product in a country, but does not separately sell all of the other products or active ingredients/components, as the case may be, included in such Combination Product in such country, the calculation of Net Sales resulting from such Combination Product shall be determined by multiplying the Net Sales by the fraction A/C where: A is the average wholesale price, in such country, of the Licensed Product contained in such Combination Product when sold as a separate Licensed Product by Licensee, its Affiliate or sublicensee, as applicable, and C is the average wholesale price, in such country, charged by Licensee, its Affiliate or sublicensee, as applicable, for the entire Combination Product.

In the event that the Licensee, its Affiliates or sublicensee does not sell a Licensed Product included in a Combination Product as a separate Licensed Product in the country where such sale occurs, but does separately sell all of the other products or active ingredients/components, as the case may be, included in the Combination Product in such country, the calculation of Net Sales resulting from such Combination Product shall be determined by multiplying the Net Sales by the fraction (C-D)/C, where: C is the average wholesale price, in such country, charged by Licensee, its Affiliate or sublicensee, as the case may be, for the entire Combination Product, and D is the average wholesale price charged by Licensee, its Affiliate or sublicensee, as the case may be, for the other products or active ingredients/components, as the case may be, included in the Combination Product.

Where the calculation of Net Sales resulting from the sale of a Combination Product in a country cannot be determined by any of the foregoing methods, the calculation of Net Sales for such Combination Product shall be that portion of the Net Sales determined in good faith by Licensee, and reasonably acceptable to Licensor, as properly reflecting the value of the Licensed Product included in the Combination Product.

1.22 " **Option Agreement** " shall mean that certain Option Agreement between the Parties dated as of June 26, 2008.

1.23 " **Patent** " shall mean any patent or patent application, including continuations, continuations-in-part (to the extent relating to existing patents or patent applications and not to any new subject matter), divisions, provisionals, substitutions, patents of addition, reissues, reexamination, certificates of invention, renewals or extensions thereof (including any supplemental certificates) and any confirmation patents or registration patents, supplementary protection certificates or the like, together with all foreign counterparts of any of the foregoing.

1.24 " **Patent Rights** " shall mean the Patents listed on Exhibit A attached hereto and any future Patents that may issue to Licensor, which will be promptly disclosed to Licensee and added to an amended and restated Exhibit A , to the extent claiming any of the Licensed Compounds or their manufacture or use in the Field.

1.25 " **Proprietary Information** " shall mean all proprietary and confidential information, including, without limitation, scientific, clinical, regulatory, marketing, financial and commercial information or data, whether communicated in writing, verbally or electronically, which is provided by one Party to the other Party in connection with this Agreement.

1.26 " **Phase II Clinical Trial** " shall mean a human clinical trial conducted for the purpose of demonstrating the efficacy and a level of safety in a particular indication tested, as well as to obtain a preliminary indication of the unit and/or daily dosage regimen required. "Commencement of Phase II" shall mean the first dosing of the first patient in the first Phase II Clinical Trial for a Licensed Product.

1.27 " **Phase III Clinical Trial** " shall mean a large scale human clinical trial conducted for the purpose of demonstrating efficacy and a level of safety in the particular indication tested that is designed for the purpose of obtaining Regulatory Approval for a Licensed Product. "Commencement of Phase III" shall mean the first dosing of the first patient in the first Phase III Clinical Trial for a Licensed Product.

1.28 " **Regulatory Approval** " shall mean any and all approvals, licenses, registrations or authorizations of any Regulatory Authority that is necessary for the Manufacture, use, storage, import, export, transport or Commercialization of Licensed Products in a country of the Territory.

1.29 " **Regulatory Authority** " shall mean any national (e.g., the FDA), supranational (e.g., the European Medicines Agency), regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity in a country that performs a function for such political subdivision similar to the function performed by the FDA for the United States with regard to the approval, licensing, registration or authorization for the Manufacture, use, storage, import, export, transport, Development, or Commercialization or Licensed Products in a country of the Territory.

1.30 " **Sublicense Income** " shall mean the amount paid to Licensee by a third party (other than an Affiliate of Licensee) for a sublicense with respect to a Licensed Product, including, without limitation, license fees and milestone payments, other than: (a) royalties paid to Licensee by a sublicensee based upon Net Sales by the sublicensee; (b) equity investments in

Licensee or any Affiliate by a sublicensee up to the amount of the fair market value of the equity purchased on the date of the investment; (c) loan proceeds paid to Licensee or any Affiliate by a sublicensee in an arms' length debt financing to the extent that such loan is not forgiven; and (d) funding for sponsored research or other services paid to Licensee by a sublicensee for research performed or to be performed by Licensee or any Affiliate.

1.31 " **Territory** " shall mean all territories other than the Republic of Korea.

1.32 " **Valid Claim** " shall mean a claim of an issued and unexpired patent included within the Patent Rights, which has not been revoked or held unenforceable or invalid by a decision of a court or other governmental agency of competent jurisdiction, unappealable or unappealed within the time allowed for appeal, and which has not been disclaimed, denied or admitted to be invalid or unenforceable through reissue or disclaimer or otherwise.

1.33 **Additional Definitions** . Each of the following definitions is set forth in the Section of this Agreement indicated below.

Definition	Section
AAA	12.2(a)
Agreement	Preamble
Buy-Out Option	6.1
Buy-Out Payment	6.2
Force Majeure	13.8
Generic Product	5.3(c)
Liability	10.1
Licensee	Preamble
Licensor	Preamble
Licensee Indemnified Party	10.2
Licensor Indemnified Party	10.1
Other Parties	8.1(b)
Party or Parties	Preamble
Term	11.1

ARTICLE 2 — LICENSE

2.1 **License Grant** . Subject to the terms and conditions of this Agreement, Licensor hereby grants to Licensee an exclusive (even as to Licensor), royalty-bearing license, with the right to grant sublicenses, under the Patent Rights and the Licensor Know-How to use, store, import, export, transport, Manufacture or have Manufactured Licensed Compounds in the Territory in the Field and to Develop, Manufacture and Commercialize Licensed Products in the Territory in the Field during the Term. Subject to the terms and conditions of this Agreement, Licensor hereby also grants to Licensee an exclusive (even as to Licensor), royalty-free right and license in the Territory, with the right to grant sublicenses as part of any sublicense of rights granted with respect to Licensed Products, to use the Licensed Trademarks in connection with using, selling and offering for sale Licensed Products in the Territory in the Field during the

Term. Licensor agrees to use commercially reasonable efforts to extend the license granted to Licensee in this Section 2.1 to the Republic of Korea prior to December 31, 2008.

2.2 No Other Licenses ; Retained Rights . Neither Party grants to the other Party any rights or licenses in or to any intellectual property, whether by implication, estoppel, or otherwise, other than the license and other rights that are expressly granted under this Agreement. Subject to the license granted to Licensee pursuant to Section 2.1, Licensor has, and shall retain all right, title and interest in and to, the Patent Rights and Licensor Know-How. Without limiting the foregoing, Licensor shall retain the rights to (and to grant to its Affiliates and to third parties the right to) develop, make, have made, export, import, use, offer for sale and sell the Licensed Compounds and products incorporating the Licensed Compounds outside the Field.

2.3 Sublicenses . Any and all sublicenses granted by Licensee under this Agreement shall be subject to the terms and conditions of this Agreement. Licensee shall notify Licensor of any sublicense hereunder. Licensee will remain liable for all milestone payments and royalty payments hereunder as a result of Net Sales made pursuant to such sublicense agreement and shall use commercially reasonable efforts to ensure that its sublicensees comply with the provisions of this Agreement applicable to them, respectively, in exercising rights under the applicable sublicense agreement. Performance or satisfaction of any of the Licensee's obligations under this Agreement by its sublicensee(s) shall be deemed performance or satisfaction of such obligations by the Licensee.

2.4 Licensee Obligations . Licensee agrees to use commercially reasonable efforts to Develop and Commercialize a Licensed Products in the Field. Licensee may seek one or more co-development partners to achieve such objectives and/or sublicense to one or more third parties to achieve these objectives. Licensee shall deliver written annual reports on its Licensed Compound Development progress on or before each anniversary of the effective date of this Agreement up to the date of the First Commercial Sale of a Licensed Product.

2.5 Section 365 (n) of the Bankruptcy Code . All rights and licenses granted under or pursuant to Section 2.1 of this Agreement are, and shall otherwise be deemed to be, for purposes of Section 365(n) of the U.S. Bankruptcy Code, licenses of rights to "intellectual property" as defined under Section 101(35A) of the Bankruptcy Code. Each Party shall retain and may fully exercise all of its rights and elections under the Bankruptcy Code or equivalent legislation in any other jurisdiction. Upon the bankruptcy of either Party, the other Party shall further be entitled to a complete duplicate of (or complete access to, as appropriate) any such intellectual property, and such, if not already in its possession, shall be promptly delivered to such other Party, unless the Party in bankruptcy elects to continue, and continues, to perform all of its obligations under this Agreement.

ARTICLE 3 — RESEARCH, DEVELOPMENT, COMMERCIALIZATION AND REGULATORY

3.1 Overview . As of the Effective Date, Licensee shall be responsible for the Development and Commercialization of Licensed Products in the Field in the Territory and for overseeing, monitoring and coordinating all regulatory actions, communications and filings with,

and submissions to, the FDA and other Regulatory Authorities in the Territory with respect to Licensed Products in the Field. Licensee shall be responsible for all of the historical records relating to the Licensed Compounds in the Field and be responsible for regulatory agency audits of historical data relating to the Licensed Compounds in the Field.

3.2 Development Costs . Licensee shall be solely responsible for all costs related to the Development and Commercialization of Licensed Products in the Field in the Territory after the Effective Date.

3.3 Materials and Regulatory Filings Transfer .

(a) Transfer of Inventory . Promptly following the Effective Date, Licensor shall transfer to Licensee, in a mutually agreed manner, all amounts of Licensed Compounds and/or Licensed Products, if applicable, in Licensor's inventory, at Licensor's' actual cost, to be used at Licensee's sole discretion for pre-clinical and clinical studies to pursue an IND, NDA and other filings for Regulatory Approval necessary to commercialize the Licensed Products in the Field. Licensor shall transfer such quantities of Licensed Compounds in Licensor's possession within thirty (30) days of the Effective Date. Licensee shall reimburse Licensor for the reasonable shipping costs associated with the transfer of such quantities of Licensed Compounds within thirty (30) days of receipt of invoice therefor. Licensor shall have no obligation to supply any further quantities of Licensed Compounds.

(b) Transfer of All Preclinical and Research Documents . As soon as practicable after the Effective Date, Licensor shall transfer to Licensee one copy of all material documents, data and records in Licensor's possession with respect to any basic research, preclinical research or other Development work documents relating to the Licensed Compounds, Licensor Know-How and/or the Licensed Products in the Field, whether finalized or in draft term.

(c) Transfer of Regulatory Applications . As soon as practicable after the Effective Date, Licensor shall transfer to Licensee all of Licensor's existing INDs and other drug approval applications covering Licensed Products in the Field. All further submissions to any Regulatory Authorities relating to such drug approval applications and/or INDs for Licensed Products in the Field shall be filed in the name of and owned by Licensee. Licensee shall hold all Regulatory Approvals for Licensed Products in the Field throughout the Territory.

(d) Transfer of Other Regulatory Documents . As soon as practicable after the Effective Date, Licensor shall transfer to Licensee one copy of all material documents and records in Licensor's possession with respect to any existing INDs and other drug approval applications covering Licensed Products in the Field in the Territory, as well as any material correspondence between Licensor and Regulatory Authorities related to Licensed Products in the Field.

(e) Transfer of Patent and Trademark Documents . As soon as practicable after the Effective Date, Licensor shall transfer to Licensee one copy of all documentation relating to the prosecution and maintenance of all Patent Rights and Licensed Trademarks, whether finalized or in draft form. Licensor shall promptly disclose to Licensee all future

Patents that issue to Licensor (or its Affiliates or sublicensees) that claim any therapeutic based on or relating to any of the Licensed Compounds.

ARTICLE 4 — MANUFACTURING

4.1 Manufacturing Responsibility . Licensee shall be responsible for the Manufacture of the Licensed Compounds and/or Licensed Products for use by Licensee, its Affiliates, and its sublicensees in the Field in the Territory.

4.2 Transfer of Manufacturing Technology . As soon as reasonably practicable after the Effective Date, Licensor shall provide or cause to be provided to Licensee, or a third party manufacturer designated by Licensee, that information within the Licensor Know-How as of the Effective Date that is necessary or useful to enable Licensee or such third party manufacturer (as appropriate) to Manufacture Licensed Compounds as of the Effective Date.

ARTICLE 5 — PAYMENTS; ROYALTIES AND REPORTS

5.1 Consideration for License . In consideration for the licenses granted to Licensee hereunder, Licensee shall pay to Licensor a one-time, non-refundable, non-creditable payment of $50,000 less all amounts paid by Licensee under the Option Agreement, which amount shall be payable within 30 days of the Effective Date.

5.2 Milestone Payments . In further consideration for the licenses granted hereunder, Licensee shall make each of the following one-time, non-refundable, non-creditable milestone payments to Licensor based on the first attainment of each milestone event indicated below with respect to a Licensed Product:

Milestone Event		Payment to Licensor
Commencement of Phase II	$	200,000
Commencement of Phase III	$	500,000
Filing of an NDA for Regulatory Approval (or equivalent in Europe or Japan)	$	1,000,000
Receipt of Regulatory Approval in the United States	$	5,000,000
Receipt of Regulatory Approval Outside the United States	$	5,000,000

Licensee shall notify Licensor in writing within ten business days after the achievement of each such milestone event giving rise to a payment obligation under this Section 5.2, and Licensee shall pay Licensor the applicable amount on the date of such notification to Licensor.

5.3 Royalties .

(a) Royalties . Subject to the terms and conditions of this Agreement, Licensee shall pay to Licensor royalties on Net Sales of Licensed Products on a country-by-country basis in the Territory in an amount equal to 5% of Net Sales; provided, however, if it shall be necessary for Licensee to obtain a license to issued Patents of any third party in order to

be able to practice the Patent Rights pursuant to the license granted hereunder in order to make, have made, use, import, sell, lease or otherwise commercially exploit a Licensed Product in the Field, Licensee shall be entitled to deduct 50% of the royalties on such Licensed Product paid to such third parties under such license during the respective Calendar Quarter from the royalties payable to Licensor hereunder for such Calendar Quarter; provided that in no event shall the royalties payable to Licensor hereunder be reduced to less than 2.5% of Net Sales for such Calendar Quarter.

(b) Term of Royalty Obligation . Royalties on Licensed Products shall commence upon the First Commercial Sale of a Licensed Product in the Field in a particular country in the Territory and will continue on a product-by-product, country-by-country basis until the later of (i) the expiration of the last to expire Valid Patent Claim covering the respective Licensed Product in the Field in such country or (ii) 10 years after the First Commercial Sale of a Licensed Product in such country.

(c) Royalty Adjustments . In the event that a Generic Product is being sold by a third party in a country before the tenth anniversary of the date of the First Commercial Sale of a Licensed Product in such country, then the royalties payable to Licensor by Licensee pursuant to Section 5.3(a) for a Licensed Product in such country shall be reduced by 50%. As used herein, a " **Generic Product** " shall mean with respect to a Licensed Product, any and all products (other than Licensed Product) containing the same active ingredient as the Licensed Product delivered by a mode of administration that is similar to that of the Licensed Product.

5.4 Sublicense Income . In addition to the payment of the royalties specified in Section 5.3 hereof, Licensee shall pay to Licensor 8% of all Sublicense Income.

