ANNOVIS BIO, INC.

FORM 424B4

(Prospectus filed pursuant to Rule 424(b)(4))

Filed 01/30/20

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CIK	0001477845
Symbol	ANVS
SIC Code	2834 - Pharmaceutical Preparations
Industry	Biotechnology & Medical Research
Sector	Healthcare
Fiscal Year	12/31

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Filed pursuant to Rule 424(b)(4)
Registration Nos. 333-232529 and
333-236126

PROSPECTUS

2,000,000 Shares

Common Stock

ANNOVIS BIO, INC.

This is a firm commitment initial public offering of 2,000,000 shares of common stock of Annovis Bio, Inc. No public market currently exists for our shares.

Our common stock has been approved for trading on the NYSE American under the symbol "ANVS."

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 14 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	$6.00	$ 12,000,000
Underwriting discounts and commissions(1)	$0.42	$ 840,000
Proceeds to us, before expenses	$5.58	$ 11,160,000

(1) Underwriting discounts and commissions do not include a non-accountable expense allowance equal to 1.0% of the public offering price payable to the underwriters. We refer you to "*Underwriting*" beginning on page 150 for additional information regarding underwriters' compensation.

We have granted the underwriters a 45-day over-allotment option to purchase up to 300,000 additional shares of common stock at the initial public offering price less underwriting discounts and commissions.

Certain of our existing stockholders have indicated an interest in purchasing an aggregate of approximately $800,000 in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, fewer or no shares in this offering to any of these stockholders, and any of these stockholders may determine to purchase more, fewer or no shares in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these stockholders as they will on any other shares sold to the public in this offering.

The underwriters expect to deliver our shares to purchasers in the offering on or about January 31, 2020

ThinkEquity
a division of Fordham Financial Management, Inc.

The date of this prospectus is January 29, 2020

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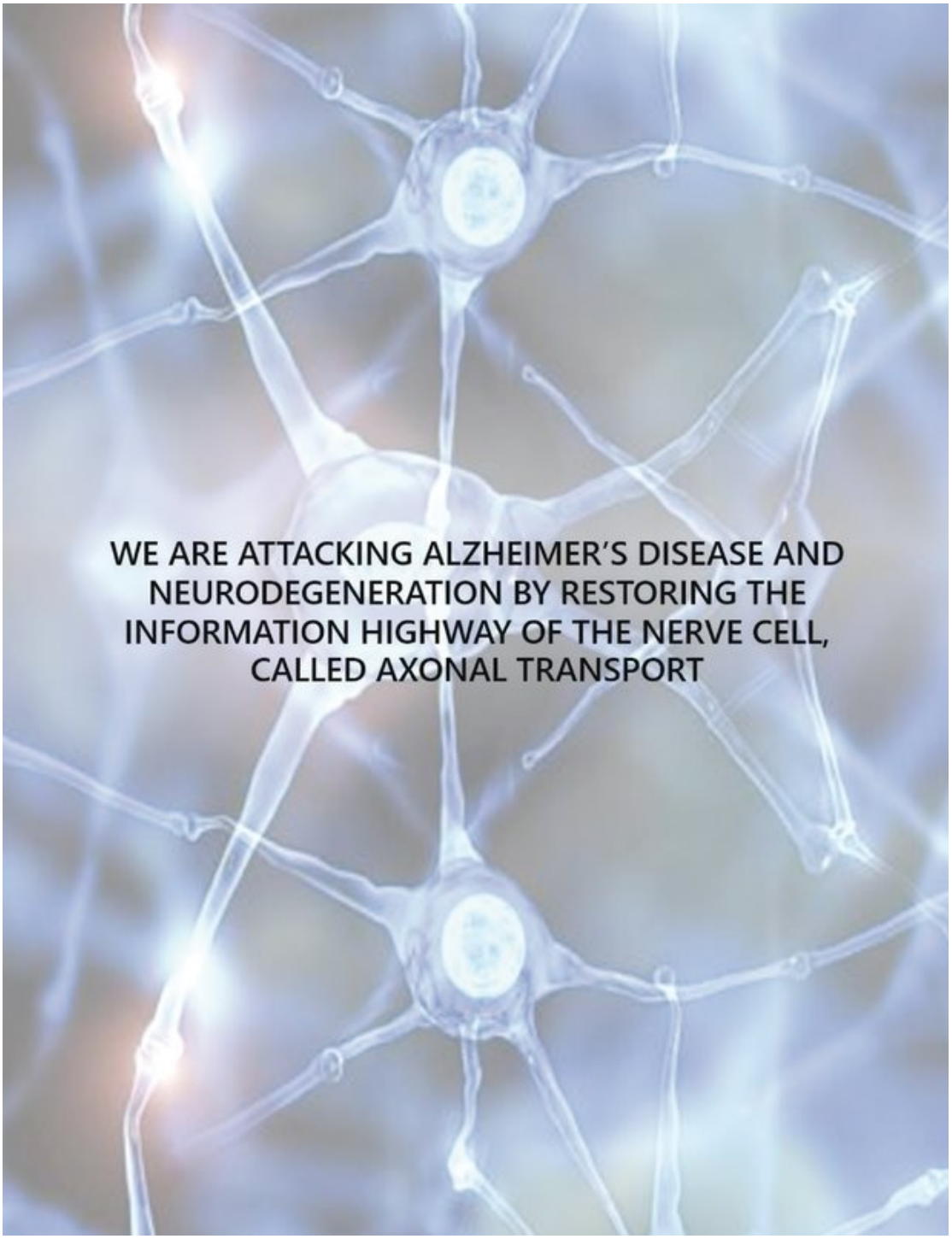

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We have not authorized anyone to provide you with different information, and we take no responsibility for any other information others may give you. If anyone provides you with different or inconsistent information, you should not rely on it. We are 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 several studies, ANVS-401 inhibited the synthesis of neurotoxic proteins—APP/Aβ (APP), tau/phospho-tau (tau) and α-Synuclein (αSYN)—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, we have shown in four mildly cognitive impaired (MCI) patients that ANVS-401 lowered the levels of these neurotoxic proteins and inflammatory factors. In preclinical studies, lower neurotoxic protein levels led to improved axonal transport, reduced inflammation, lower nerve cell death and improved function.

The industry has encountered challenges in targeting specifically one or the other neurotoxic protein, be it APP, tau or αSYN, 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 improving axonal transport 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 four 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.

We are presently conducting a Phase 2a study in AD patients in collaboration with the Alzheimer Disease Cooperative Study (ADCS) 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 AD 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 eight early to moderate AD patients. In

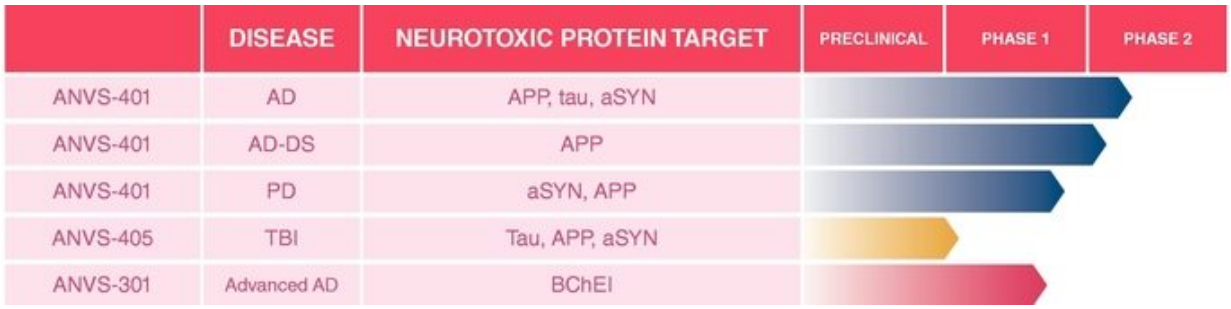
September 2019, the Data Safety Monitoring Board overseeing this study reviewed the safety data for the participants thus far and recommended the study continue without modification. We have designed the two Phase 2a studies with Parexel by applying our understanding of the underlying disease states in neurodegeneration and by measuring not just target, but also pathway validation in the spinal fluid of these patients. This means that we are proposing to measure as many factors as possible associated with the toxic cascade precipitated by impaired axonal transport. If we are able to show 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 that 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 our animal studies in DS mice, lowering their high levels of APP improved axonal transport in the brain and increased memory and learning, as described on page 6. In accordance with this animal data, we expect that lowering levels of APP, tau and αSYN in human patients will lead to an improvement in their memory, cognition and dementia. Concluding the study in AD-DS patients instead of AD patients 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 consists of ANVS-401 for chronic neurodegeneration—including AD, its orphan indication AD-DS and PD, ANVS-405 to treat acute neurodegeneration—traumatic brain injury (TBI) and stroke—and ANVS-301 for advanced AD.



ANVS-401

Our lead compound, ANVS-401 is an orally administered drug being developed for chronic indications such as AD-DS, AD and PD, because in preclinical studies it improved axonal transport in these diseases by inhibiting the overproduction of 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. ANVS-405 is the same compound as ANVS-401, but it is given intravenously in cases of acute head and brain trauma. ANVS-405 was given to rats as an injectable after TBI to ensure that it would reach the brain in less than 15 minutes rather than 1.5 hours. TBI rats that were treated after the insult exhibited enhanced memory and learning and lowered microglia activation, a measure of inflammation. To date the program has been funded by a grant from the U.S. Army and we plan to seek additional grant funding to further the development of ANVS-405 for acute indications of brain and nerve trauma.

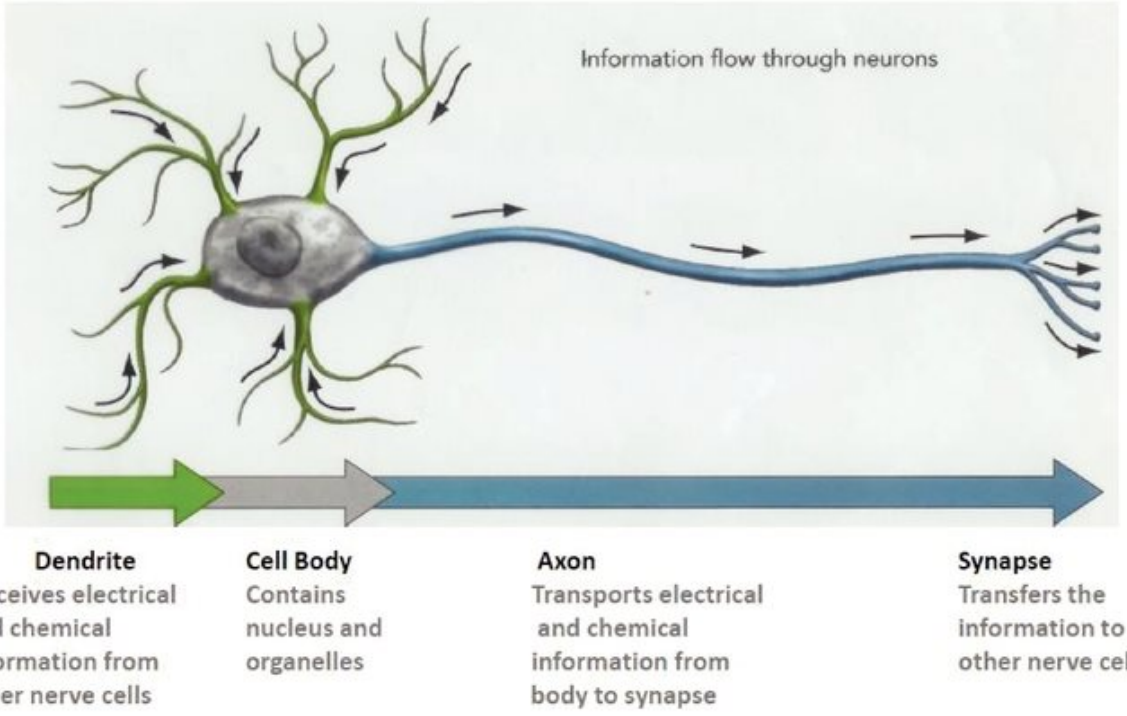
ANVS-301

We are developing our compound ANVS-301 to increase cognitive capability in later stages of AD and dementia. In preclinical studies, ANVS-301 improved memory and learning in very old rats by lowering the number of errors from six to three and shortening run times from approximately 75 to approximately 28 seconds. ANVS-301 is in a Phase 1 clinical trial that is being conducted and financed by the National Institutes of Health (NIH). The single ascending dose study is nearly complete and we, in collaboration with the NIH, are preparing to move into the multiple ascending dose study. When the single and multiple ascending dose safety studies are complete, we will review the data and decide whether to pursue the indication of advanced AD.