5.5 Royalties Payable Only Once . The obligation to pay royalties is imposed only once with respect to the same unit of Licensed Product.

5.6 Minimum Annual Payment . No later than November 30 of each Calendar Year commencing in 2009, Licensee shall pay to Licensor a non-refundable minimum annual payment of $40,000 less any amounts previously paid pursuant to Section 5.3 or 5.4 during such Calendar Year. Each such payment shall be credited against royalties and the Buy-Out Payment, if any, for that Calendar Year.

5.7 Reports; Payment of Royalty; Payment Exchange Rate and Currency Conversions .

(a) Royalties Paid Quarterly . Within 45 calendar days after the end of each Calendar Quarter following the First Commercial Sale of a Licensed Product, Licensee shall furnish to Licensor a written report for the Calendar Quarter showing the Net Sales of Licensed Products sold by Licensee, its Affiliates and its sublicensees in the Territory during such Calendar Quarter and the royalties payable under this Agreement for such Calendar Quarter. Such written report shall include the gross sales of Licensed Products on a country-by-country basis, an itemized calculation of any deductions taken from such gross sales to arrive at Net Sales for the applicable Calendar Quarter and the calculation of the amount of royalty payment due on such Net Sales. Simultaneously with the submission of the written report, Licensee shall

pay to Licensor, for the account of Licensee or the applicable Affiliate or sublicensee, as the case may be, a sum equal to the aggregate royalty due for such Calendar Quarter calculated in accordance with this Agreement.

(b) Method of Payment . All payments to be made by Licensee to Licensor under this Agreement shall be paid by bank wire transfer in immediately available funds to such bank account as is designated in writing by Licensor from time to time. Royalty payments shall be made in United States dollars. The rate of exchange to be used in any such conversion from the currency in the country where such Net Sales are made shall be the rate of exchange used by Licensee for reporting such sales for United States financial statement purposes. If, due to restrictions or prohibitions imposed by national or international authority, payments cannot be made as aforesaid, the Parties shall consult with a view to finding a prompt and acceptable solution, and Licensee will make such payments in any manner as Licensor may lawfully direct.

5.8 Maintenance of Records; Audits .

(a) Recordkeeping by Licensee . Licensee shall keep, and shall cause its Affiliates and sublicensees to keep, complete and accurate records in sufficient detail to enable the royalties and other amounts payable hereunder to be determined. Upon at least 30 days' prior written notice from Licensor, Licensee shall permit an independent certified public accounting firm of nationally recognized standing selected by Licensor and reasonably acceptable to Licensee, at Licensor's expense, to have access during normal business hours upon prearrangement to examine the pertinent books and records of Licensee, its Affiliates and/or sublicensees as may be reasonably necessary to verify the accuracy of the payment reports hereunder. The examination shall be limited to the pertinent books and records for any year ending not more than 36 months prior to the date of such request. An examination under this Section 5.8(a) shall not occur more than once in any Calendar Year. Licensee may designate competitively sensitive information which such auditor may not disclose to Licensor, provided, however, that such designation shall not encompass the auditor's conclusions. The accounting firm shall disclose to Licensor only whether the reports and payments are correct or incorrect and the specific details concerning any discrepancies. No other information shall be provided to Licensor. All such accounting firms shall sign a confidentiality agreement (in form and substance reasonably acceptable to Licensee) as to any of Licensee's, its Affiliate's and/or its sublicensee's confidential information which are provided to such accounting firms, or to which they have access, while conducting any audit pursuant to this Section 5.8(a).

(b) Underpayments/Overpayments . If such accounting firm concludes that additional payments were owed during such period, Licensee shall pay such additional payments within 30 days of the date Licensor delivers to Licensee such accounting firm's written report so correctly concluding. If such underpayment exceeds 10% of the sums correctly due Licensor then the fees charged by such accounting firm for the work associated with the underpayment audit shall be paid by Licensee. Any overpayments by Licensee will be credited against future royalty obligations.

(c) Recordkeeping by Sublicensee . Licensee shall include in each sublicense agreement entered into by it pursuant to this Agreement a provision requiring the sublicensee to make reports to Licensee, to keep and maintain records of sales made pursuant to such sublicense

agreement and to grant access to such records by Licensor's independent accountant to the same extent required of Licensee under this Agreement.

(d) Confidentiality . Licensor shall treat all financial information subject to review under this Section 5.8, or under any sublicense agreement, in accordance with the confidentiality provisions of Article 8 of this Agreement.

(e) Late Payments . Any amount owed by Licensee to Licensor under this Agreement that is not paid within the applicable time period set forth herein shall accrue interest at the rate of the one month London Inter-Bank Offering Rate plus 2% as set by the British Bankers Association as of the due date.

ARTICLE 6 — OPTION TO PURCHASE

6.1 Purchase Option . Licensor hereby grants to Licensee the exclusive right and option to purchase the Patent Rights and the Licensed Trademarks (the " **Buy-Out Option** "). The Buy-Out Option may be exercised by Licensee any time during the Term by giving written notice to Licensor of Licensee's exercise of the Buy-Out Option.

6.2 Option Price . If Licensee exercises the Buy-Out Option, the Parties will enter into an Intellectual Property Transfer Agreement negotiated in good faith and mutually agreeable to the Parties, pursuant to which Licensee will purchase the Patent Rights and Licensed Trademarks for a one-time, non-refundable purchase price (the " **Buy-Out Payment** ") determined as follows:

If the date on which the Buy-Out Option is exercised is prior to the Commencement of the first Phase II Clinical Trial, the Buy-Out Payment will be $500,000.

If the date on which the Buy-Out Option is exercised is on or after the Commencement of the first Phase II Clinical Trial and prior to the Commencement of the first Phase III Clinical Trial, the Buy-Out Payment will be $1,000,000.

If the date on which the Buy-Out Option is exercised is on or after the Commencement of the first Phase III Clinical Trial and prior to the filing of an NDA for the first Licensed Product, the Buy-Out Payment will be $5,000,000.

If the date on which the Buy-Out Option is exercised is on or after the filing of an NDA for the first Licensed Product, the Buy-Out Payment will be $8,000,000.

All amounts payable under this Section 6.2 shall be reduced by (a) all amounts paid by Licensee under the Option Agreement, and (b) all payments made by Licensee pursuant to Section 5.6 hereof for such Calendar Year.

Upon the exercise by Licensee of the Buy-Out Option this Agreement shall terminate, and Licensee shall have no further payment obligations to Licensor hereunder except for the Buy-Out Payment specified in this Article 6.

ARTICLE 7 — PATENTS

7.1 Patent Prosecution and Maintenance . From and after the Effective Date, Licensee shall have all rights to apply for, prosecute, maintain and defend all U.S. and foreign patents and patent applications, and trademarks and trademark applications, constituting part of the Patent Rights and Licensed Trademarks in the Field, as Licensee shall from time to time determine, using counsel chosen by Licensee. Licensee shall provide Licensor with copies of all relevant documentation so that both parties may be informed and apprised of the continuing prosecution, and Licensor agrees to keep this documentation confidential. The cost of preparing, filing, prosecuting and maintaining all patents and patent applications contemplated by this Agreement shall be borne by Licensee.

7.2 Enforcement of Patent Rights and Licensed Trademarks . Licensee shall control any and all Enforcement Actions, including the decision whether to undertake any such Enforcement Action. In the event that either party obtains knowledge of any challenge to the Patent Rights or Licensed Trademarks by a third party, such party shall inform the other party promptly of such challenge and provide the other party with any available evidence of such challenge. Licensee shall have the right but not the obligation to defend at its own cost and expense any challenge to any Patent in the Patent Rights in the Field or any challenge to any Licensed Trademark. If Licensee does not commence action against a third party challenger within 90 days after learning of the challenge, Licensor may commence action against the third party challenger. At the reasonable request of the party filing suit, the other party, at its own expense, shall provide reasonable assistance, including, without limitation, permitting the use of their respective names in all suits and signing all necessary documents if appropriate to the situation. Any recovery in any action brought in accordance with this Section 7.2 shall be applied first to costs incurred by the party bringing suit, and then to the costs of the party or parties providing assistance as contemplated by this Section 7.2, with the remainder to be retained by the party bringing the action.

ARTICLE 8 — CONFIDENTIALITY AND PUBLICATION

8.1 Confidentiality .

(a) Nondisclosure Obligation . Each of Licensor and Licensee shall use any Proprietary Information received by it from the other Party only in accordance with this Agreement and shall not disclose to any third party any such Proprietary Information without the prior written consent of the other Party. The foregoing obligations shall survive the expiration or termination of this Agreement for a period of ten years. These obligations shall not apply to Proprietary Information that:

(i) is known by the receiving Party at the time of its receipt, and not through a prior disclosure by the disclosing Party, as documented by the receiving Party's written records;

(ii) is at the time of disclosure, or thereafter becomes, published or otherwise part of the public domain without breach of this Agreement by the receiving Party;

(iii) is subsequently disclosed to the receiving Party by a third party who has the right to make such disclosure, as documented by the receiving Party's written records; or

(iv) is independently developed by the receiving Party or its Affiliates and without the aid, use or application of any of the disclosing Party's Proprietary Information, and such independent development can be documented by the receiving Party's written records.

To the extent it is reasonably necessary or appropriate, a Party may disclose Proprietary Information of the other Party:

(A) to any institutional review board of any entity conducting clinical trials with a Licensed Product or to any Regulatory Authority in order to gain approval to conduct clinical trials or to market a Licensed Product, provided that such disclosure may be made only to the extent reasonably necessary to obtain such authorizations; or

(B) to the extent such Proprietary Information is required to be disclosed by law, regulation, rule, act or order of any governmental authority or agency to be disclosed, provided that notice is promptly delivered to the other Party in order to provide an opportunity to seek a protective order or other similar order with respect to such Proprietary Information and thereafter the receiving Party discloses to the requesting entity only the minimum information required to be disclosed in order to comply with the request, whether or not a protective order or other similar order is obtained by the other Party.

(b) Disclosure to Agents . Notwithstanding the provisions of Section 8.1(a) and subject to the other terms of this Agreement, each of Licensee and Licensor shall have the right to disclose Proprietary Information of the other Party to their respective licensees, sublicensees, agents, consultants, Affiliates or other third parties (collectively " **Other Parties** ") in accordance with this Section 8.1(b). Such disclosure shall be limited only to those Other Parties directly involved in the Development, Manufacturing, Commercialization, marketing or promotion of Licensed Compounds or Licensed Products (or for such Other Parties to determine their interest in performing such activities) in accordance with this Agreement. Any such Other Parties must agree in writing to be bound by confidentiality and non-use obligations similar to those contained in this Agreement.

8.2 Return of Confidential Information . Upon termination of this Agreement, the receiving Party will return all documents, and copies thereof, including those in the possession of the receiving Party's Other Parties pursuant to Section 8.1(b), containing the disclosing Party's Proprietary Information, or earlier at any time upon the written request of the disclosing Party. However, the receiving Party may retain one copy of such documents in a secure location, subject to a continuing obligation of confidentiality hereunder, solely for the purposes of (a) determining its obligations hereunder, (b) complying with any applicable regulatory requirements, or (c) defending against any product liability claim.

8.3 Publicity ; **Publications and Public Presentations** . A Party may not use the name of the other Party in any publicity or advertising and may not issue a press release or otherwise publicize or disclose any information related to the existence of this Agreement or the

terms or conditions herein, except (a) on the advice of its counsel as required by law (e.g., any Securities and Exchange Commission filings and disclosures) and provided the Party who will be disclosing such information has consulted with the other Party to the extent feasible prior to such disclosure with respect to the substance of the disclosure; (b) as consented to in advance by the other Party in writing, or (c) or to persons with whom Licensee or Licensor has entered into or proposes to enter into a business relationship involving the potential transfer of rights under this Agreement or rights related to the Licensed Compounds; provided that such persons are subject to appropriate confidentiality agreements. The Parties shall agree on a form of initial press release that may be used by either Party on an ongoing basis to describe this Agreement. Licensee shall provide Licensor with reasonable advance written notice of any press release or other public disclosure of the results of any of its work on Licensed Products under this Agreement. Notwithstanding the foregoing, Licensee shall have the right to publish or publicly present the results of the Development activities contemplated hereunder. Licensor may not publish or publicly present the results of the Development activities performed under this Agreement or any Proprietary Information of Licensee without Licensee's prior written consent.

ARTICLE 9 — REPRESENTATIONS AND WARRANTIES

9.1 Representations and Warranties of Each Party . Each of Licensor and Licensee hereby represents, warrants and covenants to the other Party hereto as follows:

(a) it is a corporation duly organized and validly existing under the laws of the state or other jurisdiction of its incorporation;

(b) the execution, delivery and performance of this Agreement by such Party has been duly authorized by all requisite corporate action on the part of such Party;

(c) it has the power and authority to execute and deliver this Agreement and to perform its obligations hereunder;

(d) the execution, delivery and performance by such Party of this Agreement and its compliance with the terms and provisions herein does not and will not conflict with or result in a breach of any of the terms and provisions of or constitute a default under (i) a loan agreement, guaranty, financing agreement, agreement affecting a product or other agreement or instrument binding or affecting it or its property; (ii) the provisions of its corporate charter or other operative documents or bylaws; or (iii) any order, writ, injunction or decree of any court or governmental authority entered against it or by which any of its property is bound;

(e) except for the governmental and Regulatory Approvals required to market Licensed Products in the Territory, the execution, delivery and performance of this Agreement by such Party does not require the consent, approval or authorization of, or notice, declaration, filing or registration with, any governmental or Regulatory Authority and the execution, delivery or performance of this Agreement will not violate any law, rule or regulation applicable to such Party;

(f) this Agreement has been duly authorized, executed and delivered and constitutes such Party's legal, valid and binding obligation enforceable against it in accordance with its terms subject, as to enforcement, to bankruptcy, insolvency, reorganization and other

laws of general applicability relating to or affecting creditors' rights and to the availability of particular remedies under general equity principles;

(g) it shall comply with all applicable material laws and regulations relating to its activities under this Agreement; and

(h) during the Term of this Agreement Licensee will not use in any capacity, in connection with any activities to be performed under this Agreement, any individual who has been debarred pursuant to the United States Food, Drug and Cosmetic Act.

9.2 Licensor's Representations . Licensor hereby represents, warrants and covenants to Licensee as follows as of the Effective Date:

(a) as of the Effective Date, the Patent Rights, Licensor Know-How and Licensed Trademarks are subsisting, and to the best of Licensor's knowledge, and have not been abandoned or been held invalid or unenforceable, in whole or in part, by a decision of a court or other governmental agency;

(b) as of the Effective Date, it has, and during the Term it shall maintain the full right, power and authority to grant the license granted under Section 2.1 herein;

(c) as of the Effective Date, it is the sole owner or co-owner of the Patent Rights as indicated on Exhibit A and the sole owner of the Licensor Know-How and Licensed Trademarks, all of which are free and clear of any liens, charges and encumbrances in the Field (other than the rights of the co-owner of the Patent Rights that are identified as co-owned on Exhibit A hereto and any right or license under the Patent Rights and the Licensor Know-How granted outside the Field), and to Licensor's actual knowledge, no other person, corporate or other private entity, or governmental entity or subdivision thereof, except those entities set for on Exhibit A as co-owners of the Patent Rights, has or shall have any claim of ownership with respect to the Patent Rights, Licensor Know-How and Licensed Trademarks, whatsoever; and

(d) to Licensor's actual knowledge, as of the Execution Date, the Manufacture, Development or Commercialization of Licensed Compounds does not infringe any valid and enforceable patent rights owned or possessed by any third party;

(e) as of the Execution Date there are no claims, judgments or settlements against or owed by Licensor or pending or threatened claims or litigation against Licensor, in either case relating to Patent Rights, Licensor Know-How and Licensed Trademarks; and

9.3 No Inconsistent Agreements . Neither Party has in effect, and after the Effective Date neither Party shall enter into, any oral or written agreement or arrangement that would be inconsistent with its obligations under this Agreement.

9.4 Representation by Legal Counsel . Each Party hereto represents that it has been represented by legal counsel in connection with this Agreement and acknowledges that it has participated in the drafting of this Agreement. In interpreting and applying the terms and provisions of this Agreement, the Parties agree that no presumption shall exist or be implied against the Party which drafted such terms and provisions.

9.5 Disclaimer . Except as expressly set forth herein, THE PATENT RIGHTS, LICENSOR KNOW-HOW AND LICENSED COMPOUNDS ARE PROVIDED "AS IS," AND EACH PARTY EXPRESSLY DISCLAIMS ANY AND ALL WARRANTIES OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING, WITHOUT LIMITATION, THE WARRANTIES OF DESIGN, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, NONINFRINGEMENT OF THE INTELLECTUAL PROPERTY RIGHTS OF THIRD PARTIES, OR ARISING FROM A COURSE OF DEALING, USAGE OR TRADE PRACTICES, IN ALL CASES WITH RESPECT THERETO.

ARTICLE 10 — INDEMNIFICATION AND LIMITATION ON LIABILITY

10.1 Indemnification by Licensee . Licensee shall indemnify, defend and hold harmless Licensor and its Affiliates, and each of its and their respective employees, officers, directors and agents (each, a " **Licensor Indemnified Party** ") from and against any and all liability, loss, damage, cost, and expense (including reasonable attorneys' fees), subject to the limitations in Section 10.5, (collectively, a " **Liability** ") that a Licensor Indemnified Party may incur, suffer or be required to pay resulting from or arising out of (a) the use, storage, import, export, transport, Development, Manufacture, Commercialization, sale or other disposition of Licensed Compounds and/or Licensed Products by Licensee, its Affiliates or sublicensees in the Field, (b) the use by Licensee, its Affiliates or Sublicensees of the Licensed Trademarks in the Field and (c) any breach by Licensee of any of its representations, warranties and covenants contained in Section 9.1 herein. Notwithstanding the foregoing, Licensee shall have no obligation under this Agreement to indemnify, defend or hold harmless any Licensor Indemnified Party with respect to claims, demands, costs or judgments which result from the gross negligence or willful misconduct of Licensor, its Affiliates, or any of their respective employees, officers, directors or agents.

10.2 Indemnification by Licensor . Licensor shall indemnify, defend and hold harmless Licensee and its Affiliates, and each of its and their respective employees, officers, directors and agents (each, a " **Licensee Indemnified Party** ") from and against any Liability which a Licensee Indemnified Party may incur, suffer or be required to pay resulting from or arising in connection with any breach by Licensor of any of its representations and warranties contained in Sections 9.1 and 9.2 herein and/or the breach of any covenant or obligation of Licensor under this Agreement.

10.3 Conditions to Indemnification . The obligations of the indemnifying Party under Sections 10.1 and 10.2 are conditioned upon the delivery of written notice to the indemnifying Party of any potential Liability promptly after the indemnified Party becomes aware of such potential Liability. The indemnifying Party shall have the right to assume the defense of any suit or claim related to the Liability if it has assumed responsibility for the suit or claim in writing; however, if in the reasonable judgment of the indemnified Party, such suit or claim involves an issue or matter which could have a materially adverse effect on the business operations or assets of the indemnified Party, the indemnified Party may retain control of the defense or settlement thereof by providing written notice of such effect to the indemnifying Party, but in no event shall such action or notice be construed as a waiver of any indemnification rights that the indemnified Party may have at law or in equity. If the indemnifying Party defends the suit or claim, the indemnified Party may participate in (but not control) the defense thereof at its sole cost and

expense. The foregoing notwithstanding, the Parties acknowledge and agree that failure of the indemnified Party to promptly notify the indemnifying Party of a potential Liability shall not constitute a waiver of, or result in the loss of, such Party's right to indemnification under Section 10.1 or 10.2, as appropriate, except to the extent that the indemnifying Party's rights, and/or its ability to defend against such Liability, are materially prejudiced by such failure to notify.

10.4 Settlements . Neither Party may settle a claim or action related to a Liability without the consent of the other Party, which consent shall not be unreasonably withheld, if such settlement would impose any monetary obligation on the other Party or require the other Party to submit to an injunction or otherwise limit the other Party's rights under this Agreement. Any payment made by a Party to settle any such claim or action shall be at its own cost and expense.

10.5 Limitation of Liability . With respect to any claim by one Party against the other arising out of the performance or failure of performance of the other Party under this Agreement, the Parties expressly agree that the liability of such Party to the other Party for such breach shall be limited under this Agreement or otherwise at law or equity to direct damages only and in no event shall a Party be liable for punitive, exemplary or consequential damages. Notwithstanding the foregoing, this Section 10.5 shall not be construed to limit either Party's indemnification obligations under this Article 10 with respect to Liability for third party claims or to limit a Party's liability for breach of Article 8.

10.6 Insurance . Each Party acknowledges and agrees that during the Term of this Agreement it shall maintain adequate insurance and/or a self-insurance program for liability insurance, including products liability and contractual liability insurance, to cover such Party's obligations under this Agreement. Each Party shall provide the other Party with evidence of such insurance and/or self-insurance program, upon request.

ARTICLE 11 — TERM AND TERMINATION

11.1 Term and Expiration . This Agreement shall be effective as of the Effective Date and unless terminated earlier by mutual written agreement of the Parties, upon Licensee's exercise of the Buy-Out Option pursuant to Section 5.1, or pursuant to Section 11.2, 11.3 or 11.4 below, the Term of this Agreement shall continue in effect on a country-by-country and product-by-product basis until the expiration of Licensee's obligation to make payments under Article 5 herein (the " **Term** "). Upon expiration of this Agreement in its entirety, Licensee's licenses granted pursuant to Section 2.1 with respect to Licensor Know-How and Licensed Trademarks shall become fully paid-up, perpetual licenses.

11.2 Termination by Licensee .

(a) Licensee's Right to Terminate . Licensee shall have the unilateral right to terminate this Agreement in its entirety, with or without cause, at any time by giving 90 days advance written notice to Licensor. In the event of such termination, the rights and obligations hereunder shall terminate; provided, however, that any payment obligations due and owing as of the termination date shall continue.

(b) Effect of Termination . Notwithstanding anything contained herein to the contrary, following any termination of this Agreement in its entirety under Section 11.2(a), all rights and licenses granted to Licensee hereunder shall terminate and all rights to the Licensed Compounds, Licensed Products and Licensed Trademarks shall revert back to Licensor.

11.3 Termination for Cause .

(a) Termination for Cause . This Agreement may be terminated, in its entirety or on a country-by-country basis, by written notice by either Party at any time during the Term of this Agreement:

(i) if the other Party is in breach of its material obligations hereunder and has not cured such breach within 60 days (10 days in the event of an undisputed payment breach) after receipt of written notice requesting cure of the breach, or in the event that the breach (other than any payment breach) cannot be reasonably cured within such 60-day period, has not initiated actions reasonably expected to cure such breach within 60 days after receipt of such notice or has not cured such breach within 120 days after written notice of such breach or such later date as agreed in writing by the non-breaching Party; or

(ii) upon the filing or institution of bankruptcy, reorganization, liquidation or receivership proceedings by or against the other Party, or upon an assignment of a substantial portion of the assets for the benefit of creditors by the other Party, or in the event a receiver or custodian is appointed for such Party's business, or if a substantial portion of such Party's business is subject to attachment or similar process; provided, however, that in the case of any involuntary bankruptcy proceeding, such right to terminate shall only become effective if the proceeding is not dismissed within 60 days after the filing thereof.

(b) Effect of Termination for Cause on License . In the event this Agreement is terminated by Licensor under Section 11.3(a), the rights and the licenses granted to Licensee under Section 2.1 of this Agreement shall terminate and all rights to the Licensed Compounds, Licensed Products and Licensed Trademarks shall revert to Licensor, and Licensee shall have no further payment obligations to Licensor under this Agreement other than for payments due and owing as of the effective date of termination. In the event this Agreement is terminated by Licensee under Section 11.3(a), Licensee's licenses granted pursuant to Section 2.1 of this Agreement shall become fully paid-up, perpetual licenses. Notwithstanding the preceding sentence, Licensee shall be responsible for all undisputed amounts due and owing to Licensor prior to any written notice of termination.

11.4 Effect of Termination Generally . Expiration or termination of this Agreement shall not relieve the Parties of any obligation accruing prior to such expiration or termination, and the provisions of Sections 5.8, 9.4, 9.5, 11.2(b), 11.3(b) and 11.4, and Articles 1, 8, 10, 12 and 13 shall survive the expiration or termination of this Agreement. Any expiration or early termination of this Agreement shall be without prejudice to the rights of either Party against the other accrued or accruing under this Agreement prior to termination, including the obligation to pay royalties for Licensed Products sold prior to such termination.

ARTICLE 12 — DISPUTE RESOLUTION

12.1 Informal Discussions . In the event of any controversy or claim arising out of or relating to this Agreement, or the rights or obligations of the Parties hereunder, or the relationship between the Parties with respect to the Licensed Compounds, Licensed Products, Patent Rights, Licensor Know-How or Licensed Trademarks in the Field, the Parties shall first try to settle their differences amicably between themselves. Either Party may initiate such informal dispute resolution by sending written notice of the dispute to the other Party, and within 30 days after such notice appropriate representatives of the Parties shall meet for attempted resolution by good faith negotiations. If such representatives are unable to resolve promptly such disputed matter within the said 30 days, either Party may refer the matter by written notice to the other to the Chief Executive Officer of Licensor, or her designee, and the Chief Executive Officer of Licensee, or his designee, for discussion and resolution. If such individuals or their designees are unable to resolve such dispute within 30 days of such written notice, either Party may initiate arbitration proceedings in accordance with the provisions of this Article 12.

12.2 Arbitration . All disputes arising out of or relating to this Agreement, or the rights or obligations of the Parties hereunder, or relating in any way to the relationship between the Parties with respect to the Licensed Compounds, Licensed Products, Patent Rights, Licensor Know-How or Licensed Trademarks in the Field, shall be finally and exclusively settled by arbitration by a panel of three arbitrators.

(a) Rules Applicable . The arbitration proceeding shall be conducted under the Commercial Arbitration Rules of the American Arbitration Association (" **AAA** ") with such proceedings to be held in Chicago, Illinois, United States. Judgment upon the award rendered by arbitration may be issued and enforced by any court having competent jurisdiction.

(b) Commencement of Proceedings . If a Party intends to begin an arbitration to resolve a dispute, such Party shall provide written notice to the other Party, informing the other Party of such intention and any statement of claim required under the applicable arbitration rules (as determined in accordance with Section 12.2(a)). Within 20 business days after its receipt of such notice, the other Party shall, by written notice to the Party initiating arbitration, add any additional issues to be resolved. For clarity, the resolution of any disputes regarding such counterclaims shall be conducted in the same proceedings as the initial claims.

(c) Appointment of Arbitrators . Within 45 days following the receipt of the notice of arbitration, the Party referring the matter to arbitration shall appoint an arbitrator and promptly notify the other Party of such appointment. The other Party shall, upon receiving such notice, appoint a second arbitrator within 21 days, and the two arbitrators shall, within fifteen days of the appointment of the second arbitrator, agree on the appointment of a third arbitrator who will act with them and be the chairperson of the arbitration panel. In the event that either Party shall fail to appoint an arbitrator within 30 days after the commencement of the arbitration proceeding, the arbitrator shall be appointed by the AAA. In the event of the failure of the two arbitrators to agree within 60 days after the commencement of the arbitration proceeding to appoint the chairperson, the chairperson shall also be appointed by the AAA.

(d) Independence . All of the arbitrators shall have significant legal or business experience in pharmaceutical licensing matters. The arbitrators shall not be employees, directors or shareholders of either Party or any of their Affiliates.

(e) Right to Counsel . Each Party shall have the right to be represented by counsel throughout the arbitration proceedings.

(f) Confidentiality . To the extent possible, the arbitration hearings and award will be maintained in confidence.

(g) Binding Nature . In any arbitration pursuant to this Agreement, the award or decision shall be rendered by a majority of the members of the panel provided for herein, with each member having one vote. The arbitrators shall render a written decision with their resolution of the dispute, which decision shall set forth in reasonable detail the facts of the dispute, and the reasons for their decision. The decision of the arbitrators shall be final and non-appealable and binding on the Parties.

12.3 Injunctive Relief . By agreeing to arbitration, the Parties do not intend to deprive any competent court of such court's jurisdiction to issue a pre-arbitral injunction, pre-arbitral attachment or other order in aid of the arbitration proceedings and the enforcement of any award or judgment. Without prejudice to such provisional remedies in aid of arbitration as may be available under the jurisdiction of a national court, the court of arbitration shall have full authority to grant provisional remedies and to award damages for failure of any Party to respect the court of arbitration's order to that effect.

12.4 Expenses of Arbitration and Expert Determination . Each Party shall bear its own attorneys' fees, costs, and disbursements arising out of the arbitration, and shall pay an equal share of the fees and costs of the arbitrators; provided, however, that the arbitrators shall be authorized to determine whether a Party is the prevailing Party, and if so, to award to that prevailing Party reimbursement for its reasonable attorneys' fees, costs and disbursements (including, for example, expert witness fees and expenses, photocopy charges and travel expenses). Absent the filing of an application to correct or vacate the arbitration award as permitted by applicable law, each Party shall fully perform and satisfy the arbitration award within fifteen days of the service of the award.

ARTICLE 13 — MISCELLANEOUS

13.1 Assignment . Neither this Agreement nor any or all of the rights and obligations of a Party hereunder may be assigned, delegated, sold, transferred, sublicensed (except as otherwise provided herein) or otherwise disposed of, by operation of law or otherwise, to any third party without the prior written consent of the other Party, and any attempted assignment, delegation, sale, transfer, prohibited sublicense or other disposition, by operation of law or otherwise, of this Agreement or of any rights or obligations hereunder contrary to this Section 13.1 shall be a material breach of this Agreement by the attempting Party, and shall be void and without force or effect; provided, however, that either Party may, without such consent of the other Party, assign this Agreement and its rights and obligations hereunder to an Affiliate or in connection with the transfer or sale of all or substantially all of its assets related to the

division or the subject business, or in the event of its merger or consolidation or change in control or similar transaction, and, in the event of such a transaction (whether this Agreement is actually assigned or is assumed by the acquiring party by operation of law), intellectual property rights of the acquiring party to such transaction (if other than one of the Parties) shall not be included in the technology licensed hereunder. This Agreement shall be binding upon, and inure to the benefit of, each Party, its Affiliates, and its permitted successors and assigns. Each Party shall be responsible for the compliance by its Affiliates with the terms and conditions of this Agreement.

13.2 Governing Law . This Agreement shall be governed, interpreted and construed in accordance with the laws of the State of New York, without giving effect to its conflict of law principles. Subject to the terms of this Agreement, all disputes under this Agreement shall be governed by binding arbitration pursuant to the mechanism set forth in Article 12 herein.

13.3 Waiver . Any delay or failure in enforcing a Party's rights under this Agreement or any waiver as to a particular default or other matter shall not constitute a waiver of such Party's rights to the future enforcement of its rights under this Agreement, nor operate to bar the exercise or enforcement thereof at any time or times thereafter, excepting only as to an express written and signed waiver as to a particular matter for a particular period of time.