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

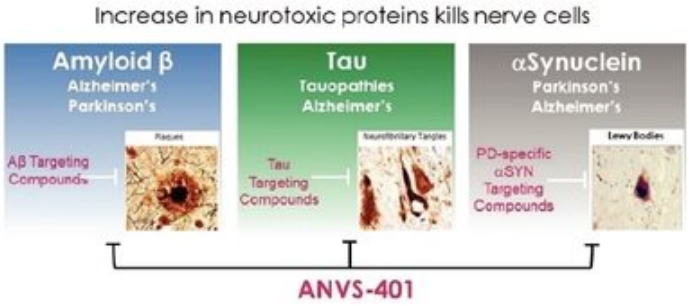


When brain cells become injured or stressed their first response is reduction and impairment of axonal transport. If the insult persists, axonal vesicle transport remains impaired resulting in decreased levels of neurotransmitters and leading to depression (serotonin), anxiety and insomnia (GABA), AD (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 preclinical pharmacokinetics analyses showing brain concentrations approximately six to eight times higher than plasma concentrations. ANVS-401 showed a mechanism of action we believe to be unique, in that it inhibited the over-translation of and, therefore, reduced the levels of several key neurotoxic proteins both *in vitro* and *in vivo*, including APP, tau and αSYN. Three Phase 1 clinical studies demonstrated that ANVS-401 was well tolerated. The third proof-of-concept study showed reduced levels of APP, tau and αSYN in the cerebrospinal fluid (CSF) of four MCI patients. Additionally, we now have preclinical data that linked lowering neurotoxic proteins to improvement of axonal transport and function. By lowering the levels of neurotoxic proteins in two AD animal models—AD transgenic (tg) mice and DS trisomic mice—ANVS-401 increased memory and learning. ANVS-401 also improved colonic motility in a PD tg mouse model of PD. See page 6.

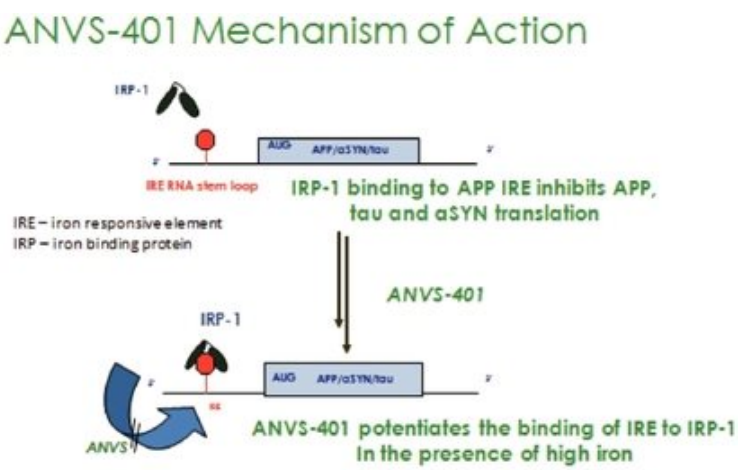
To date, all approaches that have targeted only one neurotoxic protein have failed. We believe ANVS-401 is the only drug in development that targets multiple neurotoxic proteins.



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. 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

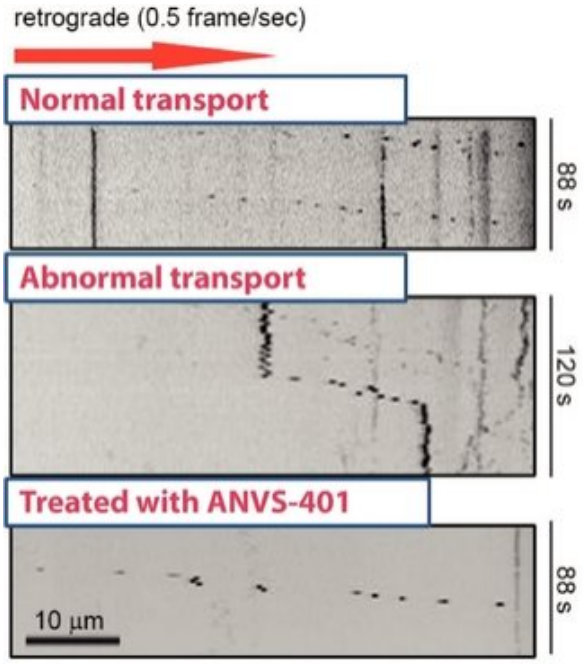
We undertook an extensive exploration of the mechanism of action of ANVS-401 on APP and αSYN synthesis and we concluded that ANVS-401 specifically inhibits translation of mRNAs coding for neurotoxic proteins only. Using five different methods we obtained overlapping results *in vitro*. mRNAs of neurotoxic 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.



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

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, discussed below, we have found that, by reducing APP, tau and αSYN levels, ANVS-401 treatment improved axonal transport and impeded the toxic cascade which leads to nerve cell death.



ANVS-401 improved 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 brain derived 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 improved and the vesicles carrying BDNF moved smoothly along the axon.

Pathway Engagement:

- Studies showed that ANVS-401 lowered levels of neurotoxic proteins and improved function:
  - AD tg mice—lowered levels of APP and its fragments and improved 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 three to four mistakes, whereas the ANVS-401 treated mice found their way with one mistake.
  - DS trisomic mice—lowered levels of APP and recovered their exploratory activity and number of entries into the maze. The trisomic mice moved 38% less and made 63% more mistakes in the maze than healthy wild-type mice. ANVS-401 increased activity and reduced mistakes of DS trisomic mice.
  - PD tg mice—lowered levels of αSYN in the brain and regulated gut motility. The PD tg mice at four months had four times slower and at seven months had seven times slower gut motility than healthy wild-type mice. ANVS-401 improved colonic motility.
  - MCI patients—in four patients, lowered levels of APP and tau statistically significantly. αSYN showed a downward trend.
- Studies showed that ANVS-401 improved retrograde and anterograde axonal transport:
  - DS trisomic mice nerve cells—in studies conducted at UCSD, inhibition 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 transport velocity of 70%. ANVS-401 also decreased the pause time by 29%. This was measured *in vitro* in isolated fully differentiated DS nerve cells.
- Studies showed that ANVS-401 increased synaptic transmission in:
  - AD tg mice—A Columbia University study showed that the AD tg mice treated with ANVS-401 had similar long-term potentiation as healthy wild-type mice, whereas long-term potentiation of the placebo treated AD tg mice was markedly reduced.
- Studies showed that ANVS-401 increased levels of neurogenesis:
  - AD tg mice brains—Two studies by the Karolinska Institute measured stem cell and nerve cell differentiation. One study found that ANVS-401 treatment increased stem cell differentiation into nerve cells by 40% in the hippocampus. The second study showed that while the data was variable and dependent on age of the mice and area of the brain, treatment with ANVS-401 improved synaptic function by modulating the maturation and plasticity of newborn neurons.
- Studies showed that ANVS-401 and/or ANVS-405 lowered inflammation in:
  - MCI patients—In a proof of concept clinical trial, four MCI patients treated with ANVS-401 showed a reduction in inflammatory factors.
  - 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. TBI rats treated with ANVS-405 had smaller microglia, showing lower inflammation.
- Studies showed that ANVS-405 protected nerve cells in:
  - TBI rats—A UCLA study stained the rat substantia nigra with a fluorescent probe. This probe, TH-immunoreactivity, binds to live cells, while dead cells do not stain. Therefore, the fluorescent signal is a surrogate marker for live cells. Rats were subjected to either TBI or to a sham, i.e., mock surgery (non-TBI rats). TBI rats treated with a placebo showed

approximately 40% less fluorescence than non-TBI rats, while TBI rats treated with ANVS-405 showed fluorescence of 100% or more as compared to non-TBI rats.

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

By lowering levels of neurotoxic proteins, ANVS-401 and ANVS-405 improved functions in all animal models we tested. These functions are: memory, learning and long-term potentiation in AD mice; memory, learning and axonal transport in DS 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 lower the CSF levels of neurotoxic proteins (at least APP, tau, and αSYN) and inflammatory markers, as previously seen in clinical and preclinical studies. In these studies, we are also planning to analyze the CSF levels for additional neurotoxic proteins, control proteins lacking the conserved mRNA sequence of neurotoxic 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. 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 conduct Phase 3 clinical studies in AD-DS and PD.

To date, we have submitted 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 Chief Financial Officer is Jeffrey McGroarty; he has extensive experience as CFO of public companies. Our Chief Medical Advisor, Jeffrey Cummings, M.D. is one of the most respected clinical Alzheimer scientists; he was previously Director of Neurology at the Cleveland Clinic. Our Chief Scientific Advisor, William Mobley, M.D., Ph.D., is one of the most respected Down Syndrome and Alzheimer's disease research scientists. He serves as executive director of UC San Diego's Down Syndrome Center for Research and Treatment and holds the Florence Riford Chair of Alzheimer's Disease Research. Our Chairman, Michael Hoffman, has extensive experience in investing in successful businesses as well as growing and leading companies.

Our scientific advisory board is composed of scientists known for their work in the area of neurodegeneration. They provide us with advice and guidance on scientific and industry matters. We believe our team, with its deep scientific background, drug development experience and industry

knowledge, 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 of ANVS-401 for the treatment of AD-DS, which is an orphan indication of AD, and to obtain regulatory approval of ANVS-401 for 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:

- ***Develop ANVS-401 through 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 and complete the study within one year.
  - Start the Phase 2a PD trial in the United States and, possibly, internationally, for the treatment of PD in the first quarter of 2020. We expect the study to be completed in one year.
  - Fully analyze both studies in early 2021.
- ***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 must first be tested for safety for six months in rats and nine months in dogs. In September 2019, we received a Notice of Award for a $1.7 million grant from the National Institute on Aging which is expected to fully cover the costs of these studies. Presently we have one month of safety studies in mice, rats and dogs, which allows us to test ANVS-401 for one month in humans.
- ***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.
- ***Pursue and obtain patent protection for our proprietary technology, inventions, improvements, platforms and our product candidates.***
  - Continue to file three families of patent applications to prolong the life of ANVS-401. In August 2019, the U.S. Patent and Trademark Office granted Patent No. US 10,383,851, the first of our patents from this family covering PD and associated diseases.
- ***Conduct a follow-on study in ANVS-405***
  - Seek a second grant from the US Army.
  - Evaluate the effect ANVS-405 administered to TBI rats at various intervals post-injury to determine how long after a TBI we can effectively treat a patient.
- ***Continue development of ANVS-301***
  - Complete single ascending dose study and move into multiple ascending dose study.
  - Seek additional funding from the NIH.

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 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 and early clinical trials may not be indicative of results obtained in later trials.

- If we are unable to obtain, maintain and defend 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	2,000,000 shares
Common stock to be outstanding after this offering	6,518,173 shares (or 6,818,173 shares if the underwriters exercise their over-allotment option in full)
Over-allotment option	300,000 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 14 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 NYSE American symbol	"ANVS"

The number of shares of our common stock to be outstanding after this offering is based on 282,614 shares of our common stock outstanding as of September 30, 2019, which excludes:

- 353,565 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2019, at a weighted-average exercise price of $0.19 per share; and
- 381,280 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 4,117,089 shares of our common stock upon the closing of this offering;
- the issuance of 118,470 shares of our common stock upon conversion of the $530,000 principal amount of our convertible promissory notes plus accrued interest as of January 31, 2020, the expected closing date 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 September 30, 2019;
- 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 125% of the initial public offering price per share or $7.50, 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 nine months ended September 30, 2019 and 2018 and the balance sheet data as of September 30, 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,		Nine Months Ended September 30,	
	2018	2017	2019	2018
			(Unaudited)	
Statement of Operations Data:				
Operating expenses:				
Research and development	$ 111.6	$ 273.4	$ 14.1	$ 98.3
General and administrative	602.3	409.0	720.6	447.6
Total operating expenses	713.9	682.4	734.7	545.9
Loss from operations	(713.9)	(682.4)	(734.7)	(545.9)
Other income (expense)	—	0.1	(55.0)	0.1
Income tax expense (benefit)	—	—	—	—
Net loss	$ (713.9)	$ (682.3)	$ (789.7)	$ (545.8)
Net loss per common share—basic and diluted(1)	$ (2.57)	$ (2.66)	$ (2.79)	$ (1.98)
Weighted average common shares outstanding—basic and diluted(1)	277,585	256,146	282,614	275,890
Pro forma net loss per common share—basic and diluted (unaudited)(2)	$ (0.16)		$ (0.18)	
Pro forma weighted average common shares outstanding (unaudited)(2)	4,394,674		4,399,703	

	As of September 30, 2019		
	Actual	Pro Forma(2)	Pro Forma As Adjusted(3)
	(Unaudited)	(Unaudited)	(Unaudited)
Balance Sheet Data:			
Cash and cash equivalents	$ 56.2	$ 56.2	$ 10,436.6
Working capital	$ (1,027.9)	$ (1,027.9)	$ 9,377.6
Total assets	$ 379.9	$ 379.9	$ 10,760.2
Convertible debt, net of unamortized deferred financing fees and debt discount	$ 498.3	$ 498.3	$ —
Redeemable convertible preferred stock	$ 7,077.0	$ —	$ —
Stockholders' equity (deficit)	$ (8,374.8)	$ (1,297.8)	$ 9,659.0

(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 4,117,089 shares of our common stock upon the closing of this offering.