13.4 Independent Relationship . Nothing herein contained shall be deemed to create an employment, agency, joint venture or partnership relationship between the Parties hereto or any of their agents or employees, or any other legal arrangement that would impose liability upon one Party for the act or failure to act of the other Party. Neither Party shall have any power to enter into any contracts or commitments or to incur any liabilities in the name of, or on behalf of, the other Party, or to bind the other Party in any respect whatsoever.

13.5 Export Control . This Agreement is made subject to any restrictions concerning the export of products or technical information from the United States of America that may be imposed upon or related to Licensor or Licensee from time to time by the government of the United States of America. Furthermore, Licensee agrees that it will not export, directly or indirectly, any technical information acquired from Licensor under this Agreement or any products using such technical information to any country for which the United States government or any agency thereof at the time of export requires an export license or other governmental approval, without first obtaining the written consent to do so from the Department of Commerce or other agency of the United States government when required by an applicable statute or regulation.

13.6 Entire Agreement ; **Amendment** . This Agreement, including the Exhibits and Schedules hereto and thereto, sets forth the complete, final and exclusive agreement and all the covenants, promises, agreements, warranties, representations, conditions and understandings between the Parties hereto and supersedes and terminates all prior agreements and understandings between the Parties with regard to the subject matter of this Agreement in the Territory. There are no covenants, promises, agreements, warranties, representations, conditions or understandings, either oral or written, between the Parties other than as are set forth herein and therein. No subsequent alteration, amendment, change, waiver or addition to this Agreement

shall be binding upon the Parties unless reduced to writing and signed by an authorized officer of each Party.

13.7 Notices . Any notice required or permitted to be given or sent under this Agreement shall be hand delivered or sent by express delivery service or certified or registered mail, postage prepaid, or by facsimile transmission (with written confirmation copy by registered first-class mail) to the Parties at the addresses and facsimile numbers indicated below.

If to Licensor, to:

TorreyPines Therapeutics, Inc.
11085 North Torrey Pines Road
Suite 300
La Jolla, CA 92037
Attn: Craig Johnson, CFO

If to Licensee, to:

QR Pharma, Inc.
1223 Foxglove Lane
West Chester, PA 19380
Attn: Maria Maccecchini, Ph.D.

Any such notice shall be deemed to have been received on the earlier of the date actually received or the date five days after the same was posted or sent. Either Party may change its address or its facsimile number by giving the other Party written notice, delivered in accordance with this Section 13.7.

13.8 Force Majeure . Failure of any Party to perform its obligations under this Agreement (except the obligation to make payments when properly due) shall not subject such Party to any liability or place them in breach of any term or condition of this Agreement to the other Party if such failure is due to any cause beyond the reasonable control of such non-performing Party (" **Force Majeure** "), unless conclusive evidence to the contrary is provided. Causes of non-performance constituting Force Majeure shall include, without limitation, acts of God, fire, explosion, flood, drought, war, riot, sabotage, embargo, strikes or other labor trouble, failure in whole or in part of suppliers to deliver on schedule materials, equipment or machinery, interruption of or delay in transportation, a national health emergency or compliance with any order or regulation of any government entity acting with color of right. The Party affected shall promptly notify the other Party of the condition constituting Force Majeure as defined herein and shall exert commercially reasonable efforts to eliminate, cure and overcome any such causes and to resume performance of its obligations with all possible speed; provided that nothing herein shall obligate a Party to settle on terms unsatisfactory to such Party any strike, lockout or other labor difficulty, any investigation or other proceeding by any public authority or any litigation by any third party. If a condition constituting Force Majeure as defined herein exists for more than 30 consecutive days, the Parties shall meet to negotiate a mutually satisfactory resolution to the problem, if practicable. If the Parties cannot in good faith reach a satisfactory resolution to the

problem within 30 days after the date of such meeting, the matter shall be handled pursuant to the dispute resolution provisions of Article 12 herein.

13.9 Severability . If any provision of this Agreement is declared illegal, invalid or unenforceable by a court having competent jurisdiction, it is mutually agreed that this Agreement shall continue in accordance with its terms except for the part declared invalid or unenforceable by order of such court; provided, however, that in the event that the terms and conditions of this Agreement are materially altered, the Parties will, in good faith, renegotiate the terms and conditions of this Agreement to reasonably substitute such invalid or unenforceable provisions in light of the intent of this Agreement.

13.10 Counterpart . This Agreement shall become binding when any one or more counterparts of it, individually or taken together, shall bear the signatures of each of the Parties hereto. This Agreement may be executed in any number of counterparts, each of which shall be an original as against either Party whose signature appears thereon, but all of which taken together shall constitute but one and the same instrument.

13.11 Captions . The captions of this Agreement are solely for the convenience of reference and shall not affect its interpretation.

13.12 Further Assurances . At the request of any Party hereto, the other Party shall execute and deliver from time to time such further instruments and shall provide reasonable cooperation in such proceedings or actions as shall be necessary or reasonably appropriate to effectuate the purposes of this Agreement. The executions, deliveries and cooperation of each Party under this Section 13.12 shall be without further consideration and at such Party's expense.

IN WITNESS WHEREOF, this Agreement has been executed by the duly authorized representatives of the Parties.

TORREYPINES THERAPEUTICS, INC.		QR PHARMA, INC.	
By:	/s/ Evelyn Graham	By:	/s/ Maria Maccecchini
Title:	Acting CEO	Title:	President & CEO

EXHIBIT 10.4

License Agreement Amendment

This license agreement amendment ("Amendment'') amends the License Agreement dated November 10, 2008 ("Agreement") by and between RAPTOR THERAPEUTICS INC., having its principal place of business at 9 Commercial Blvd., Suite 200, Novato, CA 94949 (hereinafter referred to as "Licensor''), formerly known as TorreyPines Therapeutics, Inc.; and QR PHARMA, INC., having its principal place of business at 1223 Foxglove Lane, West Chester, PA 19380 (hereinafter referred to as "Licensee").

WHEREAS, the Agreement grants to Licensee a license to certain intellectual property rights co owned by TorreyPines Therapeutics, Inc. and the Public Health Service ("PHS");

WHEREAS, Licensor changed its name from TorreyPines Therapeutics, Inc. to Raptor Pharmaceutical Corp. on September 29, 2009 and assigned the Agreement to Raptor Therapeutics Inc.;

WHEREAS, the Licensor has obtained the right to grant a license to PHS' rights in such intellectual property rights through the Interinstitutional Agreement between Raptor Therapeutics Inc. and PHS, which is identified as L-012-2012/0 and attached hereto as Exhibit 1 ("PHS Agreement"); and

WHEREAS, the Licensee desires to receive from the Licensor, a worldwide, exclusive license under PHS' intellectual property rights, effective as of the date of the PHS Agreement ("Effective Date") in the Field and in the Territory on the terms and conditions set forth in the Agreement as amended.

NOW, THEREFORE, in consideration of the foregoing premises and the mutual covenants set forth herein, the Parties, intending to be legally bound, hereby agree as follows:

Unless otherwise defined herein, capitalized terms shall be given the meaning assigned in the Agreement.

1. The following shall be deleted and replaced in their entirety as follows:

1.11 **"Field"** shall mean all fields other than the Excluded Field and Research Field.

2. The following shall be added to Article 1:

1.34 **"Research Field"** shall mean internal research and not for purposes of commercial manufacture or distribution in lieu of purchase.

1.35 **"PHS Patent Rights"** shall mean the Patent Rights as defined in section 2.1 of the PHS Agreement attached hereto as Exhibit 1.

3. Section 2.1 shall be deleted and replaced in its entirety as follows:

2.1 **License Grant.** Subject to the terms and conditions of this Agreement, and subject to the retained rights and other rights of the government under sections 2.2 and 2.6 and under the PHS Agreement, Licensor hereby grants to Licensee an exclusive (even as to Licensor), royalty-bearing license, with the right to grant sublicenses, under the Patent Rights, the Licensor Know-How and PHS Patent Rights to use, store, import, export, transport, Manufacture or have Manufactured Licensed Compounds in the Territory in the Field and to Develop, Manufacture and Commercialize Licensed Products in the Territory in the Field during the Term. Subject to the terms and conditions of this Agreement, Licensor hereby also grants to Licensee an exclusive (even as to Licensor), royalty-free right and license in the Territory, with the right to grant sublicenses as part of any sublicense of rights granted with respect to Licensed Products, to use the Licensed Trademarks in connection with using, selling and offering for sale Licensed Products in the Territory in the Field during the Term. Licensor agrees to use commercially reasonable efforts to extend the license granted to Licensee in this Section 2.1 to the Republic of Korea prior to December 31, 2008.

4. Section 2.2 shall be deleted and replaced in its entirety as follows:

2.2 No Other Licenses; Retained Rights. Neither Party grants to the other Party any rights or licenses in or to any intellectual property, whether by implication, estoppel, or otherwise, other than the license and other rights that are expressly granted under this Agreement **.** Subject to the license granted to Licensee pursuant to Section 2.1, Licensor has, and shall retain all right, title and interest in and to, the Patent Rights and Licensor Know-How **.** Without limiting the foregoing, Licensor shall retain the rights to (and to grant to its Affiliates and to third parties the right to) develop, make, have made, export, import, use, offer for sale and sell the Licensed Compounds and products incorporating the Licensed Compounds outside the Field **.** Notwithstanding anything in this Agreement to the contrary, Licensee agrees and understands that the PHS Patent Rights sublicensed under this Amendment are pursuant to the PHS Agreement, including but not limited to PHS' reservation of rights under Article 3 of the PHS Agreement, and are at all times subject to the terms and conditions of the PHS Agreement, as may be amended from time to time after the Effective Date. Without limiting the foregoing, Licensee agrees to grant such licenses or cause its sublicensee(s) to grant such licenses that PHS requires under Article 3 of the PHS Agreement.

5. Section 2.3 shall be deleted and replaced in its entirety as follows:

2.3 Sublicenses. Any and all sublicenses granted by Licensee under this Agreement shall be subject to the terms and conditions of this Agreement **.** Licensee shall notify Licensor of any sublicense hereunder **.** Licensee will remain liable for all milestone payments and royalty payments hereunder as a result of Net Sales made pursuant to such sublicense agreement and shall use commercially reasonable efforts to ensure that its sublicensees comply with the provisions of this Agreement applicable to them, respectively, in exercising rights under the applicable sublicense agreement. Performance or satisfaction of any of the Licensee's obligations under this Agreement by its sublicensee(s) shall be deemed performance or satisfaction of such obligations by the Licensee. Licensee agrees that the terms of any sublicense of its rights hereunder will include a requirement that any and all sublicensees comply with requirements of the PHS Agreement. Licensee agrees to provide copies of any licenses and sublicenses to PHS as required by section 5.5 of the PHS Agreement.

6. The following shall be added to Article 2:

2.6 Federal Funding. Licensee understands that the PHS Patent Rights may have been conceived or may have been (or in the future may be) first actually reduced to practice with funding from the U.S. government **.** All rights granted herein shall be limited by and subject to the rights of and obligations to the U.S. government, including those set forth in 35 U.S.C. §200 et seq.

7. Article 4 shall be deleted and replaced in its entirety as follows:

4.1 Manufacturing Responsibility. Licensee shall be responsible for the Manufacture of the Licensed Compounds and/or Licensed Products for use by Licensee, its Affiliates, and its sublicensees in the Field in the Territory. The Manufacture of Licensed Compounds and/or Licensed Products embodying the PHS Patent Rights, or produced through use of the PHS Patent Rights, shall be subject to Sections 2.6 and 13.5 and the PHS Agreement, which requires that products embodying PHS Patent Rights, or produced through use of PHS Patent Rights, shall be manufactured substantially in the United States unless a waiver is granted by PHS.

4.2 Transfer of Manufacturing Technology. As soon as reasonably practicable after the Effective Date, Licensor shall provide or cause to be provided to Licensee, or a third party manufacturer designated by Licensee, that information within the Licensor Know-How as of the Effective Date that is necessary or useful to enable Licensee or such third party manufacturer (as appropriate) to Manufacture Licensed Compounds as of the Effective Date. The Manufacture of Licensed Compounds and/or Licensed Products embodying the PHS Patent Rights, or produced through use of the PHS Patent Rights, shall be subject to Sections 2.6 and 13.5 and the PHS Agreement, which requires that products embodying PHS Patent

Rights, or produced through use of PHS Patent Rights, shall be manufactured substantially in the United States unless a waiver is granted by PHS.

8. Section 5.2 shall be deleted and replaced in its entirety as follows:

5.2 Milestone Payments. In further consideration for the licenses granted hereunder, Licensee shall make each of the following one-time, non-refundable, non-creditable milestone payments to Licensor based on the first attainment of each milestone event indicated below with respect to a Licensed Product:

Milestone Event	Licensed Products not Incorporating PHS Patent Rights	Licensed Products Incorporating PHS Patent Rights
Commencement of Phase II	$ 200,000	$ 230,000
Commencement of Phase III	$ 500,000	$ 575,000
Filing of an NDA for Regulatory Approval (or equivalent in Europe or Japan)	$ 1,000,000	$ 1,150,000
Receipt of Regulatory Approval in the United States	$ 5,000,000	$ 5,750,000
Receipt of Regulatory Approval Outside the United States	$ 5,000,000	$ 5,750,000

Licensee shall notify Licensor in writing within ten business days after the achievement of each such milestone event giving rise to a payment obligation under this Section 5.2, and Licensee shall pay Licensor the applicable amount on the date of such notification to Licensor.

9. Section 5.3(a) shall be deleted and replaced in its entirety as follows:

5.3 Royalties.

(a) Royalties . Subject to the terms and conditions of this Agreement, Licensee shall pay to Licensor royalties on Net Sales of Licensed Products on a country by-country basis in the Territory in an amount equal to 5.00% for Licensed Products not incorporating PHS Patent Rights or 5.75% for Licensed Products incorporating PHS Patent Rights of Net Sales; provided, however, if it shall be necessary for Licensee to obtain a license to issued Patents of any third party in order to be able to practice the Patent Rights pursuant to the license granted hereunder in order to make, have made, use, import, sell, lease or otherwise commercially exploit a Licensed Product in the Field, Licensee shall be entitled to deduct 50% of the royalties on such Licensed Product paid to such third parties under such license during the respective Calendar Quarter from the royalties payable to Licensor hereunder for such Calendar Quarter; provided that in no event shall the royalties payable to Licensor hereunder be reduced to less than 2.50% for Licensed Products not incorporating PHS Patent Rights or 2.875% for Licensed Products incorporating PHS Patent Rights of Net Sales for such Calendar Quarter.

10. Section 5.4 shall be deleted and replaced in its entirety as follows:

5.4 Sublicense Income. In addition to the payment of the royalties specified in Section 5.3 hereof, Licensee shall pay to Licensor 8.0% of all Sublicense Income attributable to Licensed Products not incorporating PHS Patent Rights or 9.2% of all Sublicense Income attributable to Licensed Products incorporating PHS Patent Rights.

11. Section 5.6 shall be deleted and replaced in its entirety as follows:

5.6 Minimum Annual Payment. No later than November 30 of each Calendar Year commencing in 2009, Licensee shall pay to Licensor a non-refundable minimum annual payment of $46,000 less any amounts previously paid pursuant to Section 5.3 or 5.4 during

such Calendar Year. Each such payment shall be credited against royalties and the Buy-Out Payment, if any, for that Calendar Year.

12. The following shall be added to Article 5:

5.9 Development Reporting Requirements. Licensee shall submit to Licensor and PHS an annual report in compliance with section 7.2 of the PHS Agreement.

5.10 Negotiation Costs. Licensee shall reimburse Licensor within thirty (30) days for any and all attorneys' fees and costs associated with negotiating this Amendment and the PHS Agreement.