(3) Reflects the effect of our issuance and sale of 2,000,000 shares of our common stock in this offering at an initial public offering price of $6.00 share, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us and the issuance of 118,470 shares of our common stock upon conversion of the $530,000 principal amount of our convertible promissory notes plus accrued interest as of January 31, 2020, the expected closing date of this offering, into shares of our common stock at a 20% discount to the public offering price.

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 $0.8 million and $0.5 million for the nine month periods ended September 30, 2019 and 2018, respectively. As of September 30, 2019, we had an accumulated deficit of $8.6 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 FDA to complete two Phase 3 trials to support a 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 September 30, 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 September 30, 2019, we had net operating loss carryforwards, or NOLs, of $4.1 million for federal income tax purposes and $4.1 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 $1.4 million generated after December 31, 2017 are not subject to expiration but are limited to 80% of taxable income in future years for federal income tax purposes. In general, under Section 382 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 Section 382 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 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 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 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 for those indications. 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 rights to the compound outright. 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 maintain patent protection for our technology licensed from Horizon 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, maintain and defend patent protection in the United States and other countries with respect to ANVS-401 and any future 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. 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.

If we are unable to obtain additional patent protection for the applications filed by Annovis to prolong the patent life of our compounds, we may not be able to continue development of our compounds.

We seek to protect and prolong our proprietary position by filing patent applications in the United States and abroad related to our development programs and product candidates. 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 and our company could cease to exist.

Annovis has filed three families 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 using ANVS-401 is limited. The first patent application family we filed, which would be expected to expire in 2031, covers the use of ANVS-401 at much lower doses and expands its use to the treatment of AD, PD and other neurodegenerative disorders such as Huntington's disease, prion diseases, amyotrophic lateral sclerosis, tauopathies and frontotemporal dementia, based on our preclinical research. In August 2019, the U.S. Patent and Trademark Office granted Patent No. US 10,383,851, the first of our Annovis patents from this family covering Parkinson's disease and Lewy body diseases. The second patent application family covers ANVS-405's use in acute brain and nerve trauma and would be expected to expire in 2036, before any patent term adjustments or extensions. The third patent application family relates to the use of the mechanism of action of ANVS-401 and ANVS-405 to prevent and treat neurodegenerative diseases and would be expected to expire in 2038, before any patent term adjustments or extensions.

While the issuance of our new patent gives us some comfort that the patent life relating to methods of using ANVS-401 may be prolonged to 2031, the fact that only a portion of the family claims has so far been allowed could result in very limited patent coverage as the patent claims issued thus far are limited to treating PD and Lewy body 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.

Our patents may be challenged in courts or in patent offices which could result in the invalidation, narrowing or unenforceability of our patents and our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

There is no assurance that all 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 during which we could market a product candidate under patent protection could be reduced.

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 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 third party infringement 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. Proceedings challenging our patents or those that we license 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 on 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 our 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 on 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 (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 provide 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. The total patent

term including the extension cannot exceed 14 years following regulatory approval. 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 or right to use. 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, disruption of our operations, damage to 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 43.6% of the voting power of our outstanding common stock, or approximately 42.1% 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 initial public offering price of $6.00 per share, you will experience immediate dilution of $4.52 per share, representing the difference between our net tangible book value per share, after giving effect to this offering, and the 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 NYSE American, 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.

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. Information that is based on estimates, forecasts, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information based on various factors, including those discussed in "Risk Factors."

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 2,000,000 shares of our common stock in this offering will be approximately $10.4 million, 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 $12.1 million, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

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 to completion of the Phase 2a PD trial of ANVS-401 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 to completion of 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 of ANVS-401 in AD-DS for the treatment of memory loss and dementia in DS;
- approximately $1.7 million to conduct the chronic toxicology studies of ANVS-401 in rats and dogs;
- approximately $0.7 million for payments under our license agreement with Horizon Therapeutics, PLC;
- the rest for general and administrative expenses, including intellectual property legal costs, research and development related to ANVS-401, ANVS-405 and ANVS-301 and to provide sufficient liquidity until we raise additional capital for the Phase 3 studies of ANVS-401 in AD-DS and PD.

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. In September 2019, we received a Notice of Award for a $1.7 million grant from the National Institute on Aging which is expected to fully cover the costs of the chronic toxicology studies of ANVS-401 in rats and dogs. We previously received a grant from the US Army to conduct the study of ANVS-405 described under Business—Preclinical Animal Studies—TBI in Rats in this Prospectus. We are in the process of writing a second grant proposal to conduct a follow-on study to evaluate the effect of ANVS-405 administered to TBI rats at various intervals post-injury to determine how long after a TBI we can effectively treat a patient. The ongoing study of ANVS-301 continues to be funded by the NIH and further development of ANVS-301 may be funded by future grants.

The 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 September 30, 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 4,117,089 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 2,000,000 shares of our common stock in this offering at an initial public offering price of $6.00 per share, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us and the issuance of 118,470 shares of our common stock upon conversion of the $530,000 principal amount of our convertible promissory notes plus accrued interest as of January 31, 2020, the expected closing date 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 September 30, 2019		
	Actual	Pro Forma	Pro Forma As Adjusted
	(in thousands, except share and per share data)		
Cash and cash equivalents	$ 56.2	$ 56.2	$ 10,436.6
Convertible debt, net of unamortized deferred financing fees and debt discount	$ 498.3	$ 498.3	$ —
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 282,614 shares issued and outstanding, actual; 35,000,000 shares authorized, pro forma and pro forma as adjusted and 4,399,703 shares issued and outstanding, pro forma and 6,518,173 shares issued and outstanding, pro forma as adjusted	$ —	$ 0.4	$ 0.7
Additional paid-in capital	201.0	7,277.5	18,234.1
Accumulated deficit	(8,575.8)	(8,575.8)	(8,575.8)
Total stockholders' equity (deficit)	$ (8,374.8)	$ (1,297.8)	$ 9,659.0
Total capitalization	$ (799.5)	$ (799.5)	$ 9,659.0

The table above does not include:

- 353,565 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2019, at a weighted-average exercise price of $0.19 per share; and

- 381,280 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.

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 September 30, 2019 was $(8.4) million, or $(29.63) 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 282,614 shares of our common stock outstanding as of September 30, 2019.

Our pro forma net tangible book value deficit as of September 30, 2019, was $(1.3) million, or $(0.29) 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 4,117,089 shares of our common stock upon the closing of this offering.

After giving further effect to our issuance and sale of 2,000,000 shares of our common stock in this offering at an initial public offering price of $6.00 per share, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us and after giving further effect to the issuance of 118,470 shares of our common stock upon conversion of the $530,000 principal amount of our convertible promissory notes plus accrued interest as of January 31, 2020 the expected closing date 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 September 30, 2019 would have been $9.7 million, or $1.48 per share. This represents an immediate increase in pro forma net tangible book value per share of $1.77 to our existing stockholders and immediate dilution in net tangible book value per share of $4.52 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 initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Initial public offering price per share		$ 6.00
Historical net tangible book value deficit per share as of September 30, 2019	$ (29.63)	
Increase per share attributable to the automatic conversion of preferred stock in connection with this offering	29.34	
Pro forma net tangible book value deficit per share as of September 30, 2019	(0.29)	
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	1.77	
Pro forma as adjusted net tangible book value per share after this offering		1.48
Dilution per share to new investors purchasing common stock in this offering		$ 4.52

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 $1.66 and dilution per share to new investors purchasing common stock in this offering would be $4.34, at an initial public offering price of $6.00 per

share, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The following table summarizes, as of September 30, 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 initial public offering price of $6.00 per share, 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	
			(in thousands)		
Existing stockholders	4,518,173	69.3%	$ 6,224.8	34.2%	$ 1.38
New investors	2,000,000	30.7	12,000.0	65.8	6.00
Total	6,518,173	100.0%	$ 18,224.8	100.0%	

The table above assumes no exercise of the underwriters' over-allotment option. If the underwriters' over-allotment option is exercised in full, upon completion of this offering, the percentage of common stock held by existing stockholders would be reduced to 66.3%, and the percentage of common stock held by new investors purchasing common stock in this offering would be increased to 33.7%.

The tables above do not include:

- 353,565 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2019, at a weighted-average exercise price of $0.19 per share; and
- 381,280 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.

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 nine months ended September 30, 2019 and 2018 and the balance sheet data as of September 30, 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,		Nine Months Ended September 30,	
	2018	2017	2019	2018
			(Unaudited)	
Statement of Operations Data:				
Operating expenses:				
Research and development	$ 111.6	$ 273.4	$ 14.1	$ 98.3
General and administrative	602.3	409.0	720.6	447.6
Total operating expenses	713.9	682.4	734.7	545.9
Loss from operations	(713.9)	(682.4)	(734.7)	(545.9)
Other income (expense)	—	0.1	(55.0)	0.1
Net loss	$ (713.9)	$ (682.3)	$ (789.7)	$ (545.8)
Net loss per common share—basic and diluted(1)	$ (2.57)	$ (2.66)	$ (2.79)	$ (1.98)
Weighted average common shares outstanding—basic and diluted(1)	277,585	256,146	282,614	275,890
Pro forma net loss per common share—basic and diluted (unaudited) (2)	$ (0.16)		$ (0.18)	
Pro forma weighted average common shares outstanding—basic and diluted (unaudited)(2)	4,394,674		4,399,703	

(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 4,117,089 shares of our common stock upon the closing of this offering. Does not include the issuance of 118,470 shares of our common stock upon conversion of the $530,000 principal amount of our convertible promissory notes plus accrued interest as of January 31, 2020, the expected closing date of this offering, into shares of our common stock at a 20% discount to the public offering price.

(in thousands)	As of September 30, 2019 (Unaudited)
Balance Sheet Data:	
Cash	$ 56.2
Working capital(1)	(1,027.9)
Total assets	379.9
Convertible debt, net of unamortized deferred financing fees and debt discount	498.3
Redeemable convertible preferred stock	7,077.0
Stockholders' equity (deficit)	(8,374.8)

(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 addressing neurodegeneration such as Alzheimer's disease in Down Syndrome (AD-DS), Alzheimer's disease (AD), Parkinson's disease (PD). 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—amyloid precursor protein APP/Aβ (APP), tau/phospho-tau (tau) and α-Synuclein (αSYN)—thereby improving axonal transport. Human studies in four MCI patients have shown that ANVS-401 lowered the levels of neurotoxic proteins and inflammatory factors. In preclinical studies, lower neurotoxic protein levels led to improved axonal transport, reduced inflammation, lower nerve cell death and improved function.

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 condition. 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 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 preclinical pharmacokinetics analyses showing brain concentrations approximately six to eight times higher than plasma concentrations. ANVS-401 has a mechanism of action that we believe to be unique, in that it inhibited the over-translation of and, therefore, reduced the levels of several neurotoxic proteins both *in vitro* and *in vivo* including APP, tau and αSYN.

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 ADCS 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 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. If we are able to show 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 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 nine months ended September 30, 2019 and 2018 were $789,724 and $545,820, respectively, and our accumulated deficit at September 30, 2019 was $8,575,772. 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 candidates. 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 125,701 options with exercise prices of $0.14 per share. During the year ended December 31, 2017, we issued an additional 154,754 options with exercise prices of $0.14 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 $0.36 per share. We used the Option Pricing Model (OPM) Backsolve method utilizing the Series A preferred stock price of $0.50 per share, which equates to a conversion price to common stock of $0.70 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 123,800 options with exercise prices of $0.25 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 $0.85 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, which equates to a conversion price to common stock of $1.26 per share.

Results of Operations

Operating expenses were comprised of the following:

	Year Ended December 31,		Nine Months Ended September 30,	
	2018	2017	2019	2018
			(Unaudited)	
Research and development	$ 111,608	$ 273,370	$ 14,074	$ 98,319
General and administrative	602,329	409,063	720,586	447,562
	$ 713,937	$ 682,433	$ 734,660	$ 545,881

Years Ended December 31, 2018 and 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.

Nine Months Ended September 30, 2019 and 2018

Research and Development Expenses

Research and development expenses decreased by $84,245, or 86%, to $14,074 for the nine months ended September 30, 2019 from $98,319 for the nine months ended September 30, 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 $273,024, or 61%, to $720,586 for the nine months ended September 30, 2019 from $447,562 for the nine months ended September 30, 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 September 30, 2019, our principal source of liquidity was our cash, which totaled $56,250.

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 nine months ended September 30, 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 candidates and seek marketing approval and, subject to obtaining such approval, the eventual commercialization of our product candidates. If we obtain marketing approval for our product candidates, 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 candidates;
- the clinical development plans we establish for our product candidates;
- 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,		Nine Months Ended September 30,	
	2018	2017	2019	2018
			(Unaudited)	
Statement of Cash Flows Data:				
Total net cash provided by (used in):				
Operating activities	$ (558,609)	$ (537,481)	$ (424,014)	$ (482,449)
Financing activities	246,449	332,495	444,952	246,449
Increase (decrease) in cash and cash equivalents	$ (312,160)	$ (204,986)	$ 20,938	$ (236,000)

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 14,286 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 50,131 shares of our common stock.

Nine Months Ended September 30, 2019 and 2018

Operating Activities

For the nine months ended September 30, 2019, cash used in operations was $424,014 compared to $482,449 for the nine months ended September 30, 2018. The decrease in cash used in operations was primarily the result of an increase in accounts payable and accrued expense balances.

Financing Activities

Cash provided by financing activities was $444,952 for the nine months ended September 30, 2019, attributable to the $530,000 proceeds from the sale of convertible promissory notes partially offset by the payment of $76,747 of deferred offering costs and $8,301 of fees on the issuance of the convertible promissory notes. Cash provided by financing activities was $246,449 for the nine months ended September 30, 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 14,286 shares of our common 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 did 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 did not have an impact on our 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 elected to apply the provisions of this ASU in our 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
Chief Medical Advisor

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 several studies, ANVS-401 inhibited the synthesis of neurotoxic proteins—APP/Aβ (APP), tau/phospho-tau (tau) and α-Synuclein (αSYN)—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, we have shown in four mildly cognitive impaired (MCI) patients that ANVS-401 lowered the levels of neurotoxic proteins and inflammatory factors. In preclinical studies, lower neurotoxic protein levels led to improved axonal transport, reduced inflammation, lower nerve cell death and improved function.

The industry has encountered challenges in targeting specifically one or the other neurotoxic protein, be it APP, tau or αSYN, 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 improving axonal transport 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 four 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: in all four patients, ANVS-401 reduced the levels of APP, tau and αSYN (αSYN is an unpublished, not statistically significant observation) and lowered inflammatory factors.

We are presently conducting a Phase 2a study in AD patients in collaboration with the Alzheimer Disease Cooperative Study (ADCS) 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 AD 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 eight early to moderate AD patients. Under an agreement with UC San Diego, where ADCS is located, we have contracted 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. This means that we are proposing to measure as many factors as possible associated with the toxic cascade precipitated by impaired axonal transport. If we are able to show 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 that 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, because in DS the APP gene is triplicated, leading to early onset AD with similar pathology as sporadic AD. In our animal studies in DS mice, lowering their high levels of APP improved axonal transport in the brain and increased memory and learning as described on page 89. In accordance with this animal data, we expect that lowering levels of APP, tau and αSYN in DS human patients will lead to an improvement in their memory, cognition and dementia. Conducting the study in AD-DS patients instead of AD patients 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 one or two new drug applications (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 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 Aβ to date have failed, but since Aβ 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.

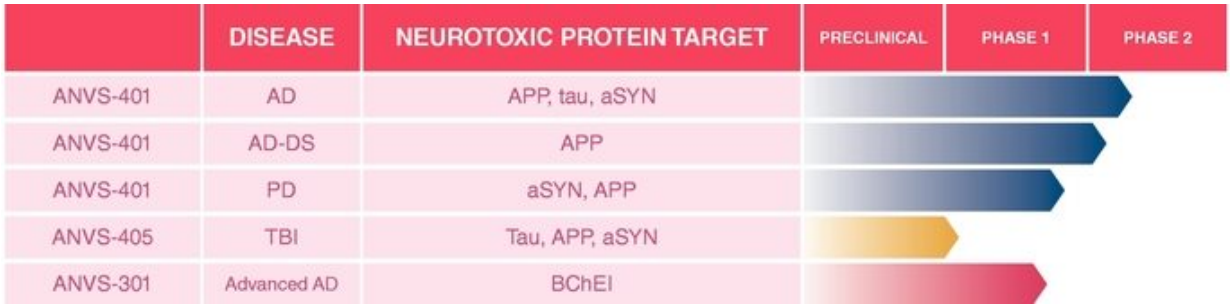
Why have all DMD approaches failed to date? In 1906 Alois Alzheimer opened the brain of a woman that had died with severe dementia and he found plaques, tangles and brain shrinkage. He called the condition Alzheimer's disease. Today we are still calling this condition AD. However, what Alois Alzheimer 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 consists of ANVS-401 for chronic neurodegeneration—including AD, its orphan indication AD-DS and PD, ANVS-405 to treat acute neurodegeneration—traumatic brain injury (TBI) and stroke—and ANVS-301 for advanced AD.



ANVS-401

Our lead compound, ANVS-401 is an orally administered drug being developed for chronic indications such as AD-DS, AD and PD, because in preclinical studies it improved axonal transport in these diseases by inhibiting the overproduction of 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. ANVS-405 is the same compound as ANVS-401 but it is given intravenously in cases of acute head and brain trauma. ANVS-405 was given to rats as an injectable after TBI to ensure that it would reach the brain in less than 15 minutes rather than 1.5 hours. TBI rats that were treated with ANVS-405 after the insult exhibited enhanced memory and learning and lower microglia activation, a measure of inflammation. To date the program has been funded by a grant from the US Army and we plan to seek additional grant funding to further the development of ANVS-405 for acute indications of brain and nerve trauma. We plan to conduct a follow-on study to evaluate the effect of ANVS-405 administered to TBI rats at various intervals post-injury to determine how long after a TBI we can effectively treat a patient. We would then seek further funding to conduct the toxicology and pharmacokinetics (PK) studies in animals, file the initial new drug application (IND), conduct the safety and PK studies in humans and continue with Phase 2 and Phase 3 efficacy studies.

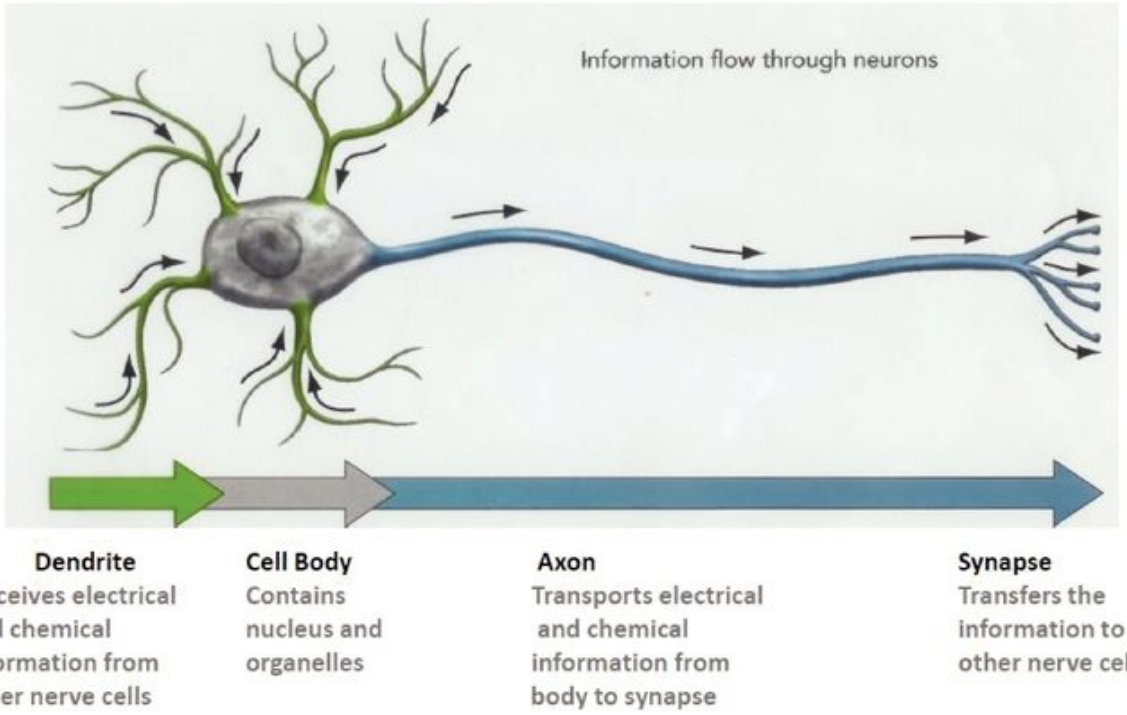
ANVS-301

We are developing our compound ANVS-301 to increase cognitive capability in later stages of AD and dementia. ANVS-301 improved memory and learning in very old rats by lowering the number of errors from six to three and shortening run times from approximately 75 to approximately 28 seconds. ANVS-301 is in a Phase 1 clinical trial that is being conducted and financed by the National Institutes of Health (NIH). The single ascending dose study is nearly complete and we, in collaboration with the NIH, are preparing to move into the multiple ascending dose study. When the single and multiple ascending dose safety studies are complete, we will review the data and decide whether to pursue the indication of advanced AD.

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 preclinical pharmacokinetics analyses showing brain concentrations approximately six to eight times higher than plasma concentrations. In different studies we found slightly different ratios because of the time of measurement after administration; on average brain levels are approximately six to eight times higher than plasma concentrations. ANVS-401 showed a mechanism of action we believe to be unique, in that it inhibited the over-translation of and, therefore, reduced the levels of several key neurotoxic proteins both *in vitro* and *in vivo*, including APP, tau and αSYN. Three Phase 1 clinical studies demonstrated that ANVS-401 was well tolerated. The third proof-of-concept study showed that it also reduced levels of APP, tau and αSYN (αSYN is an unpublished, not stastically significant observation) in the cerebrospinal fluid (CSF) of four MCI patients. Additionally, we now have preclinical data that linked the lowering of neurotoxic proteins to axonal transport improvement and restoration of function. By lowering the levels of neurotoxic proteins in AD transgenic (tg) and DS trisomic mice models, ANVS-401 increased memory and learning. ANVS-401 also improved colonic motility in a PD tg mouse model of PD. See pages 89-90.

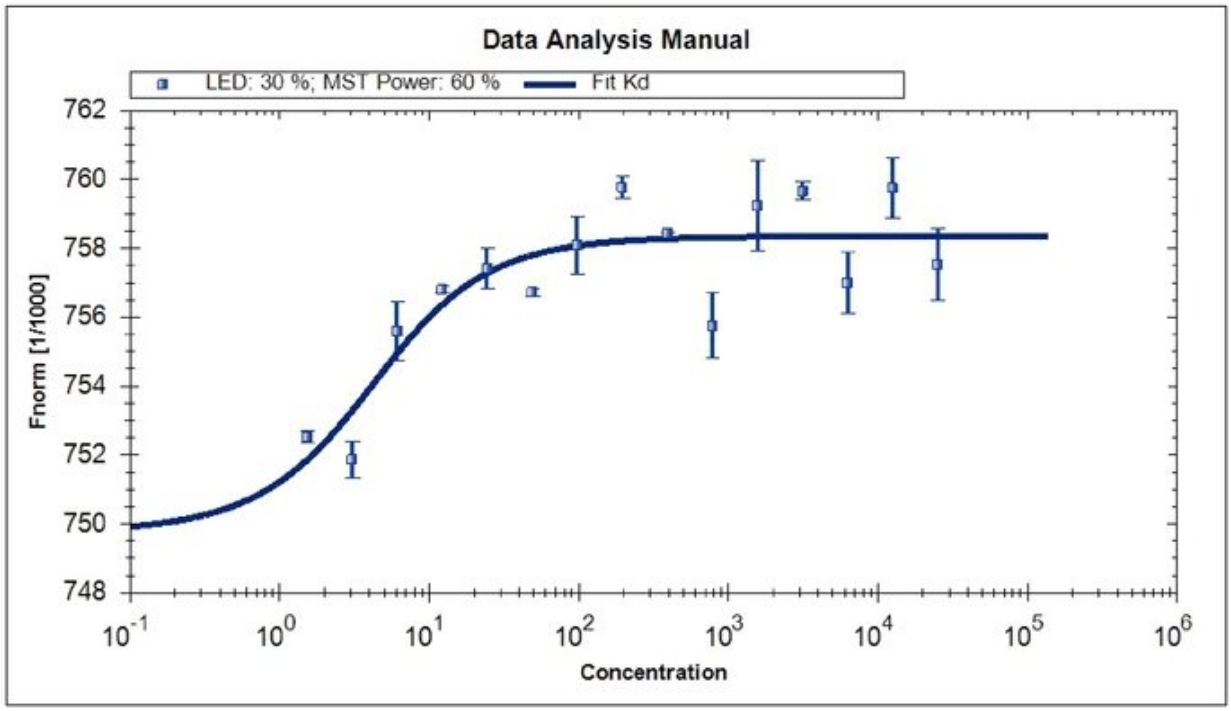
By targeting multiple neurotoxic proteins, ANVS-401 resembles a combination therapy approach, with the added convenience of being a single drug with a single drug target. Therefore, we have worked to understand how ANVS-401 is able to inhibit the translation of more than one neurotoxic protein.