13. Section 6.1 shall be deleted and replaced in its entirety as follows:

6.1 Purchase Option. Licensor hereby grants to Licensee the exclusive right and option to purchase Licensor's rights in the Patent Rights (to the extent permitted under the PHS Agreement) and the Licensed Trademarks solely owned by licensor (the **"Buy-Out Option").** The Buy-Out Option may be exercised by Licensee any time during the Term by giving written notice to Licensor of Licensee's exercise of the Buy-Out Option. For the avoidance of doubt, the Buy-Out Option does not apply o PHS' rights or the U.S. government's rights in the Patent Rights. Moreover, the Buy-Out Option that does not involve PHS Patent Rights shall not be affected in any way by the PHS Agreement.

14. Section 7.1 shall be deleted and replaced in its entirety as follows:

7.1 Patent Prosecution and Maintenance. From and after the Effective Date, Licensee shall have all rights to apply for, prosecute, maintain and defend all U.S. and foreign patents and patent applications, and trademarks and trademark applications, constituting part of the Patent Rights and Licensed Trademarks in the Field, as Licensee shall from time to time determine, using counsel chosen by Licensee. Licensee shall provide Licensor and PHS with copies of all relevant documentation so that all parties may be informed and apprised of the continuing prosecution, and Licensor agrees to keep this documentation confidential. The cost of preparing, filing, prosecuting and maintaining all patents and patent applications contemplated by this Agreement shall be borne by Licensee. Licensee will comply with the patent prosecution provisions of Article 4 of the PHS Agreement.

15. Section 7.2 shall be deleted and replaced in its entirety as follows:

7.2 Enforcement of Patent Rights and Licensed Trademarks. To the extent permitted under the PHS Agreement, Licensee shall control any and all Enforcement Actions, including the decision whether to undertake any such Enforcement Action, after consulting with Licensor and PHS. In the event that either party obtains knowledge of any challenge to the Patent Rights or Licensed Trademarks by a third party, such party shall inform the other party in writing promptly of such challenge and provide the other party with any available evidence of such challenge. Licensee will assume responsibility for and comply with Licensor's obligations regarding enforcement under Section 8 of the PHS Agreement, including but not limited to the obligations under section 8.1 to notify the Government of infringement and eliminate infringement, and the obligations under section 8.2 to reimburse the Government for any costs, expenses or fees. To the extent permitted under the PHS Agreement, Licensee, after consulting with Licensor and PHS, shall have the right but not the obligation to defend at its own cost and expense any challenge to any Patent in the Patent Rights in the Field or any challenge to any Licensed Trademark. If Licensee does not commence action against a third party challenger within ninety (90) days after learning of the challenge, Licensor or PHS may commence action against the third party challenger. At the reasonable request of the party filing suit, the other party, at its own expense, shall provide reasonable assistance, including, without limitation, permitting the use of their respective names in all suits and signing all necessary documents if appropriate to the situation. Any recovery in any action brought in accordance with this Section 7.2 shall be applied first to costs incurred by the party bringing suit, and then to the costs of the party or parties providing assistance as contemplated by this Section 7.2, with the remainder to be retained by the party bringing the action.

16. Section 13.6 shall be deleted and replaced in its entirety as follows:

13.6 Entire Agreement; Amendment. This Agreement, including the Exhibits and Schedules hereto and thereto, sets forth the complete, final and exclusive agreement and all the covenants, promises, agreements, warranties, representations, conditions and understandings between the Parties hereto and supersedes and terminates all prior agreements and understandings between the Parties with regard to the subject matter of this Agreement in the Territory. The Licensee has been provided a copy of the PHS Agreement between the Licensor and PHS, and hereby agrees that if there are any inconsistencies, Licensee will comply with the more stringent of the two provisions, and will in all cases ensure that it complies with obligations under Articles 3, 4, 7, 8, and Sections 11.1 and 11.2 of the PHS Agreement. No subsequent alteration, amendment, change, waiver or addition to this Agreement shall be binding upon the Parties unless reduced to writing and signed by an authorized officer of each Party.

17. Section 13.7 shall be deleted and replaced in its entirety as follows:

13.7 Notices. All notices required or permitted by this Agreement shall be given by prepaid, first class, registered or certified mail or by an express/overnight delivery service provided by a commercial carrier, properly addressed to the other party at the address below, or to the other address as may be designated in writing by such other Party. Agreement notices shall be considered timely if the notices are received on or before the established deadline date or sent on or before the deadline date as verifiable by U.S. Postal Service postmark or dated receipt from a commercial carrier. Parties should request a legibly dated U.S. Postal Service postmark or obtain a dated receipt from a commercial carrier or the U.S. Postal Service. Private metered postmarks shall not be acceptable as proof of timely mailing.

If to Licensor, to:

Raptor Therapeutics Inc.
9 Commercial Blvd., Suite 200
Novato, CA 94949
Attn: Kim Tsuchimoto

If to Licensee, to:

QR Pharma, Inc.
1223 Foxglove Lane
West Chester, PA 19380
Attn: Maria Maccecchini, Ph.D.

If to PHS, to:

Chief, Monitoring & Enforcement Branch
Office of Technology Transfer, NIH
6011 Executive Boulevard, Suite 325
Rockville, Maryland 20852-3804

Except as modified hereby, all of the terms and conditions of the Agreement shall remain in full force and effect.

The parties execute this valid and binding amendment in one or more counterparts, each of which shall be deemed an original but all of which taken together constitute one and the same instrument.

RAPTOR THERAPEUTICS INC.	**QR PHARMA, INC.**
/s/ Kim R. Tsuhimoto	/s/ Maria Maccecchini
Name	Name
CFO	President & CEO
Title	Title
11/18/11	11/29/2011
Date	Date

EXHIBIT 1

PHS Agreement

L#: L-012-2012/0

PUBLIC HEALTH SERVICE

PHS INTERINSTITUTIONAL AGREEMENT

INSTITUTION-LEAD

This **Agreement** is entered into between the National Institutes of Health (" **NIH** ") or the Food and Drug Administration (" **FDA** "), hereinafter singly or collectively referred to as " **PHS** ", agencies of tire United States Public Health Service within the Department of Health and Human Services (" **HHS** ") through the Office of Technology Transfer, **NIH** , having an address at 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804, U.S.A. and Raptor Therapeutics Inc., hereinafter referred to as the " **Institution** ", having an address at 9 Commercial Blvd Novato, CA 94949, U.S.A.

1. BACKGROUND

1.1 In the course of fundamental research programs at the **PHS** and by the **Institution** , **Inventor(s)** Greig, Nigel H.; Shaw, Karen T. Y.; Yu, Qiang-Sheng; Holloway, Harold W.; Soncrant, Timothy T.; Brossi, Arnold; Giordano, Anthony; Powers, Gordon; Davidson, Diane; Sturgess, Michael; Utsuki, Tada; Ingram, Donald K.; and Hausman, Marvin made or reduced to practice certain inventions which are included within the **Patent Rights** , as defined in Paragraph 2.1.

1.2 It is the mutual desire of the **Institution** and the **PHS** that their respective undivided interests in the **Patent Rights** be administered in a manner to ensure the rapid commercialization of the **Patent Rights** and to make their benefits widely available to the public. Therefore, in accordance with 35 U.S.C. §202(e) and 37 C.F.R. §401.10. **PHS** is granting an exclusive license to **PHS'** rights in the **Patent Rights** to the **Institution** under tile conditions set forth herein.

1.3 It is acknowledged that **Institution** has in place an exclusive (patent commercial) License Agreement with **QR Pharma** , dated November 10, 2008.

2. DEFINITIONS

2.1 " **Patent Rights** " means:

(a) Patent applications (including provisional patent applications and PCT patent applications) or patents as follows:

(i) U.S. Patent Application Serial No./U.S. Provisional Patent Application Serial No. 60/052,087(provisional), **HHS** Reference number E-247-1997/0, filed July 9, 1997, entitled Highly Selective Butyrylcholinestcrase Inhibitors for the Treatment and Diagnosis of Alzheimer's Disease and Dementias, and

(ii) U.S. Patent Application Serial No./U.S. Provisional Patent Application Serial No, 60/245,329 (provisional), **HHS** Reference number E-141-2000/0, filed November 2, 2000, entitled Agents useful for reducing amyloid precursor protein and treating dementia and methods of use thereof,

and any U.S. and foreign patent application(s) claiming the benefit of priority thereof including all divisions and continuations of these applications, all patents issuing from these applications, divisions,

and continuations, and any reissues, reexaminations, and extensions of all these patents to the extent that at least one **Inventor** from the **Institution** is an **Inventor** thereon;

(b) to the extent that the following contain one or more claims directed to the invention or inventions disclosed in 2.1(a) and to the extent that at least one **Inventor** from the **Institution** is an **Inventor** ;

(i) continuations-in-part of 2.1(a);

(ii) all divisions and continuations of these continuations-in-part;

(iii) all patents issuing from these continuations-in-part, divisions, and continuations;

(iv) priority patent application(s) of 2.1(a); and

(v) any reissues, reexaminations, and extensions of all these patents; and

(c) to the extent that the following contain one or more claims directed to the invention or inventions disclosed in 2.1(a) and to the extent that at least one **Inventor** from the **Institution** is an Inventor: all counterpart foreign and U.S. patent applications and patents to 2.1(a) and 2.1(b); and

(d) **Patent Rights** shall *not* include 2.1(b) or 2.1(c) to the extent that they contain one or more claims directed to new matter which is not the subject matter disclosed in 2.1(a).

2.2 " **Net Revenues** " means all consideration received by **Institution** from the licensing of the **Patent Rights** pursuant to this **Agreement** , less (a) **Expenses** and then (b) fifteen percent (15%) of the remaining consideration for administrative overhead. In the event that a license is executed by **Institution** with a third party wherein the **Patent Rights** are licensed together with other technologies not failing under the definition of the Patent Rights, all consideration received by **Institution** from the licensing of the **Patent Rights** pursuant to this **Agreement** through the third-party executed license shall correspond to the **Patent Rights'** percentage contribution to the total amount received for all licensed technologies as determined by **Institution** .

2.3 " **Expenses** " means all reasonable and actual out-of-pocket costs, excluding those reimbursed by a third party, paid by the **Institution** for the preparation, filing, prosecution, and licensing of United States and foreign patent applications, extraordinary expenses as provided in Paragraph 4.6, and the maintenance of the resulting patents or patent applications, exclusive or any salaries, administrative, or other indirect costs.

2.4 " **Research License** " means a nontransferable, nonexclusive license to make and to use any tangible embodiment of the **Patent Rights** and to practice any process(es) included within the **Patent Rights** for purposes of internal research and not for purposes of commercial manufacture or distribution or in lieu of purchase.

2.5 " **Practical Application** " means to manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the ease of a machine or system; and in each case, under such conditions as to establish that the invention is being utilized and that its benefits are, to the extent permitted by law or by regulations of the Government of the United States of America (hereinafter referred to as " **Government** "), available to the public on reasonable terms.

2.6 " **Effective Date** " means the date when this **Agreement** is signed by all parties.

2.7 " **QR Pharma** " means QR Pharma, Inc., a company having an address at 1055 Westlakes Drive, Suite 300, Berwyn, PA, U.S.A., and the company that is currently sublicensing this technology under **Institution** License Agreement dated November 10, 2008.

3. GRANT AND RESERVATION OF RIGHTS

3.1 **PHS** hereby grants and the **Institution** accepts, subject to the terms and conditions of this **Agreement** , an exclusive license, including the right to sublicense, under the **Patent Rights** to make and have made, to use and have used, to sell and have sold, to offer to sell, and to import any tangible embodiment of the **Patent Rights** and to practice and have practiced any process included within the **Patent Rights** .

3.2 In accordance with 35 U.S.C. 202 et seq and 37 CFR 404 et seq, the **Government** shall have the irrevocable, royalty-free, paid-up right to practice and have practiced the **Patent Rights** throughout the world by or on behalf of the **Government** and on behalf of any foreign government or international organization pursuant to any existing or future treaty or agreement to which the **Government** is a signatory. Any license granted by the **Institution** under the terms of this **Agreement** shall be subject to this right of the **Government** .

3.3 In accordance with 35 U.S.C. 202 et seq and 37 CFR 404 et seq, **PHS** reserves the right to require the **Institution** , or its licensees or sublicensee, to grant sublicenses to responsible applicants, on terms that are reasonable under the circumstances when necessary to fulfill health or safety needs or when necessary to meet requirements for public use specified by Federal regulations.

3.4 In addition to the reserved right of Paragraph 3.3, **PHS** reserves the right to require **Institution** to grant Research Licenses on reasonable terms and conditions. The purpose of these **Research Licenses** is to encourage basic research, whether conducted at an academic or corporate facility.

4. PATENT PROSECUTION AND PROTECTION

4.1 The **Institution** or its licensee or sublicensee shall file, prosecute, and maintain patent application(s) relating to the **Patent Rights** and shall within a reasonable time provide to **PHS** all serial numbers and filing dates, together with copies of all these applications, including copies of all Patent Office actions, responses, and all other Patent Office communications. In addition, the **Institution** , shall file with Patent Offices, a Power of Attorney, that names both the **Institution** and **PHS** . This Power of Attorney shall be filed with every Patent Office involved in prosecuting all patent applications pertaining to **Patent Rights** . The **Institution** shall consult with **PHS** , when so requested, prior to communicating with any Patent Office with respect to the **Patent Rights** .

4.2 The **Institution** or its licensee or sublicensee shall make an election with respect to foreign filing, upon consultation with **PHS** , including which countries foreign filing shall be done prior to the election, within eight (8) months of any United States filing. If any foreign patent applications are filed, the **Institution** or its licensee or sublicensee shall provide to **PHS** within a reasonable time all serial numbers and filing dates. The **Institution** or its licensee or sublicensee also shall provide **PHS** copies of foreign patent applications and Patent Office actions. The **Institution** shall consult with **PHS** , when so requested, prior to communication with any Patent Office with respect to the **Patent Rights** .

4.3 The **Institution** or its licensee or sublicensee shall within a reasonable time record Assignments of domestic **Patent Rights** in the United States Patent and Trademark Office and shall promptly provide **PHS** with the original of each recorded Assignment with respect to **PHS** .

4.4 Notwithstanding any other provision of this **Agreement** , the **Institution** or its licensee or sublicensee shall not abandon the prosecution of any patent application, including provisional patent applications (except for purposes of filing continuation application(s)) or the maintenance of any patent contemplated by this **Agreement** , without prior written notice to **PHS** . Upon receiving the written notice, **PHS** may, at its sole option, take over the prosecution of any patent application, or the maintenance of any patent.

4.5 The **Institution** or its licensee or sublicensee shall promptly provide **PHS** with copies of all issued patents under this **Agreement** .

4.6 In the event that the **Institution** anticipates incurring any **Expenses** that are extraordinary expenditures arising from the preparation, filing, prosecution, licensing, or defense of any patent application or patent contemplated by this **Agreement** , including, without limitation, interferences, reexaminations, reissues and oppositions, the **Institution** shall: (a) provide **PHS** with all relevant information; (b) shall consult

with PHS on a mutually acceptable course of action prior to incurring such extraordinary expenditures; and (c) shall include such extraordinary expenditures as **Expenses** only upon written agreement of **PHS** .

5. LICENSING

5.1 The **Institution** shall diligently seek licensees for the commercial development of the **Patent Rights** and shall administer the **Patent Rights** for the mutual benefit of the parties and in the public interest. The **Institution** shall ensure that any license granted for the **Patent Rights** is subject to the provisions of 37 C.F.R. Part 401 and the rights retained by the **Government** under this **Agreement** , including the requirement for substantial manufacture in the United States as stated in Paragraph 11.1.