Novel Mechanism of Action and Target Engagement

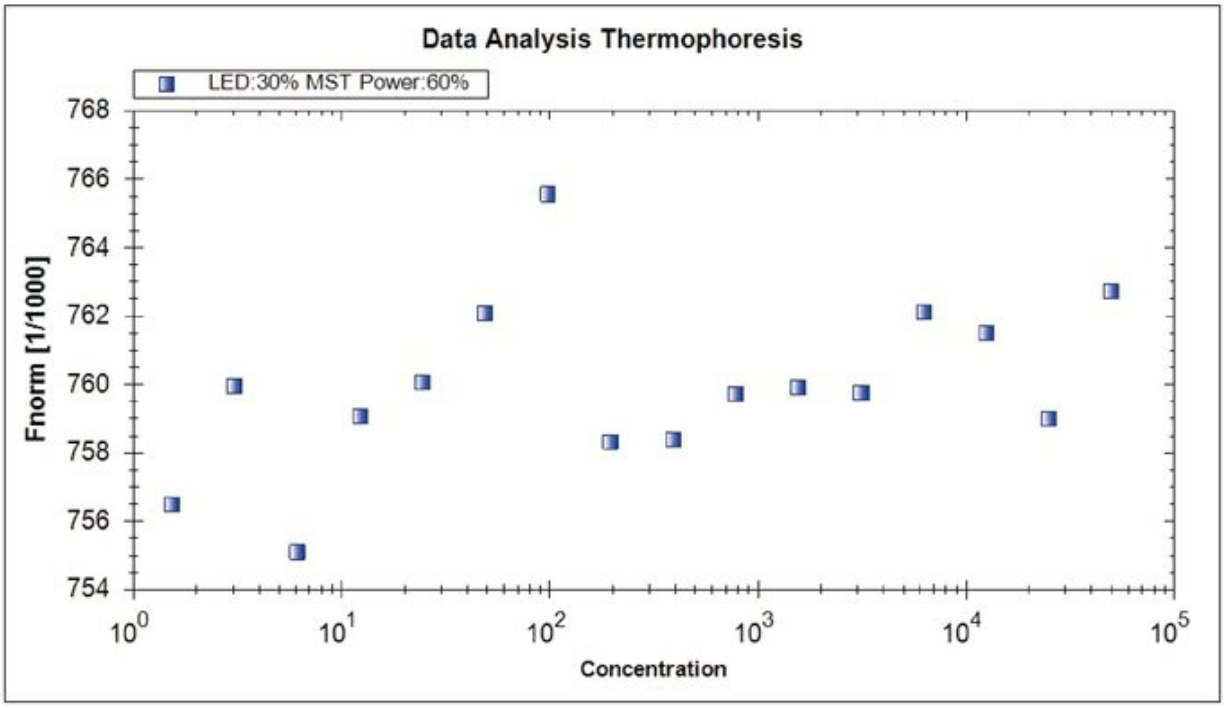
We undertook an extensive exploration of the mechanism of action of ANVS-401 on APP and αSYN synthesis and we concluded that ANVS-401 specifically inhibits translation of mRNAs coding for neurotoxic proteins only. Using 5 different methods we obtained overlapping results *in vitro*. mRNAs of neurotoxic 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 these *in vitro* studies, ANVS-401 specifically bound to the IRE/IRP1 complex of mRNAs coding for neurotoxic proteins and inhibited 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 ferroportin or other protein mRNAs.



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

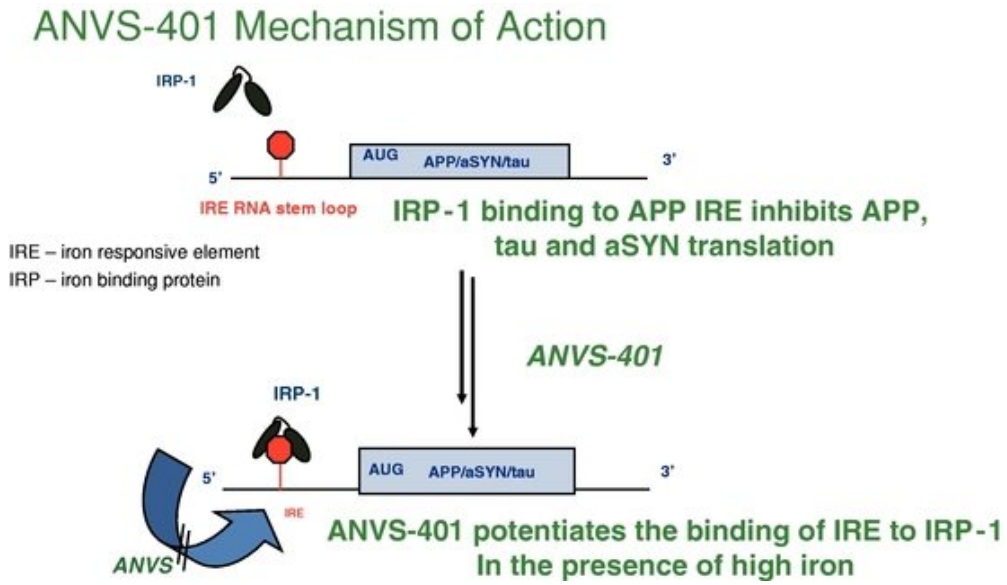


Ferritin IRE/IRP1/ANVS-401 no Kd

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

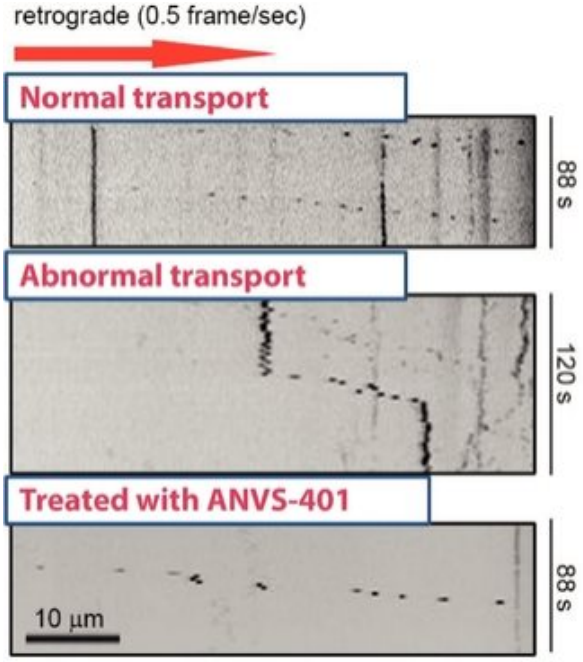
Since the 5' UTR IRE is highly conserved among the mRNAs of neurotoxic proteins, we believe ANVS-401 can inhibit the translation of several neurotoxic proteins by having just one binding site and by increasing the binding of that conserved IRE to IRP1 under high iron conditions (see graph below). We have data showing that homologous IRE type II loops are also present in the 5'UTR of mRNAs that code for APP and αSYN as well as for other neurotoxic proteins: tau, Prion protein (PrP) and huntingtin (Htt). Furthermore, we have binding data confirming the interaction of IRP1 with the IREs from human APP, αSYN, tau, PrP and Htt (not shown). Finally, our data shows that ANVS-401 only increases the binding of IREs of neurotoxic 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).

As discussed above, 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 mRNAs under high iron conditions.



Axonal Transport and Pathway Engagement

APP, tau, and αSYN impair axonal transport and synaptic transmission, causing inflammation, forming aggregates, and, finally, leading to nerve cell death. Through several studies, discussed below, we have found that, by reducing APP, tau and αSYN levels, ANVS-401 treatment improved axonal transport and impeded the toxic cascade which leads to nerve cell death.



ANVS-401 improved 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 brain derived 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 improved and the vesicles carrying BDNF moved smoothly along the axon.

ANVS-401 is being developed for chronic indications as an oral administered drug. ANVS-405 is the same compound as ANVS-401, but it is given intravenously in cases of acute head and brain trauma. Both modes of administration have shown in animal studies that they lower neurotoxic proteins and inflammation. The difference between ANVS-401 and 405 is not in their mode of action or activity, but in their mode of administration, kinetics and dose. Our pharmacokinetic studies show that in rats,

injectable ANVS-405 enters the brain in less than 15 minutes, while oral ANVS-401 takes approximately 1.5 hours. Our dosing studies in rats show that the dose of injectable form is about seven times lower than the oral form. Accordingly, we expect their toxicology profiles to be different, with ANVS-405 very likely showing adverse events at much lower doses than ANVS-401. ANVS-401 has been tested in mouse, rat and dog toxicology studies as well as in human safety studies for one month. ANVS-405 was given to rats as an injectable, but for humans it first needs to be formulated into an injectable and the safety must be established in two animal species and in humans before we can study it in human TBI or stroke patients.

Pathway Engagement:

- Studies showed that ANVS-401 lowered levels of neurotoxic proteins and improved function:
  - AD tg mice—lowered levels of APP and its fragments and improved 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 three to four mistakes, whereas the ANVS-401 treated mice found their way with one mistake.
  - DS trisomic mice—lowered levels of APP and recovered memory and learning. The trisomic mice moved 38% less and made 63% more mistakes in the maze than healthy wild-type mice. ANVS-401 increased activity and reduced mistakes of DS trisomic mice.
  - PD tg mice—lowered levels of αSYN in the brain and gut and regulated gut motility. The PD tg mice at four months had four times slower and at seven months had seven times slower gut motility than healthy wild-type mice. ANVS-401 improved colonic motility.
  - MCI patients—in four patients, lowered levels of APP and tau stastically significantly. αSYN showed a downward trend.
- Studies showed that ANVS-401 improved retrograde and anterograde axonal transport:
  - DS trisomic mice nerve cells—in studies conducted at UCSD, inhibition 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 transport velocity of 70%. ANVS-401 also decreased the pause time by 29%. This was measured *in vitro* in isolated fully differentiated DS nerve cells.
- Studies showed that ANVS-401 increased synaptic transmission in:
  - AD tg mice—A Columbia University study showed that the AD tg mice treated with ANVS-401 had similar long-term potentiation as healthy wild-type mice, whereas long-term potentiation of the placebo treated AD tg mice was markedly reduced.
- Studies showed that ANVS-401 increased levels of neurogenesis:
  - AD tg mice brains—Two studies by the Karolinska Institute measured stem cell and nerve cell differentiation. One study found that ANVS-401 treatment increased stem cell differentiation into nerve cells by 40% in the hippocampus. The second study showed that while the data was variable and dependent on age of the mice and area of the brain, treatment with ANVS-401 improved synaptic function by modulating the maturation and plasticity of newborn neurons.
- Studies showed that ANVS-401 and/or ANVS-405 lowered inflammation in:
  - MCI patients—In a proof of concept clinical trial, all four MCI patients treated with ANVS-401 showed a reduction in inflammatory factors.
  - TBI rats—rats with traumatic brain injury had much larger microglia than normal rats. Enlarged microglia means that the microglia are activated and shows inflammation. TBI rats treated with ANVS-405 had smaller microglia, showing lower inflammation.

- Studies showed that ANVS-405 protected nerve cells in:

  - TBI rats—A UCLA study stained the rat substantia nigra with a fluorescent probe. This probe, TH-immunoreactivity, binds to live cells, while dead cells do not stain. Therefore, the fluorescent signal is a surrogate marker for live cells. Rats were subjected to either TBI or to a sham, i.e., mock surgery (non-TBI rats). TBI rats treated with a placebo showed approximately 40% less fluorescence than non-TBI rats, while TBI rats treated with ANVS-405 showed fluorescence of 100% or more as compared to non-TBI rats.

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

By lowering levels of neurotoxic proteins, ANVS-401 and ANVS-405 improved functions in all animal models we tested. These functions are: memory, learning and long-term potentiation in AD mice; memory, learning and axonal transport in DS 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 lower the CSF levels of neurotoxic proteins (at least APP, tau, and αSYN) and inflammatory markers, as previously seen in clinical and preclinical studies. In these studies, we are also planning to analyze the CSF levels for additional neurotoxic proteins, control proteins lacking the conserved mRNA sequence of neurotoxic 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 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.