5.2 The **Institution** shall not issue any royalty-free or paid-up licenses or assign **Patent Rights** to any third party, notwithstanding any other provision of this **Agreement** , without the prior written consent of **PHS** .

5.3 The **Institution** shall consult with **PHS** in the negotiation of any exclusive or partially-exclusive licenses, not withstanding any other provision of this **Agreement** , and shall not grant these licenses without the prior review, opportunity for comment, and written approval of **PHS** . In the case of existing License Agreement dated November 10, 2008 with **QR Pharma** , **Institution** agrees to provide **PHS** an opportunity to comment on the modification to License Agreement dated November 10, 2008 to comply with the terms and obligations of this **Agreement** , said license to be modified within 90 (ninety) days of the **Effective Date** of this **Agreement.**

5.4 Before licensing of the **Patent Rights** or any part thereof by the **Institution** , the **Institution** shall first notify and confer with **PHS** regarding any research funding related to the **Patent Rights** so as to determine **PHS'** interest in participating in any funded collaborative research project.

5.5 The **Institution** shall promptly provide **PHS** with complete copies of all licenses and sublicenses granted for the **Patent Rights** .

5.6 **Institution** agrees that its licensees shall supply, to the Mailing Address for **Agreement** notices indicated on the Signature Page, the Office of Technology Transfer, **NIH** with inert samples of the licensed products or licensed processes, as covered by the **Patent Rights** , or their packaging for educational and display purposes only.

6. ROYALTIES AND EXPENSES

6.1 The **Institution** shall distribute **Net Revenues** to **PHS** concurrently with distributions it makes under the **Institution's** patent policy, but in any case not later than April 1 for the preceding calendar year, on the following basis: (a) eighty five percent (85%) of the **Net Revenues** as a royalty to the **Institution** and (b) fifteen percent (15%) of the **Net Revenues** as a royalty to **PHS** .

6.2 All payments to **PHS** , required under this **Agreement** , shall be in U.S. dollars and payment options are listed in Appendix A.

(a) Any loss of exchange, value, taxes, or other expenses incurred in the transfer or conversion to U.S. dollars shall be paid entirely by **Institution** ; and

(b) Additional royalties may be assessed by **PHS** on any payment that is more than ninety (90) days overdue at the rate of one percent (1%) per month. This one percent (1%) per month rate may be applied retroactively from the original due date until the date of receipt by **PHS** of the overdue payment and additional royalties. The payment of any additional royalties shall not prevent **PHS** from exercising any other rights it may have as a consequence of the lateness of any payment.

6.3 **Institution** shall submit to **PHS** annual statements of itemized **Expenses** as defined in Paragraph 2.3 and shall deduct the **Expenses** as provided for in Paragraph 2.2, except where **PHS** has identified discrepancies in billing by **Institution** , in which case, deduction of the contested item(s), as a part of **Expenses** as provided for in Paragraph 2.2, shall be delayed pending resolution thereof.

6.4 in no event shall **PHS** be obligated to bear directly any costs for **Expenses** under this **Agreement** without written agreement of **PHS** .

6.5 Each party shall be solely responsible for calculating and distributing to its respective **Inventor(s)** of the **Patent Rights** any share of **Net Revenues** in accordance with its respective patent policy, royalty policy, or Federal law during the term of this **Agreement** .

7. RECORDS AND REPORTS

7.1 The **Institution** shall keep complete, true, and accurate accounts of all **Expenses** and of all **Net Revenues** received by it from each licensee of the **Patent Rights** and shall permit **PHS** or **PHS'** designated agent, upon reasonable notice, to examine its books and records in order to verify the payments due or owed under this **Agreement** .

7.2 The **Institution** shall submit to **PHS** an annual report, not later titan April 1 of each year, setting forth the status of all patent prosecution, commercial development, and licensing activity relating to the **Patent Rights** for the preceding calendar year.

8. PATENT INFRINGEMENT

8.1 In the event **PHS** or the **Institution** , including its licensees, shall learn of the substantial infringement of any patent subject to this **Agreement** , the party who learns of the infringement shall promptly notify the other party in writing and shall provide the other party with all available evidence of the infringement. The **Institution** and its licensees, in cooperation with **PHS** , shall use their best efforts to eliminate the infringement without litigation. If the efforts of the parties are not successful in eliminating the infringement within ninety (90) days after the infringer has been formally notified of the infringement by the **Institution** , the **Institution** or its licensee or sublicensee shall have the right, after consulting with **PHS** , to commence suit on its own account. **PHS** may join the **Institution's** or its licensee(s)' or sublicensee(s)' suit at **Institution's** or licensee's or sublicensee's expense but shall join if required by law or a court of competent jurisdiction; or **PHS** may commence its own suit at its own expense.

8.2 The **Institution** may permit its licensees or sublicensee to bring suit on their own account. **PHS** shall retain the right to join any licensee's or sublicensee's suit at its own expense but shall join if required by law or a court of competent jurisdiction. Should the **Government** be sued or added as a party to any suit arising out of the subject matter of this **Agreement** , Licensee shall reimburse the **Government** for any costs, expenses, or fees which the **Government** incurs as a result of the motion or other action, including all costs incurred by the **Government** in opposing the motion or other action. In all cases, licensee or sublicensee agrees to keep **PHS** reasonably apprised of the status and progress of any litigation.

8.3 Neither a licensee nor the **Institution** shall take action to compel **PHS** either to initiate or to join in any suit for patent infringement. Should the **Government** be made a party to any suit by motion or any other action of a licensee or sublicensee or the **Institution** , the licensee or sublicensee or the **Institution** shall reimburse the **Government** for any costs, expenses, or fees which the **Government** incurs as a result of the motion or other action, including any and all costs incurred by **PHS** in opposing any joinder action,

8.4 Legal action or suits to eliminate infringement or recover damages pursuant to Paragraph 8.1 shall be at the full expense of the party by whom suit is brought. All damages recovered thereby shall first be used to reimburse each party for its expenses relating to the legal action, and the remainder of the damages shall be considered **Net Revenues** .

8.5 Each party agrees to cooperate with the other in litigation proceedings. **PHS** may be represented, at its expense, by counsel of its choice in any suit.

9. GOVERNING LAWS, SETTLING DISPUTES

9.1 This **Agreement** shall be construed in accordance with U.S. Federal law, as interpreted and applied by the U.S. Federal courts in the District of Columbia. Federal law and regulations shall preempt any conflicting or inconsistent provisions in this **Agreement** . The **Institution** agrees to be subject to the jurisdiction of U.S. courts.

9.2 Any controversy or any disputed claim by either party against the other arising under or related to this **Agreement** shall be submitted jointly to the **Institution's** President or designee and to the Director of the

NIH or designee for resolution. The **Institution** and **PHS** shall be free after written decisions are issued by those officials to pursue all administrative or judicial remedies which may be available.

10. TERM AND TERMINATION

10.1 This **Agreement** is effective on the **Effective Date** , unless the provisions of Paragraph 11.9 are not fulfilled, and shall extend to the expiration of the last to expire of the patents included within the **Patent Rights** unless otherwise terminated by operation of law or by acts of the parties in accordance with the terms of this **Agreement** .

10.2 The **Institution** may terminate this **Agreement** upon at least sixty (60) days written notice to **PHS** , but in any event not less than sixty (60) days prior to the date on which any pending Patent Office actions need be taken to preserve patent rights for the benefit of the parties hereto.

10.3 In the event the **Institution** has made no commitments to any third party for exclusive license rights relating to the **Patent Rights** , **PHS** may terminate this **Agreement** for any reason upon thirty (30) days written notice to the **Institution** . During the term of any option agreement or license agreement to any third party for exclusive license rights relating to the **Patent Rights** between the **Institution** and an optionee or licensee, **PHS** may terminate this **Agreement** when:

(a) it is determined by **PHS'** Office of Technology Transfer that:

(i) The **Institution** or its licensee or sublicensee has not taken and is not expected to take effective steps to achieve **Practical Application** of the **Patent Rights** under the requirements of 35 U.S.C. §203;

(ii) Termination is necessary to alleviate health or safety needs which are not reasonably satisfied by the **Institution** or its licensee tinder the requirements of 35 U.S.C. §203;

(iii) Termination is necessary to meet requirements for public use specified by Federal law or regulations and these requirements are not reasonably satisfied by the **Institution** or its licensees or sublicensee under 35 U.S.C. §203; or

(iv) Termination is necessary because tire requirements of 35 U.S.C. §204 have not been satisfied or waived or because a licensee of the exclusive right to use or sell the **Patent Rights** in the United States is in breach of its agreement obtained pursuant to Section 204;

(b) the **Institution** or affected third party has been notified of this determination and has been given at least thirty (30) days to provide a response to this determination, and

(c) the **Institution's** or affected third party's response to the determination of Paragraph 10.3(a)(i)-(iv) is determined to be unsatisfactory by the Office or Technology Transfer.

10.4 **PHS** may terminate this **Agreement** in whole or in part if;

(a) the **Institution** fails to make any payment or periodic reports required by this **Agreement** ;

(b) the **Institution** has willfully made a false statement of, or willfully omitted, a material fact in the negotiation of the **Agreement** or in any report required by the **Agreement** ;

(c) the **Institution** has committed a substantial breach of a covenant or duty contained in this **Agreement** ; or

(d) **PHS** and the **Institution** are involved in a dispute under this **Agreement** which cannot be resolved under the procedures specified in Paragraph 9.2. If this **Agreement** is

terminated under this Paragraph 10.4, **PHS** agrees to provide affected licensees an opportunity to license the **Patent Rights** subject to the restrictions of 37 C.F.R. Part 404 , under terms as may have been agreed to by the **Institution** ; and

(e) Prior to **PHS** exercising its right to terminate this **Agreement** as a result of **Institution's** breach of this **Agreement** (described in 10.4 (a) through 10.4(d)), the **Institution** shall have a reasonable opportunity to cure its breach.

10.5 Following termination by **PHS** , **PHS** shall have no further rights or obligations under this **Agreement** , except that tire **Institution** shall be obligated to administer subsequent gross proceeds from licensing the **Patent Rights** according to the Institution policy, and to distribute royalties to **PHS** for **PHS Inventor(s)** as though they were **Inventor(s)** of the **Institution** under that policy with respect to royalties and payment schedules.

11. GE NERAL

11.1 The **Institution** agrees that, for use and sale of the **Patent Rights** in the United States, any products embodying the **Patent Rights** , or produced through use of the **Patent Rights** , shall be manufactured substantially in the United States unless a waiver is granted by **PH** S.

11.2 All **Agreement** notices required or permitted by this **Agreement** shall be given by prepaid, first class, registered or certified mail or by an express/overnight delivery service provided by a commercial carrier, properly addressed to the other party at the address designated on the following Signature Page, or to the other address as may be designated in writing by such other party. **Agreement** notices shall be considered timely if the notices are received on or before the established deadline date or sent on or before the deadline date as verifiable by U.S. Postal Service postmark or dated receipt from a commercial carrier. Parties should request a legibly dated U.S. Postal Service postmark or obtain a dated receipt from a commercial carrier or the U.S. Postal Service. Private metered postmarks shall not be acceptable as proof of timely mailing.

11.3 This **Agreement** shall not be construed to confer on any person any immunity from or defenses under the antitrust laws or from a charge of patent misuse, and the acquisition and use of rights pursuant to this **Agreement** shall not be immunized from the operation of state or Federal law by reason of the source of the grant.

11.4 It is agreed that no waiver by either party hereto of any breach or default of any of the covenants or agreements herein set forth shall be deemed a waiver as to any subsequent or similar breach or default.

11.5 This **Agreement** is binding upon and shall inure to the benefit of the parties hereto and their successors or assigns, but this **Agreement** may not be assigned by either party without the prior written consent of the other party, except in the event of an assignment of one hundred percent (100%) of the assets of the **Institution** relating to **Patent Rights** with a full assumption of **Institution's** obligations hereunder as part of the sale.

11.6 This **Agreement** confers no license or rights by implication, estoppel, or otherwise under any patent applications or patents of the **PHS** other than the **Patent Rights** regardless of whether such patents are dominant or subordinate to the **Patent Rights** .

11.7 Any modification to this **Agreement** must be in writing and agreed to by both parties.

11.8 It is understood and agreed by the **Institution** and **PHS** that this **Agreement** constitutes the entire agreement between the parties, and that all prior agreements respecting the subject matter hereof, either written or oral, expressed or implied, shall be abrogated, canceled, and are null and void and of no effect.

11.9 The terms and conditions of this **Agreement** , which will become valid and binding as of the **Effective date** , shall, at **PHS'** sole option, be considered by **PHS** to be withdrawn from **Institution's** consideration and the terms and conditions of this **Agreement** , and the **Agreement** itself to be null and void, unless this **Agreement** is executed by the **Institution** and a fully executed original is received by **PHS** within sixty (60) days from the date of **PHS** signature found at the Signature Page.

SIGNATURES BEGIN ON NEXT PAGE

PHS INTERINSTITUTIONAL AGREEMENT — INSTITUTION

SIGNATURE PAGE

IN WITNESS WHEREOF, the parties hereto have executed this **Agreement** in duplicate originals by their respective duly authorized officers, who have affixed their signatures hereunto, on the day and year hereinafter written. Any communication or notice to be given shall be forwarded to the respective addresses listed below.

For **PHS** :

Richard U. Rodriquez
Director, Division of Technology Development and Transfer Office of Technology Transfer
National Institutes of Health

Date

Mailing Address or E-mail Address for Agreement notices and reports:

Chief, Monitoring & Enforcement Branch
Office of Technology Transfer
National Institutes of Health
6011 Executive Boulevard, Suite 325
Rockville, Maryland 20852-3804 U.S.A.

E-mail: LicenseNotices_Reports@mail.nih.gov

For the **Institution** :

Upon information and belief, the undersigned expressly certifies or affirms that the contents of any statements of the **Institution** made or referred to in this **Agreement** are truthful and accurate.

Kim R. Tsuchimoto
Chief Financial Officer
Raptor Pharmaceutical Corp.
Raptor Therapeutics Inc.

Date

Official and Mailing Address for **Agreement** notices:

Kim R. Tsuchimoto
Chief Financial Officer
Raptor Pharmaceutical Corp.
Raptor Therapeutics Inc.
Raptor Discoveries Inc.
9 Commercial Blvd., Suite 200
Novato, CA 94949

Phone: 415-382-1390
Fax: 415-382-1368
Email: ktsuchimoto@raptorpharma.com

EXHIBIT 10.6

License Agreement Amendment Number 2

This license agreement amendment number 2 ("Amendment Number 2"), effective as of May 2, 2012 ("Effective Date"), amends the License Agreement dated November 10, 2008, as amended November 18, 2011 (collectively, the "Current Agreement") by and between RAPTOR THERAPEUTICS INC., having its principal place of business at 9 Commercial Blvd., Suite 200, Novato, CA 94949 (hereinafter referred to as "Licensor"), formerly known as TorreyPines Therapeutics, Inc.; and QR PHARMA, INC., having its principal place of business at 1055 Westlakes Drive, Suite 300, Berwyn, PA 19312 (hereinafter referred to as "Licensee")..

WHEREAS, the Current Agreement grants to Licensee a license to certain intellectual property rights co-owned by Licensor and the Public Health Service ("PHS"), subject to any applicable provisions under the PHS Agreement;

Whereas, the Parties desire to amend the Current Agreement to provide as set forth in this Amendment Number 2; and·

Whereas, the Current Agreement, as amended hereby, is hereinafter referred to as "this Agreement."

NOW, THEREFORE, in consideration of the foregoing premises and the mutual covenants set forth herein, the Parties, intending to be legally bound, hereby agree as follows:

Unless otherwise defined herein, capitalized terms shall be given the meaning assigned in the Agreement.

1. The following shall be deleted and replaced in their entirety as follows:

1.11 "Field" shall mean all fields.

2. Section 1.9, "Excluded Field" and Section 1.34 "Research Field" shall be deleted in their entirety.

3. Section 2.1 shall be deleted and replaced in its entirety as follows:

2.1 License Grant . Subject to the terms and conditions of this Agreement, and subject to the retained rights and other rights of the government under sections 2.2 and 2.6 and under the PHS Agreement, Licensor hereby grants to Licensee an exclusive (even as to Licensor), royalty-bearing license, with the right to grant sublicenses, under the Patent Rights, the Licensor Know-How and PHS Patent Rights to use, store, import, export, transport, Manufacture or have Manufactured Licensed Compounds in the Territory in the Field and to Develop, Manufacture and Commercialize Licensed Products in the Territory in the Field during the Term. Subject to the terms and conditions of this Agreement, Licensor hereby also grants to Licensee an exclusive (even as to Licensor), royalty-free right and license in the Territory, with the right to grant sublicenses as part of any sublicense of rights granted with respect to Licensed Products, to use the Licensed Trademarks in connection with using, selling and offering for sale Licensed Products in the Territory in the Field during the Term.

4. Section 2.2 shall be deleted and replaced in its entirety as follows:

2.2 No Other Licenses; Retained Rights . Neither Party grants to the other Party any rights or licenses in or to any intellectual property, whether by implication, estoppel, or otherwise, other than the license and other rights that are expressly granted under this Agreement. Subject to the license granted to Licensee pursuant to Section 2.1, Licensor has, and shall retain all right, title and interest in an to, the Patent Rights and Licensor Know-How. Notwithstanding anything in this Agreement to the contrary, Licensee agrees and understands that the PHS Patent Rights sublicensed under this Agreement are pursuant to the PHS Agreement, including but not limited to PHS' reservation of rights under Article 3 of the PHS Agreement, and are at all times subject to the terms and conditions of the PHS Agreement, as may be amended from time to time after the Effective Date. Without limiting the foregoing,

Licensee agrees to grant such licenses or cause its sublicensee(s) to grant such licenses that PHS requires under Article 3 of the PHS Agreement.

5. Article 4 shall be deleted and replaced in its entirety as follows:

4.1 Manufacturing Responsibility . Licensee shall be responsible for the Manufacture of the Licensed Compounds and/or Licensed Products for use by Licensee, its Affiliates, and its sublicensees in the Field in the Territory. The Manufacture of Licensed Compounds and/or Licensed Products embodying the PHS Patent Rights, or produced through use of the PHS Patent Rights, shall be subject to Sections 2.6 and 13.5 of this Agreement and to the PHS Agreement (including but not limited to section 11.1 of the PHS Agreement}, which requires that products embodying PHS Patent Rights, or produced through use of PHS Patent Rights, shall be manufactured substantially in the United States unless a waiver is granted by PHS.

4.2 Transfer of Manufacturing Technology . As soon as reasonably practicable after the Effective Date, Licensor shall provide or cause to be provided to Licensee, or a third party manufacturer designated by Licensee, that information within the Licensor Know-How as of the Effective Date that is necessary or useful to enable Licensee or such third party manufacturer (as appropriate) to Manufacture Licensed Compounds as of the Effective Date. The Manufacture of Licensed Compounds and/or Licensed Products embodying the PHS Patent Rights, or produced through use of the PHS Patent Rights, shall be subject to Sections 2.6 and 13.5 of the Agreement and the PHS Agreement (including but not limited to section 11.1 of the PHS Agreement), which requires that products embodying PHS Patent Rights, or produced through use of PHS Patent Rights, shall be manufactured substantially in the United States unless a waiver is granted by PHS.

6 Section 5.6 shall be deleted and replaced in its entirety as follows:

5.6 Minimum Annual Payment . No later than November 30 of each Calendar Year commencing in 2009 and continuing through 2011, Licensee shall pay to Licensor a non-refundable minimum annual payment of $40,000 less any amounts previously paid pursuant to Section 5.3 or 5.4 during such Calendar Year. No later than November 30 of each Calendar Year commencing in 2012, Licensee shall pay to Licensor a non-refundable minimum annual payment of $46,000 less any amounts previously paid pursuant to Section 5.3 or 5.4 during such Calendar Year. Each such payment shall be credited against royalties and the Buy Out Payment, if any, for that Calendar Year. Notwithstanding anything to the contrary set forth above, until such time, from and after January 1, 2012, as Licensee shall raise equity financing of at least $2 million in new cash, payment of all amounts payable pursuant to this Section 5.6 may be deferred by Licensee.

7. Notwithstanding anything to the contrary set forth in this Amendment Number 2 or in the Agreement, Licensor makes no representation under Sections 9.2(b) and 9.3 of the Agreement as to the grant of rights as of the Effective Date in the field of human chemical and bioterrorism defense or in the Republic of Korea.

Except as modified hereby, all of the terms and conditions of the Agreement shall remain in full force and effect.

The Parties execute this valid and binding Amendment Number 2 as of the Effective Date in one or more counterparts, each of which shall be deemed an original but all of which taken together constitute one and the same instrument.

RAPTOR THERAPEUTICS INC.	**QR PHARMA, INC.**
/s/ Kim R. Tsuchimoto	/s/ Maria Maccecchini
Name	Name
CFO	President & CEO
Title	Title
5/2/12	5-2-2012
Date	Date

EXHIBIT 10.7

Investigator-Initiated Clinical Trial Agreement

This Clinical Trial Agreement ("Agreement") is made and entered into effective as of the full execution hereof ("Effective Date"), by and between The Regents of the University of California, a California constitutional corporation, on behalf of its San Diego campus, located at 9500 Gilman Drive, La Jolla, CA 92093, California ("Institution"), and QR Pharma, Inc., a Delaware corporation having its principal place of business at 1055 Westlakes Drive, Suite 300, Berwyn PA 19312 ("Company"), (each may be individually referred to as a "Party" and collectively, as "the Parties").

Whereas, **Howard Feldman, M.D.** an employee of Institution ("Principal Investigator"), desires to conduct a clinical study ("Study"), funded by the National Institutes of Health ("NIH") under a protocol entitled " **A Safety and PK/PD Study of Posiphen in Subjects with Mild Alzheimer's Disease (PSN)** " ("Protocol"), a copy of which is attached hereto as Exhibit A;

Whereas, Principal Investigator has authored the Protocol, and Institution and Principal Investigator have the expertise and facilities to conduct the Study;

Whereas, Company is providing - Study Drug (as defined herein) for use in the Study;

Whereas, the Study is intended to advance scientific and medical knowledge, and Institution considers the Study to be research done in the public interest;

Now, therefore, in consideration of the mutual promises set forth in this Agreement, the Parties hereby agree as follows:

1. Scope of Work.

1.1 Principal Investigator . Institution shall conduct the Study under the direction of the Principal Investigator. Principal Investigator may appoint such other Institution employees to provide services on behalf of Institution to conduct such Study ("Study Staff"). If Principal Investigator becomes unable or unwilling to continue to conduct the Study, Institution shall promptly notify Company in writing. If a mutually acceptable substitute Principal Investigator is not identified within thirty {30) days after the date of Institution's notice, then either Party shall have the option to terminate the Study upon ten (10) days prior written notice and pursuant to Section 8.4 below.

1.2 Institution as Study Sponsor . Institution and Principal Investigator shall act as "Sponsor" of the Study, as such term is defined by the U.S. Food and Drug Administration ("FDA") Federal Code of Regulations, 21 C.F.R. 312.3(b) or 21 C.F.R. 812.3(n).

1.3 Company as Investigational New Drug Application ("IND") Holder . To the extent required to do so by Applicable Law, Company will obtain and maintain IND #72.654 pursuant to FDA regulations.

1.4 Study Staff . Institution, through Principal Investigator, shall supervise Study Staff in their performance of the Study and ensure that all Study Staff are qualified to perform the duties assigned to such person. Institution shall take reasonable and appropriate steps to inform Study Staff of their obligations under this Agreement.

1.5 Conduct of the Study . Institution shall, and shall cause the Principal Investigator and Study Staff (collectively, "Study Team") to, conduct the Study in accordance with this Agreement, the Protocol, and all applicable foreign, federal and state laws and regulations ("Applicable Law"); provided, however, that Institution may deviate from the Protocol and such instructions to the extent that the safety of Study subjects so requires. For clinical Studies, such conduct includes compliance with International Conference on Harmonization Good Clinical Practice (ICH GCP), but only to the extent that the ICH GCP guidelines comport with FDA regulations.

1.6 IRB Approval . Institution shall obtain approval of the Study, the Protocol, and an informed, consent from the appropriate institutional review board ("IRB") and shall seek any other approvals required for the Study from applicable safety or review boards or other authorities.

1.7 Informed Consent . Prior to a Study subject's participation in Study, Institution shall obtain from each Study subject participating in the Study or such Study subject's legal representative an informed consent, signed by the Study subject or his or her legal representative, unless such signature is waived by the IRB.

1.8 Protocol Ownership and Changes to the Protocol . Company and Investigator jointly authored the Study Protocol and research design of the Study. Institution shall inform Company of any changes to the Protocol that significantly affect Study objectives or the safety of Study.

1.9 Multi-Center Study . In the event of a multi-center Study, Institution agrees that each site involved in the Study (each a "Study Site" and collectively "Study Sites") shall enter into a written agreement with Institution regarding such Study Site's participation in the Study with Institution and Sponsor. Institution and Investigator shall be responsible for the conduct of the Study at all Study Sites, and shall ensure that the Study Sites comply with the terms and conditions of this Agreement and all Applicable Laws.

1.10 Provision of Study Drug and Study Supplies . Company shall provide to Institution, without cost, a necessary quantity of Sponsor's study drug to be encapsulated and blister packed, blinded and distributed to conduct the Study pursuant to the Protocol ("Study Drug"), as well as placebo (collectively, "Study Supplies") which the Protocol specifies that Company

will deliver to conduct the Study. Institution shall be responsible for costs associated with encapsulation, blister packing, labeling, and distribution by Frontage.

2 Access and Auditing.

2.4 Access to Study Data . Upon prior written request to Institution, at mutually agreeable times during Institution's regular business hours, and subject to the terms of this Agreement and Applicable Law, Company or its agents may access and make copies of Institution's Study data in the form in which it is available, except that direct identifiers of any Study subject, including, but not limited to, Study subject's name, birth date, street address, telephone, social security, medical record or health plan beneficiary numbers ("Direct Identifiers") shall not be made available to Company. In the event Study data contains Direct Identifiers, such Direct Identifiers shall be redacted. Compliance with HIPAA and CMIA . The Parties shall comply with all Applicable Laws governing patient privacy and confidentiality of health information, including without limitation the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") and its implementing regulations, and the State of California Confidentiality of Medical Information Act ("CMIA"). The Parties shall take all actions necessary to comply with such laws and regulations, including agreeing to amend this Agreement as necessary for compliance.

2.5 Adverse Event Reporting . Company is solely responsible for reporting adverse events in the course of the Study in accordance with Applicable Law and the Protocol to the FDA and other regulatory authorities, as applicable. Institution shall provide Company with a copy of any adverse event reports. Company shall be responsible for submission of IND Safety Report to the FDA.

2.6 Debarment . Institution certifies that it will not use the services of any Study Staff to perform services in connection with the Study who is (i) debarred, disqualified or banned from conducting clinical studies under the Generic Drug Enforcement Act of 1992, as amended, or (ii) excluded, debarred or suspended from participation in, or is otherwise ineligible to participate in, any federal health care program or federal procurement or non-procurement program. Institution further certifies that neither it, nor any person or entity it utilizes to perform services pursuant to this Agreement, has been convicted of a criminal offense that falls within the ambit of 42 U.S.C. § 1320a-7(a) or is otherwise related to the provision of healthcare items or services. Institution agrees to inform Company in writing of any change to this certification.

3. Ownership of Data and Intellectual Property

4.1 Study Data . All rights, title and interest in Study data shall be the sole and exclusive property of Institution; provided, however, that Company shall have the right to use the Study data for regulatory filings and all other lawful purposes.

4.2 Final Report . Within a reasonable time, but no longer than 90 days, following completion of the Study, Institution shall provide Company with a final report of the research results of the Study. Company may request reports as needed.

4.3 Study Inventions . Institution shall own all patentable inventions and discoveries conceived and reduced to practice in the direct performance of the Study and which necessarily use or necessarily incorporate the Study Drug ("Study Inventions"). Institution shall promptly disclose each Study Invention to Company. Study Inventions shall be deemed the Confidential Information of the Party holding rights to such inventions.

4.4 Option to License . Institution shall grant to Company (i) a worldwide, royalty-free, fully paid, nonexclusive, perpetual license to use all Study Inventions for non-commercial purposes; and (ii) a time-limited first right to negotiate an exclusive or non-exclusive commercial (at Company's election) license to Institution's rights in any Study Invention as set forth below. Company will advise Institution in writing within sixty (60) days of Institution's disclosure of each Study Invention whether or not Company wishes to secure a commercial license ("Election Period"). Company shall have one hundred twenty (120) days from the date of election to enter into a license agreement with Institution ("Negotiation Period"). In such event, Institution shall negotiate in good faith, and shall not enter into negotiations with any third party during the Negotiation Period. In the event it is necessary in the opinion of Institution to file any patent application to protect a Study Invention during the Election or Negotiation Period, Company will reimburse Institution for any incurred patent costs during such period, provided that Company is continuing to pursue negotiation of a commercial license at that time. If such license is not agreed upon within the Negotiation Period, neither Party shall have any further obligation to the other with respect to such Study Invention other than the nonexclusive license granted to Company in accordance with clause (i) above.

4.5 No Rights to Other Proprietary Interests . Nothing contained in this Agreement shall be deemed to grant either directly or by implication, estoppel, or otherwise, any rights under any patents, patent applications or other proprietary interests, whether dominant or subordinate, or any other invention, discovery or improvement of either Party, other than the specific rights covering Study Inventions under this Agreement.

4. Confidentiality

5.1 Institution Confidential Information . Institution shall only disclose confidential information necessary for Company's support of the Study. "Institution Confidential Information" shall mean and include all data and other information which are disclosed by Institution to Company, for the purposes of conducting Study which is marked as "Confidential "at the time of disclosure, or (i) in the case of oral disclosures, identified at the time of such oral disclosure as confidential and summarized in writing and marked as "Confidential" within thirty (30) days of oral disclosure; (ii) if not marked, regarded as confidential if a reasonable person in the relevant field would consider such information to be Institution's confidential information given its content and the circumstances of the disclosure.

Institution Confidential Information shall not include information to the extent that it: (i) is, or later becomes, publicly known other than through a breach of this Agreement by Company, its employees, or its agents; (ii) is lawfully made available to Company, its employees or its agents, by a third party that Company reasonably believes owes no obligation of confidentiality to Institution; or (iii) was already known to or is independently developed by Company, its employees, or its agents. During the term of this Agreement and for a period of five (5) years after its expiration or earlier termination, Company shall maintain the confidentiality of Institution Confidential Information and may not transfer or disclose Institution Confidential Information to any third party without Institution 's prior written consent other than as required by Applicable Law or as permitted pursuant to the terms of this Agreement.