Dr. Greig also synthesized a group of analogs that had no acetylcholinesterase activity, which were of no importance to him at that time. 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, both those with and without AChEI activity. 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 licensed them to Axonyx Inc. He published extensively and patented his inventions.

Axonyx Inc. conducted preclinical toxicology studies 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 IND with the FDA. In 2006 phenserine failed and Axonyx merged with TorreyPines Therapeutics, Inc., which merged with Raptor

Pharmaceuticals, Inc. in 2009. 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/Aβ, tau/p-tau and αSYN and protect nerve cells from dying. They are expected to be DMDs and change the course of neurodegeneration.

The toxicology studies which were completed in mice, rats and dogs lasted 30 days. With 30 days of animal safety data we can treat humans, whether healthy volunteers or patients for 30 days. For us to conduct a two-year clinical study, the FDA requires the completion of two animal toxicology studies—a six-month study in rats and a nine-month study in dogs. The successful completion of those toxicology studies is a prerequisite for us to start our planned Phase 3 studies in AD-DS and PD.

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 doses of 80 mg once a day or 60 mg four times a day. 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 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 72 healthy volunteers including placebo**
  - Drug determined to be well-tolerated, with no AEs at 80 mg with a maximum tolerated dose (MTD) of 160 mg
  - Dose limiting toxicity was nausea
- **Multiple ascending doses (MAD) in 48 healthy volunteers including placebo**
  - Drug determined to be well-tolerated with no AEs and no symptoms indicative of inhibition of either acetyl- or butyryl cholinesterase at doses up to 240 mg/day (60 mg four times a day)
- **Proof of Concept (POC) in four MCI patients**
  - Concentrations of ANVS-401 in the brain, extrapolated from blood and CSF, were eight times higher than in plasma
  - ANVS-401 lowered CSF levels of neurotoxic proteins and inflammatory markers. See pages 94 and 95.

In the four MCI patients, ANVS-401 had a half-life of five hours in plasma and more than 12 hours in CSF. The longer 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. T_{max} was 1.3–1.6 hours post dose, independent of dose and comparable for both sexes in plasma and CSF. ANVS-401 is stable, orally available and enters the brain, therefore we are developing it as an oral drug candidate.

Summary of Safety in Humans

ANVS-401's pattern of AEs was similar to that seen in typical studies in healthy 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 (one placebo and one 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, four patients with MCI were treated for 10 days with ANVS-401 with a dose of 60 mg four times a day (240 mg/day), which we knew from our MAD study to be a well tolerated level. CSF and plasma were drawn over 12 hours on Day 0 before any administration of ANVS-401 and on Day 11 after the last administration of ANVS-401. During each 12-hour period, a total of nine CSF samples were taken and levels of ANVS-401 and metabolites were measured in plasma and CSF at all time points.

Pharmacokinetics

ANVS-401 pharmacokinetics (PK) in plasma corresponded to what we had seen in the previous clinical safety studies: a half-life of five hours. In CSF, however, ANVS-401 showed a much longer half-life of over 12 hours. We 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, we were 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 we have in mice, where in several studies, ANVS-401 levels were found to be approximately six to eight 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 αSYN for the whole period tested (12 hours). The extended effect of ANVS-401 in the four human patients 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 four times a day were far in excess of levels we believe are required to down-regulate APP and αSYN. The doses of ANVS-401 needed to lower the levels of neurotoxic proteins are similar for the toxic proteins, suggesting similar dosing in AD, AD-DS and PD. We further compared ANVS-401 brain levels of mice that showed improved memory, learning and colonic motility and calculated that the optimum brain levels measured were between 150 and 500 nM. Using three different extrapolation/comparison calculations we calculated that a daily dose of 5mg to 60 mg should achieve potentially desired brain levels in humans.

Pharmacodynamics

ANVS-401 pharmacodynamics was performed on the same 18 CSF samples taken from each person as above. Since we had data for four patients with 18 time points each, it was possible to conduct statistical analysis of the data using a repeated measure mixed model analysis of variance. The p-value represents the probability that the difference between compared groups is due to chance rather than drug effect, and when that probability is less than 5%, or $p<0.05$, the result is considered statistically significant. FDA evidentiary standards for drug approval require that the trial design must permit a valid comparison with a control group to permit a quantitative assessment of the effect of the drug, which may include demonstration of statistical significance.

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

	LAB 1		LAB 2	
Human Biomarker	**CSF % of Baseline**	**p-Value**	**CSF % of Baseline**	**p-Value**
sAPP α	–59.9%	0.0006	–34.1%	0.0661
sAPP β	–57.7%	0.0001	–34.0%	0.0901
Aβ42	–51.4%	0.0533	–45.2%	0.0995
Tau	–46.2%	0.0020	–74.1%	0.0150
p-Tau	–61.0%	0.0005		
αSYN	–41.2%	0.0910*		

* Represents unpublished results.

MCI patients showed high levels of sAPP, tau and αSYN in their CSF. They were treated for 10 days with ANVS-401 and their CSF was analyzed for neurotoxic proteins. In all four patients, the levels of neurotoxic proteins decreased. The percentages shown in the table were calculated using all nine time points after treatment compared to all nine time points prior to treatment. Due to the variability in the CSF measurements of sAPPα, sAPPβ, Aβ42 and tau, we had all samples analyzed by two different laboratories using different methodologies.

Inflammation

The same CSF samples were also analyzed for inflammatory factors and microglia activation factors as well as a control factor. All patients reacted by lowering their levels of inflammatory markers and not lowering the level of the control protein.

The statistical analysis again was performed with a repeated measure mixed model analysis of variance. Three inflammatory markers were lowered to a statistically significant level: Complement C3, MCP-1 and YKL-40. The fourth inflammatory marker, sCD14, showed a downward trend. We also measured Factor FH, a complement regulatory protein involved in blood clotting, which served as our control factor. As we had expected, Factor FH was not downregulated by ANVS-401.

CSF INFLAMMATORY MARKERS AFTER 10 DAYS OF ORAL ANVS-401 IN FOUR MCI PATIENTS

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 showed high levels of inflammatory factors and microglia activation factors in their CSF. ANVS-401 statistically significantly lowered the levels of three inflammatory markers in all four patients.

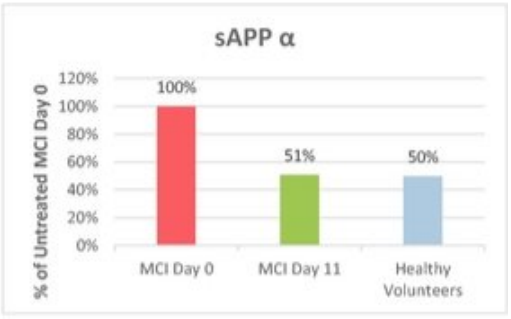
Comparison with Healthy Volunteers

We then compared the levels found in four healthy volunteers with the levels seen in the four MCI patients before and after 10 days of ANVS-401 administration. The heathy volunteers did not go through the entire study as did the MCI patients. They gave one CSF sample taken by lumbar puncture in the morning and that sample was only used to measure sAPPα, sAPPβ and tau.

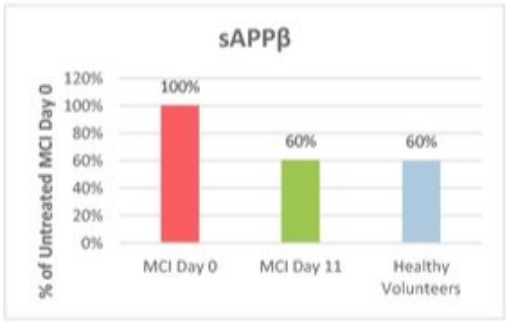
In order to make the comparison as accurate as possible, we used a single measurement from the same time point in each of the mornings of Day 0 and Day 11 for each MCI patient because this was similar to the timing for the healthy volunteers. In this very limited comparison we were able to show that all four patients experienced a decrease in sAPPα, sAPPβ and tau. These reductions brought the average levels of sAPPα, sAPPβ and tau in the treated MCI patients close to the average levels we measured in healthy volunteers.

LEVELS OF NEUROTOXIC PROTEINS IN FOUR MCI PATIENTS COMPARED TO FOUR HEALTHY VOLUNTEERS

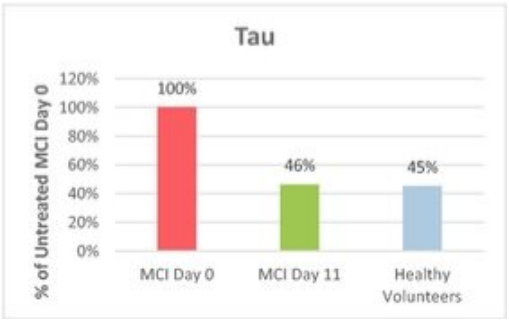
sAPPα					
MCI Patients				Healthy Volunteers	
ID	Day 0	Day 11	Decrease	ID	Single Sample
A	8,089	5,096	37%	1	4,450
B	11,517	5,700	51%	2	6,553
C	16,861	7,409	56%	3	6,876
D	11,137	6,093	46%	4	5,912
Avg.	11,901	6,075	49%		5,948



sAPPβ					
MCI Patients				Healthy Volunteers	
ID	Day 0	Day 11	Decrease	ID	Single Sample
A	1,125	569	49%	1	502
B	1,009	573	43%	2	575
C	1,090	673	38%	3	517
D	1,012	747	26%	4	946
Avg.	1,059	641	40%		635



Tau					
MCI Patients				Healthy Volunteers	
ID	Day 0	Day 11	Decrease	ID	Single Sample
A	689	400	42%	1	305
B	794	266	66%	2	363
C	663	255	62%	3	308
D	626	361	42%	4	279
Avg.	693	321	54%		314



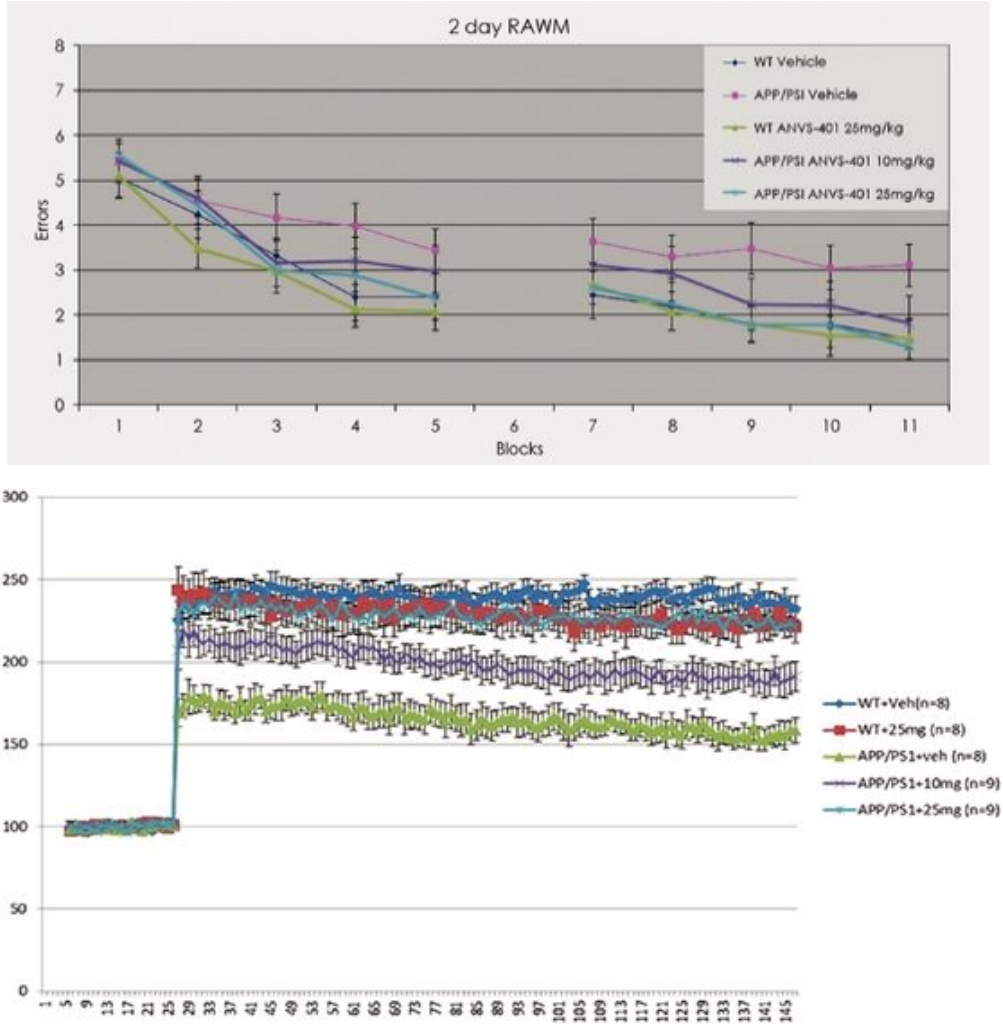
The tables above show the CSF levels of sAPPα, sAPPβ and tau in the four MCI patients and the four healthy volunteers. The percentages in the bar diagrams are derived from each of the tables, with red representing average of MCI patients at Day 0 before ANVS-401 treatment; green representing average of MCI patients at day 11 after 10 days of ANVS-401 treatment; and blue representing average of untreated healthy volunteers. The average of MCI patients at Day 0 was considered the base at 100%. We then calculated the averages of MCI patients at Day 11 and the healthy volunteers as a percentage of the base.