5.2 Company Confidential Information . Company shall only disclose confidential information necessary for Institution's performance of the Study. "Company Confidential Information" shall mean and include all data and other information which are disclosed by Company to Institution for the purposes of conducting Study which is marked as "Confidential" at the time of disclosure, or (i) in the case of oral disclosures, identified at the time of such oral disclosure as confidential and summarized in writing and marked as "Confidential" within thirty (30) days of oral disclosure; (ii) if not marked, regarded as confidential if a reasonable person in the relevant field would consider such information to be Company's confidential information given its content and the circumstances of the disclosure. Company Confidential Information shall not include information to the extent that it: (i) is, or later becomes, publicly known other than through a breach of this Agreement by Institution, its employees, or its agents, including the Principal Investigator; (ii) is lawfully made available to Institution, its employees or its agents, including Principal Investigator, by a third party that Institution reasonably believes owes no obligation of confidentiality to Company; or (iii) was already known to or is independently developed by Institution, its employees, or its agents, including Principal Investigator. During the term of this Agreement and for a period of five (5) years after its expiration or earlier termination, Institution shall maintain the confidentiality of Company Confidential Information and may not transfer or disclose Company Confidential Information to any third party without Company's prior written consent other than as required by Applicable Law or as permitted pursuant to the terms of this Agreement.

5.3 Permitted Uses and Disclosures of a Disclosing Party ' s Confidential Information . "Disclosing Party" as used herein means, with respect to Institution Confidential Information or Company Confidential Information, the Party who owns or otherwise controls such confidential information, and has disclosed such confidential information under this Agreement. A Disclosing Party's confidential information may be used by the Party receiving such confidential information ("Receiving Party") to the extent that it: (i) is disclosed for the purpose of performing the Study, provided that the Receiving Party has obligated its employees and agents to hold such Institution Confidential Information or Company Confidential Information in confidence at least to the same degree of care as the Receiving Party uses to protect its own confidential information hereunder; or (ii) is disclosed to medical professionals in order to provide reasonable and necessary medical care to a Study subject, provided that the Receiving Party advises such medical care

provider(s) of the need to maintain the confidentiality of such Institution Confidential Information or Company Confidential Information.

5.4 Required Disclosures of Institution Confidential Information and Company Confidential Information . Notwithstanding any provisions of this Agreement, the Receiving Party may disclose Institution Confidential Information or Company Confidential Information which it is required by governmental order, subpoena or Applicable Law to disclose. The Receiving Party agrees to cooperate with any reasonable effort of the Disclosing Party to challenge a court- ordered, open records, or similar required disclosure at the Disclosing Party's expense; provided, however, that, with respect to an open records disclosure, the Receiving Party independently has determined that the information the Disclosing Party seeks to protect is exempted from disclosure under Applicable Law.

5.5 Return of Confidential Information . At any time and upon the Disclosing Party's advance written request, the Receiving Party shall return to the Disclosing Party promptly, or destroy, any and all Institution Confidential Information or Company Confidential Information furnished to the Receiving Party under this Agreement, and all copies thereof; provided, however, that the Receiving Party may retain one copy in a secure location solely for purposes of compliance with this Agreement and Applicable Law. The Receiving Party shall not be required to delete or destroy any electronic back-up tapes or other electronic back-up files that have been created solely by the automatic or routine archiving and back-up procedures of the Receiving Party, to the extent created and retained in a manner consistent with its or their standard archiving and back-up procedures.

5.6 Accessibility of Institution Records . Institution, as an instrumentality of the State of California, is subject to certain state regulations and resolutions regarding access to Institution's records, including the requirement that Institution make available the terms and conditions of contracts. The actual contract agreement must be released upon request, although portions of the document may be withheld when redaction meets one of the legal exemptions under the California Public Records Act. As such, the general terms and conditions of this Agreement will be released to the public upon request. To the extent disclosure of other records, including the Protocol, terms of compensation and related documents, is requested, Institution will use reasonable efforts to notify Company and work with Company to redact material which can be withheld from disclosure, to the extent permitted by law and at Company's request and expense. Furthermore, for the avoidance of doubt, Institution maintains a publicly accessible listing of all proposals and awards. The listing includes the name of the campus, sponsor, award amount, begin and end dates, principal investigator and co-investigator's name, project type, award instrument, indirect cost rate, account and fund number, department and academic discipline.

5.7 Use of Name . Company shall not use the name, logo, mark or image of Institution in any publicity or advertising without Institution's written approval. California Education Code Section 92000 prohibits use of Institution's names to suggest that Institution endorses a product or service.

6. Publication

6.1 Right of Publication . Institution may freely publish and disseminate the results of the Study, or otherwise publish or submit for publication an article, manuscript, abstract, report, poster, presentation, or other material containing or dealing with results of the Study {"Publication").

6.2 Review Period of Publications . Institution shall send Company a copy of any proposed Publication thirty {30) days prior to submission for Publication ("Review Period"). Company may comment upon, but may not make any editorial changes to the proposed Publication. Upon Company's timely written request prior to submission to Publication, Institution shall delete any Company Confidential Information in the proposed Publication. At Company's request, Institution shall delay Publication for an additional thirty (30) days in order to protect the potential patentability of an invention described therein.

6.3 Registration of Study . Company shall register and report the results of the Study in accordance with the International Committee of Medical Journal Editors (ICMJE) clinical trial requirements for publication and as required under Applicable Law.

7. Indemnification, Subject Injury and Insurance

7.1 Company Indemnification . Company shall defend, indemnify and hold harmless Institution, its directors, officers, agents, subcontractors and employees, including Principal Investigator ("Institution lndemnitees") from and against any and all claims, liabilities, expenses (including reasonable attorneys' fees), actions or demands that may be made or instituted against any of them by a third party by reason of injury (including death) to any person, or damage to property, arising out of or in connection with the Study Drug or any procedures required under the Protocol ("Claims"); provided Company shall have no liability with respect to such injury to the extent caused by: (i) Institution's failure to comply with all applicable laws, regulations and directives, the Protocol, this Agreement, all written instructions delivered by Company concerning administration of the Research Drugs, all communications from IRBs, guidelines governing good clinical practice; or (ii) Institution's negligence, willful malfeasance or breach of this Agreement by Institution, the Principal Investigator or any employee or agent of Institution. Institution shall promptly notify Company in writing after receipt by Institution of any Claim subject to this Section.

7.2 Institution Indemnification . Institution shall defend, indemnify and hold harmless Company, its directors, officers, agents and employees ("Company lndemnitees") from and against any and all Claims arising out of Institution's breach of this Agreement or the negligence or willful malfeasance of Institution, the Principal Investigator or any employee or agent of Institution. Company shall promptly notify Institution in writing after receipt by Company of any Claim subject to this Section.

7.3 Management of Indemnification . Each Party shall have the right to manage the defense and settlement of any Claim for which it is the indemnifying Party, provided however, that the indemnifying Party shall not admit any liability or wrongdoing on the part of the indemnified Party or indemnitees, or settle any Claim which would involve such an admission, without the prior written consent of the indemnified Party, which consent will not be unreasonably withheld. The indemnified Party shall reasonably cooperate with the indemnifying Party regarding any such Claims. Subject to the foregoing, each indemnitee may participate in any such Claims at its/his/her own cost and expense.

7.4 Reimbursement for Subject Injury . Company shall reimburse Institution for all reasonable and necessary expenses for the diagnosis or treatment of any injury or illness that is a direct result of Study Subject's participation in the Study; provided, however, that such obligation of Company shall not apply to the extent the injury or illness results from (i) the negligence or reckless or intentional misconduct of, or violation of law by, Institution, the Principal Investigator, or Institution's agents or employees; (ii) any failure of Institution, the Principal Investigator, or Institution's agents or employees to adhere to the terms of the Protocol or any provision of this Agreement; or (iii) the natural progression of the Study Subject's underlying, preexisting medical condition. Institution shall provide Company with sufficient documentation to review and process any Study Subject injury reimbursements. In the event that such costs are properly paid by the Study Subject's private insurer, government payor or other responsible third party, Company shall have no reimbursement obligation with respect thereto.

7.5 Insurance . Each Party shall have sufficient liability insurance and other adequate forms of protection to satisfy the obligations set forth in this Agreement. The amount of a Party's insurance coverage shall not be construed as creating a limit on such Party's obligations assumed herein.

8. Term and Termination

8.1 Term . This Agreement shall take effect on the Effective Date and shall continue until the earlier of: (i) completion of such Study; (ii) upon full execution of this agreement; or (iii) until Study is sooner terminated or suspended as provided for in this Agreement and pursuant to the Protocol.

8.2 Termination . Either Party may terminate this Agreement: (i) upon thirty (30) days prior written notice to the other Party, in its sole discretion; or (ii) upon written notice to the other Party, if the terminating Party determines that termination of the Study is necessary for the safety of the Study subjects.

8.3 Early Termination Procedures . If this Agreement is terminated before completion of the Study, the Parties shall negotiate in good faith on the phase-out for Study subjects and subsequent treatment of Study subjects. Company shall reimburse Institution for (i) obligations incurred in accordance with the Study budget that cannot be cancelled or

mitigated by Institution using reasonable efforts; (ii) reasonable costs incurred in connection with the safe withdrawal of Study subjects; and (iii) any other post-termination expenses mutually agreed to by the Parties in writing.

8.4 Return of Property . Within thirty (30} days following the expiration or earlier termination of this Agreement: (a) Institution shall return to Company, at Company's sole and reasonable expense (i) any remaining Study Supplies (except as required by Applicable Law and (iii) subject to the terms of Section 5 of this Agreement, any copies of Company Confidential Information provided by Company that are in the possession of or are under the control of Institution; (b) Company shall return to Institution, at Company's sole and reasonable expense, subject to the terms of Section 5 of this Agreement, any copies of Institution Confidential Information provided by Institution that are in the possession of or are under the control of Company.

8.5 Survival . The following provisions shall survive expiration or termination of this Agreement: Sections 1.2, 1.3, 1.4, 2.1, 2.2, 3, 4, 5, 6, 7, 8.4, 8.5, 8.6 and 9.

9. Miscellaneous

9.1 Independent Contractor . All research performed by Institution, Principal Investigator and any Study Staff pursuant to this Agreement shall be performed as an independent contractor. The relationship between the Parties does not constitute a partnership, joint venture, or agency. Neither Party shall have the authority to bind the other Party without that other Party's express and written consent.

9.2 Equitable Relief . Each Party hereby acknowledges and agrees that damages at law may be an inadequate remedy for any breach by a Party of its obligations under Section 2.1, Section 4 or Section 5 of this Agreement, and, accordingly, each Party agrees that, in the event of such a breach, the other Party may be entitled to such temporary, preliminary and permanent injunctive relief as may be necessary to remedy or limit such breach and including specific performance of such obligations and an order enjoining the breaching Party from the continuation of, or from any threatened, breach of such obligations.

9.3 Remedies and Waiver . The remedies provided in this Agreement are not exclusive and the Party suffering from breach or default of this Agreement may pursue all other remedies, both legal and equitable. No express or implied waiver by a Party of any breach or default will be construed as a waiver of a future or subsequent breach or default. The failure or delay of any Party in exercising any of its rights under this Agreement will not constitute a waiver of any such right, and any single or partial exercise of any particular right by any Party will not exhaust the same or constitute a waiver of any other right provided in this Agreement.

9.4 Assignment . Neither Party may assign any of its rights or delegate any of its duties under this Agreement without the prior written consent of the other Party, except that Company

may assign this Agreement to a third party in connection with a merger or sale of all or substantially all of its assets relating to the Study Drug, and Company may delegate its obligations or assign its rights under this Agreement to a contractor, provided that Company remains liable for the performance of all delegated obligations and written notice is provided to Institution. Any unauthorized attempted assignment shall be null and void and of no force or effect.

9.5 Governing Law . This Agreement is governed by the laws of the State of California without regard to its conflict of law provisions.

9.6 No Implied Right or License . No implied right or license is granted under this Agreement by either Party except those specifically set forth herein. Nothing contained in this Agreement shall impose an obligation of exclusivity on one Party to the other Party.

9.7 Severability . If any provision of this Agreement is held to be unenforceable for any reason, that unenforceability shall not affect the enforceability of any other provision of this Agreement. The Parties shall negotiate in good faith to substitute an enforceable provision with similar terms.

9.8 Entire Agreement . This Agreement, and any Exhibits thereto, constitutes the entire agreement between the Parties and supersedes all prior agreements and understandings relating to its subject matter. This Agreement, and any Exhibits thereto, may not be altered, modified or waived in whole or part except in writing signed by duly authorized representatives of both Parties. In the event of a conflict between the provisions of this Agreement and Exhibit A or other Study document, the provisions of this Agreement will govern.

9.9 Counterparts: Electronic or Facsimile Transmission . This Agreement may be executed in counterparts, via facsimile or .pdf file and each of which shall be deemed to be an original, but all of which constitute one instrument. An executed counterpart of this Agreement may be transmitted to the other Party by electronic or facsimile transmission, with the same effect as if the Parties had delivered an executed original Agreement.

9.10 Force Majeure . If either Party's performance of this Agreement or Study is prevented, restricted or delayed, either totally or in part, for reasons beyond the affected Party's reasonable control and is not due to the action or inaction of such Party, the affected Party will, upon giving notice to the other Party, be excused from such performance to the extent of such prevention, restriction or delay; provided, that the affected Party will use reasonable efforts to avoid or remove such causes of non-performance and will continue its performance whenever such causes are removed. For purposes of this Section, a lack of funds shall not be considered a cause beyond the reasonable control of the Parties.

9.11 Order of Precedence . The terms of this Agreement and the Protocol shall take precedence over other documentation, including but not limited to the Informed Consent in the interpretation and resolution of disputes concerning this Study. In the event that there is a conflict between the terms of the Protocol and the terms of this Agreement, the terms of this Agreement will govern with respect to legal contract terms, but the Protocol will govern with respect to the scientific/clinical conduct of the Study.

9.12 Notices . All notices required or permitted hereunder must be in writing, and will be deemed to be effective only when delivered personally or sent by certified or registered mail, postage prepaid, return receipt requested, and addressed to the Parties as follows or at such other address as a Party shall have given notice of pursuant hereto:

To Institution:	UCSD OCGA Attn: Karim Hussein 9500 Gilman Drive #0934 La Jolla, CA 92093-0934 (858) 822-5180
With a copy to the Principal Investigator:	Howard Feldman 9500 Gilman Drive, 0949 La Jolla, CA 92093
To Company:	QR Pharma, Inc. 1055 Westlakes Drive, Suite 300 Berwyn PA 19312 Attention: Maria L. Maccecchini, Ph.D. President and CEO

In witness whereof, the Parties have caused this Agreement to be executed by their duly authorized representatives.

QR PHARMA, INC.

By: /s/ Maria L. Maccecchini

Print Name: Maria L. Maccecchini

Title: President and CEO

Date: 6-17-2016

By: /s/ Karim Hussein

Print Name: Karim Hussein

Title: Principal Contract Officer

Date: 06/27/2016

WHILE NOT A PARTY TO THIS AGREEMENT I HAVE READ THE AGREEMENT AND ACKNOWLEDGE MY RESPONSIBILITIES AS THE PRINCIPAL THE PRINCIPAL INVESTIGATOR:

/s/ Howard Fedman

Name: Howard Feldman

Title: Principal Investigator

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the use in this Preliminary Prospectus constituting a part of this Registration Statement on Form S-1 of Annovis Bio, Inc. of our report dated May 15, 2019, except for the effects on the financial statements of the restatement described in Note 12, as to which the date is July 2, 2019, relating to the balance sheets of Annovis Bio, Inc. as of December 31, 2018 and 2017, and the related statements of operations, changes of redeemable convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the two years in the period then ended.

We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ WithumSmith+Brown, PC

East Brunswick, New Jersey
July 2, 2019