Preclinical Animal Studies

By inhibiting the overexpression of neurotoxic proteins, ANVS-401 improved or prevented the symptoms associated with chronic as well as acute neurodegeneration in several animal models. The data most relevant to the present application are shown.

APP/PS1 tg Mouse Model of AD

ANVS-401 improved spatial-working memory as shown in a 2-day radial arm water maze test in this mouse AD model at a 25 mg/kg oral dose (p=0.0033, figure below-top) and showed a dose response at 10 mg/kg oral dose. In the same study ANVS-401 improved synaptic function and long-term potentiation in hippocampal slices at both doses in a dose-dependent fashion (figure below-bottom). ANVS-401 treatment did not affect wild-type (WT) mice.

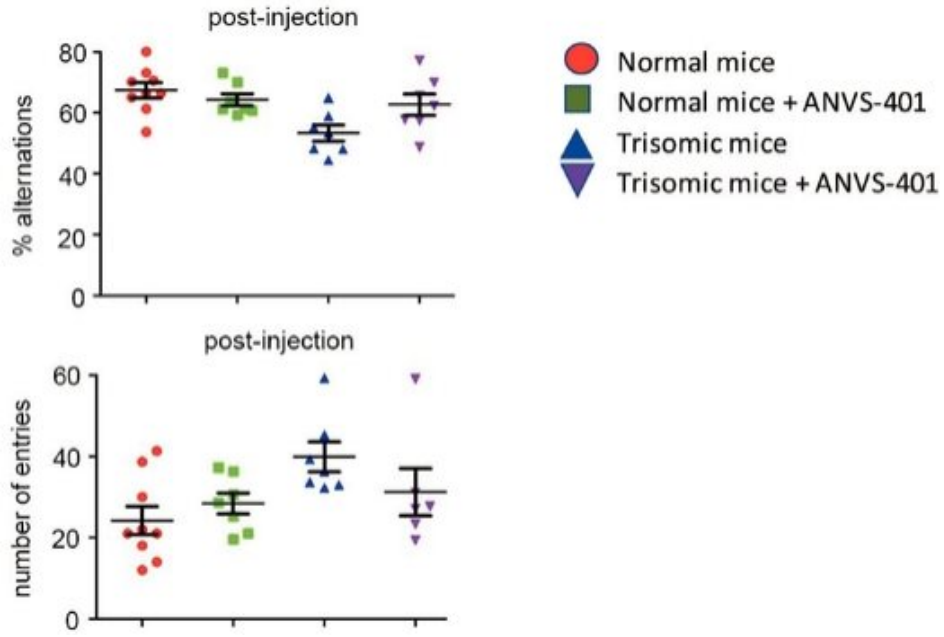


APP/PS1 AD tg mice were treated for one month with ANVS-401, before the behavioral evaluation. 2-day radial arm water maze test results are shown on the top, and electrophysiology (extracellularly recorded field excitatory postsynaptic potentials – fEPSP) between Shaffer collateral and pyramidal neurons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

Trisomic Mouse Model of AD-DS

DS trisomic mice display several abnormal behaviors reminiscent of AD, including memory loss. They have elevated levels of APP that has been shown in mice to contribute to deficient memory and learning, cognitive impairment as well as dementia. DS trisomic mice are used as a model for AD, because they exhibit similar deficits as seen in AD. Thus, we considered whether ANVS-401 could re-establish healthy behavior in these mice like that seen in wild-type mice. We measured the rate of

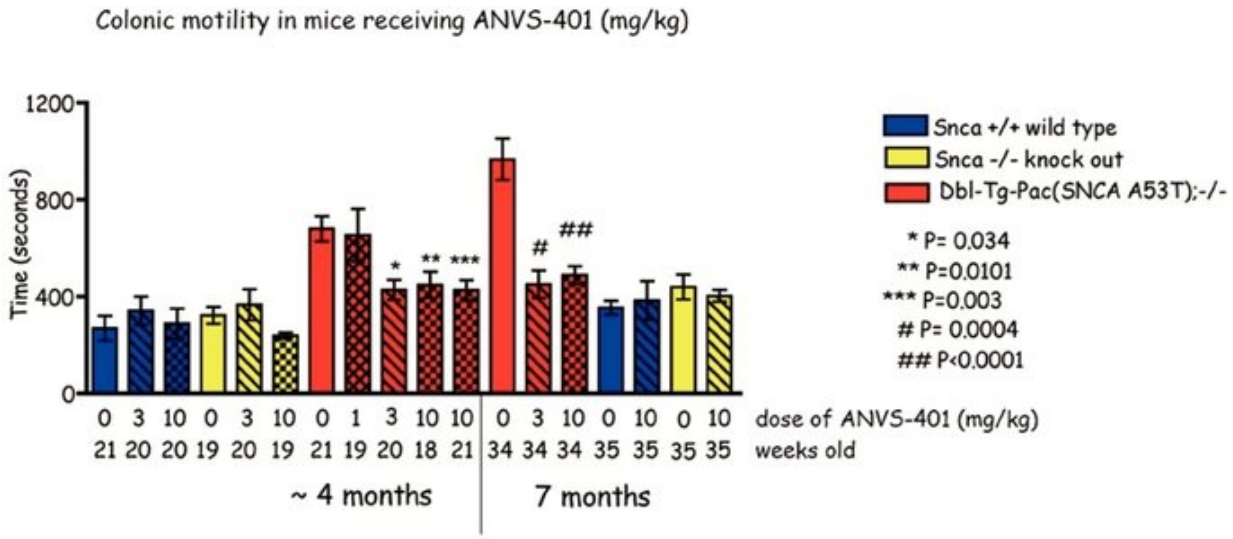
spontaneous alternations in a Y-maze and found that the alternation rate is significantly lower in DS trisomic mice versus wild-type mice reflecting impaired working memory. While ANVS-401 treatment increased alternation rate in DS trisomic mice it had no obvious effects in wild-type mice. We also found an effect on the exploratory activity reflected by the number of arm entries, again reflecting impaired working memory. All DS trisomic mice treated with ANVS-401 displayed improved working memory to a variable extent.



DS trisomic mice were tested for correct alternations into a Y-maze and they made 38% less alternations (p=0.005), left above. At the same time, they made 63% more entries into the maze (p=0.01), left, than wild-type mice. ANVS-401 treatment improved working memory deficit in DS trisomic mice. Mobley Laboratory, UCSD, manuscript in preparation.

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

We used these PD tg mice as models of early gastrointestinal dysfunction, which is common in PD patients and precedes the onset of motor symptoms by many years to decades. Untreated PD tg mice resemble pre-Parkinson's patients, showing symptoms of constipation by three months of age. Here we assessed the colonic motility by measuring the time required to expel a glass bead inserted into the colon at four and seven months of age. ANVS-401 statistically significantly (p=0.034 at four months and p=0.0001 at seven months) decreased the bead expulsion time between ANVS-401 treated and placebo treated mice; thus, it improved the colonic motility of PD tg mice (figure below). Furthermore, even after we stopped treatment for nine 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.



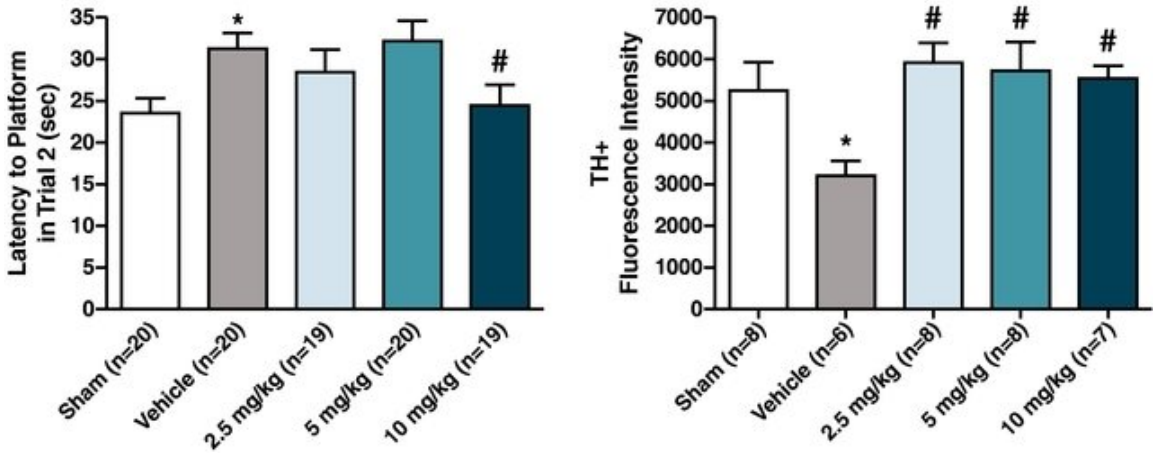
$SNCA^{A53T}$ and $SNCA^{A30P}$ mice (producing human mutant αSYN associated with familial PD) were treated intraperitoneally with vehicle or ANVS-401 beginning at six weeks up to seven months of age. ANVS-401 prevented the impaired gut motility of the $SNCA^{A53T}$ and $SNCA^{A30P}$ mice at 3 and 10 mg/kg. Older mice demonstrate a more severe phenotype that nonetheless responded 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. Several studies have analyzed changes in the brain after TBI and identified up-regulation of neurotoxic proteins, such as APP, tau, and αSYN.

Annovis received a $1.5 million grant 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.

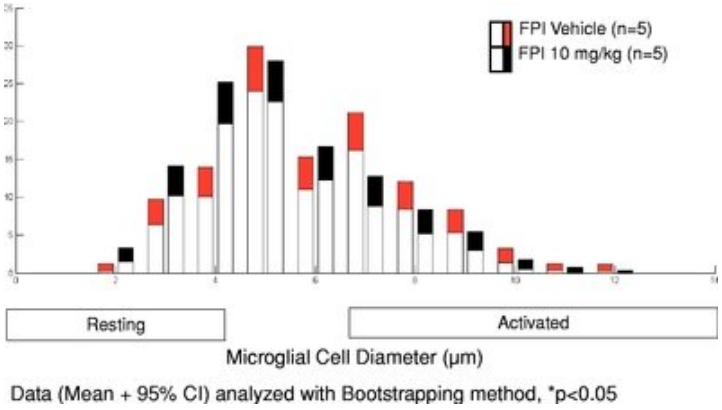
In our study (manuscript in preparation), rats were subjected to either fluid percussion injury (FPI) or sham operation to one side of the brain. Three different ANVS-405 doses or saline were given intraperitoneally to rats subjected to FPI for four weeks, with the first dose administered one hour post-injury. 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 of living cells and determination of microglia activation. As shown, 10 mg/kg ANVS-405 improved 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 three doses of ANVS-405 showed higher TH staining in the ipsilateral area of the brain than 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-FPI-Vehicle vs. FPI-10mg/kg ANVS-405#; *p=0.035 by one-way ANOVA, Bonferroni comparison. Right: TH immunoreactivity in the ipsilateral area of rats-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 µm. Fully activated amoeboid microglia had a mean cell body diameter of 7-14 µm. 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 show ANVS-401 and ANVS-405 reduced the toxic effects of neurotoxic proteins *in vivo*, in several animal models of both chronic and acute neurodegeneration.

Reproducible Results Across Species—Mouse, Rat, Human

As mentioned, lowered levels of APP, tau and αSYN have been shown in spinal fluid of humans treated with ANVS-401 in the human POC study as well as in brains of mice in AD tg mice, DS trisomic mice and PD tg mice and rats treated with ANVS-405 in the TBI study.

Furthermore, reduced inflammation has been shown in spinal fluid of four humans treated with ANVS-401 in the human POC study and in brains of rats treated with ANVS-405 in the TBI study.

As discussed, ANVS-401 and -405 have a mechanism of action we believe to be unique that allows them to inhibit the over-translation of and reduce the levels of APP, tau and αSYN, which play a central role in the pathogenesis of both AD and PD. That, in combination with our supporting data showing results in AD-DS, AD and PD mouse models, and lowering 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 mRNAs of multiple neurotoxic proteins, applicable to multiple diseases.

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 αSYN. So far neither drugs attacking tau nor αSYN have been tested in Phase 3. Hence there is an enormous need for a different disease-modifying strategy. There is more than one neurotoxic protein in the brain of AD and of PD patients, and the same neurotoxic 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 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 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.

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

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 four to five 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, non-DS 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. 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 similar symptoms to sporadic AD, but in a much younger population with accelerated disease progression.

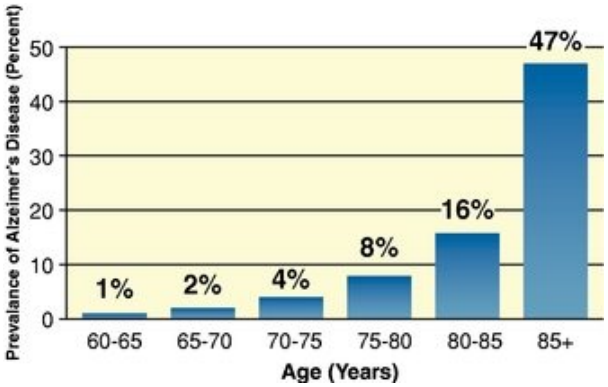
In the US AD-DS is an orphan indication, because about 50,000 DS people have AD and about 120,000 are at risk to develop AD in the next 5 to 10 years.

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 over 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 DMTs that can slow or prevent PD progression.

Mixed Pathologies Market

In addition to the unmet need of AD and PD patients, approximately 50% of patients exhibit 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 these 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 αSYN 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 Aβ plaques and tau-containing neurofibrillary tangles for a secondary diagnosis of Alzheimer's disease, and these pathologies may act synergistically with αSYN pathology to confer a worse prognosis.

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/Lewy body dementia, 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 addresses Aβ, tau or αSYN won't help people with mixed pathologies. Since ANVS-401 inhibits more than one neurotoxic 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-Aβ 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 Aβ, the main constituent of amyloid plaques in the brains of patients with AD. Aβ 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 Colombia, which is home to nearly 5,000 people who share the risk for a rare genetic mutation. This mutation, presenilin 1, causes early-onset AD 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 Aβ Vaccine Phase 1b Study for AD-DS

AC Immune has completed recruitment for the high-dose cohort of the ACI-24 Phase 1b study for the treatment of AD-like characteristics in adults with 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 Aβ-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 Aβ 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 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 Aβ 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 Aβ42, but all Aβ42 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 several neurotoxic proteins—amyloid precursor protein and its toxic fragments Aβ42 and IC99, a well as tau and αSYN—a DMD drug needs to target more than just one toxic protein to be efficacious. We believe that 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 Mini-Mental State Exam 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 one to five 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 inhibitors and the monoamine oxidase (MAO) inhibitors allow patients to reduce L-DOPA dosing levels. Several 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 αSYN 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 αSYN approaches in development right now.

Product	Company	MOA	Ph	Status/ Outcome
PRX002	Prothena/Roche	Anti-αSYN-mAb	2	Good safety profile, CSF/Serum 0.3%. P2 primary outcome (MDS UPURS at 52w) is expected in 2020
BIIB054	Neurimmune/Biogen	Anti-αSYN-mAb	2	Good safety profile, CSF/Serum 0.2%. P2 primary outcome (safety, PD at 52w) is expected 2021
Kenterin	Enterin	Shark-derived αSYN inhibitor	2	Primary outcome (safety, PKPD, efficacy) of phase 1/2 a study results expected in 2019
Affiris	Affiris	Therapeutic vaccine for αSYN	1	Good safety profile with immune responses. Responses were shown in several efficacy outcomes (PR: no details reported).
PD03	Affiris	Therapeutic vaccine for αSYN	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 αSYN	1	Phase 1 study completed in 2016 but results not reported
MEDI1341	AstraZeneca Takeda	Anti-αSYN-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 few 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, tyrosine hydroxylase and GTP cyclohydrolase 1, 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 the program.

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 September 30, 2019, our portfolio of owned and licensed patents totaled 36 issued or pending patents consisting of eight issued U.S. patents, two pending U.S. patent applications, 15 issued foreign patents and 11 pending foreign applications. These include three classes of 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 2022 and 2026.

Annovis has filed an additional three families 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.

The patents have expiration dates between 2031 and 2038. In August 2019, the U.S. Patent and Trademark Office granted Patent No. US 10,383,851, the first of our Annovis patents from this family covering PD and associated diseases.

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 AD 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 2022.
- 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.

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

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 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 2031 in the United States. This patent family covers AD and PD as well as Huntington's disease, prion diseases, amyotrophic lateral sclerosis, tauopathies and frontotemporal dementia. In August 2019, the U.S. Patent and Trademark Office granted Patent No. US 10,383,851, the first of our Annovis patents from this family covering PD and associated diseases. We are filing one or more continuation applications in order to capture further patentable subject matter in this application. While the notice of allowance gives us some comfort that the patent life of ANVS-401 may be prolonged to 2031, the fact that only a portion of the application family claims has so far been allowed could result in very limited patent coverage and the constraint of our development efforts to PD alone. It is further 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 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-405. The acute brain or nerve injury may be traumatic brain injury, stroke, microinfarcts, post-operative cognitive decline resulting from anesthesia or surgery-induced inflammation, or acute brain injury induced by brain ischemia, insufficient oxygen supply to the brain, anoxia or hypoxia, concussion, drowning, whip lash, bicycle crashes, automobile accidents, shaken baby syndrome, falling, 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.

- 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 AD or PD, 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 AD, 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.

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 Raptor Pharmaceuticals, Inc. and 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 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 (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 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 comply with cGMP requirements and are 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 for the 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 (IMM) 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. 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 influences 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 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 if 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 the FDA-approved products for a particular indication. Also, third-party payors may refuse to include a 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 based on 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 January 20, 2020, we had 2 employees.

Facilities

Our offices are 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	69	Founder, President and CEO and director
Jeffrey McGroarty	50	Chief Financial Officer
Directors		
Michael Hoffman	69	Chairman of the Board(2)
Claudine Bruck	64	Board Member(1)
Robert Whelan	67	Board Member(1)(2)(3)
Mark White	63	Board Member(1)(3)

(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 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

Jeffrey L. Cummings MD
Chief Medical Advisor

Dr. Cummings is our Chief Medical Advisor and served as our Chief Medical Officer from January 2019 to August 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.

William Mobley, M.D., Ph.D.
Chief Scientific Advisor

Dr. Mobley is our Chief Scientific Advisor, 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 a Distinguished Professor of Neurosciences, Florence Riford Chair for Alzheimer's Disease Research and Associate Dean for Neurosciences Initiatives at UC San Diego. 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 advisors and 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 NYSE American. 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 governance committee monitors 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 three standing committees—audit, compensation and nominating and governance—each of which operates under a charter that has been approved by our board of directors. Each committee's charter will be available under the Corporate Governance section of our website at *www.annovisbio.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 assists our board of directors in its oversight of our accounting and financial reporting process and the audits of our financial statements. We have adopted an audit committee charter, which details 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, Claudine Bruck and Mark White. Mr. Whelan serves as chairperson of the committee. All members of our audit committee meet the requirements for financial literacy under the applicable listing rules of NYSE American, or the NYSE American rules, and meet the independence requirements of Rule 10A-3 under the Exchange Act and the applicable NYSE American rules. Mr. Whelan qualifies as an audit committee financial expert under Item 407 of Regulation S-K.

Compensation Committee

Our compensation committee assists our board of directors in the discharge of its responsibilities relating to the compensation of our executive officers. We have adopted a compensation committee charter, which details 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. Mr. Hoffman serves as the chairperson of the committee. Our board of directors has determined that Mr. Hoffman and Mr. Whelan are independent under the applicable NYSE American rules, including the NYSE American 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.

Nominating and Governance Committee

Our nominating and governance committee assists our board of directors in its oversight of our corporate governance principles. We have adopted a nominating and governance committee charter, which details the principal functions of the nominating and governance committee, including:

- identifying nominees for election to the board, consistent with the qualifications and criteria approved by the board;
- determining the composition of the committees of the board;

- recommending to the board the director nominees for the annual meeting of stockholders;
- developing, overseeing and making recommendations to the board regarding our corporate governance guidelines and procedures;
- establishing and monitoring a process of assessing the board's effectiveness; and
- overseeing the evaluation of the board.

The members of our nominating and governance committee are Mark White and Robert Whelan. Mr. White serves as the chairperson of the committee. Our board of directors has determined that Mr. White and Mr. Whelan are independent under the applicable NYSE American rules, including the NYSE American rules specific to oversight of director nominations.

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 have adopted 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 NYSE American, our code of business conduct and ethics will be available under the Corporate Governance section of our website at *www.annovisbio.com*. In addition, we intend to post on our website all disclosures that are required by law or the NYSE American 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 for the year ended December 31, 2019, 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 "Summary Compensation Table" below and the non-employee members of our board of directors. In 2019, our "named executive officers" and their positions were:

- Maria Maccecchini, President and Chief Executive Officer
- Jeffrey McGroarty, Chief Financial 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.

Summary Compensation Table

The following table sets forth information concerning the compensation of our named executive officers for the years ended December 31, 2019 and 2018.

Name and Principal Position	Year	Salary ($)	Option Awards ($)(1)	Total ($)
Maria Maccecchini	2019	120,000	—	120,000
President and Chief Executive Officer	2018	120,000	35,165	155,165
Jeffrey McGroarty(2)	2019	—	—	—
Chief Financial Officer				

(1) Amounts reflect the full grant date fair value of stock options granted, computed in accordance with ASC Topic 718, rather than the amounts paid to or realized by the named individual. 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. No options were granted to our named executive officers during the year ended December 31, 2019.

(2) Mr. McGroarty became our Chief Financial Officer in April 2019.

Bonuses

Our named executive officers did not participate in an annual cash bonus program or receive bonuses for 2019 or 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 2018 Plan, please see the section titled "Equity Compensation Plans" below.

Retirement, Health and Welfare Plans

Maria Maccecchini is covered by a medical plan. No other plans were covered by the Company in 2019 or 2018.

Outstanding Equity Awards

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, 2019.

		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	85,714	—	$ 0.14	4/1/2027
	4/6/2018	50,000	—	$ 0.25	4/5/2028
Jeffrey McGroarty	—	—	—	—	—

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.

Director Compensation Table

Name	Year	Option Awards ($)(1)	Total ($)
Michael Hoffman	2019	—	—
	2018	5,062	5,062
Robert Whelan	2019	—	—
	2018	5,062	5,062
Mark White	2019	—	—
	2018	5,062	5,062
Claudine Bruck	2019	—	—
	2018	5,062	5,062

(1) Amounts reflect the full grant date fair value of stock options granted, computed in accordance with ASC Topic 718, rather than the amounts paid to or realized by the named individual. 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. No options were granted to our directors during the year ended December 31, 2019.

Scientific Advisory Board Compensation

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

Scientific Advisor Compensation Table

Name	Year	Option Awards ($)(1)	Total ($)
Jeffrey Cummings	2019	—	—
	2018	3,374	3,374
Peter Davies	2019	—	—
	2018	3,374	3,374
Sidney Strickland	2019	—	—
	2018	5,062	5,062
Gregory Petsko	2019	—	—
	2018	5,062	5,062
Rudy Tanzi	2019	—	—
	2018	5,062	5,062

(1) Amounts reflect the full grant date fair value of stock options granted, computed in accordance with ASC Topic 718, rather than the amounts paid to or realized by the named individual. 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. No options were granted to our scientific advisors during the year ended December 31, 2019.

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 376,123 shares. If grants of stock options or stock awards under the Plan or our prior equity incentive plan are canceled or forfeited, the shares subject to such grants will again be available under the Plan.

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 Plan, 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 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, 2019 and 2018, 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
- Mark White purchased an aggregate of 16,167 shares for $14,550, through an angel investment partnership

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
- Mark White purchased an aggregate of $14,550, through an angel investment partnership
- Claudine Bruck purchased an aggregate of $5,000

Participation in This Offering

Certain of our existing stockholders have indicated an interest in purchasing an aggregate of approximately $800,000 in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, fewer or no shares in this offering to any of these stockholders, and any of these stockholders may determine to purchase more, fewer or no shares in this offering.

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, 2019 and 2018 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 September 30, 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 4,399,703 shares of common stock outstanding as of September 30, 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 exercisable within 60 days of September 30, 2019 and shares of our common stock that will be issued upon conversion of our $530,000 principal amount convertible promissory notes plus accrued interest as of January 31, 2020, the expected closing date 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 c/o Annovis Bio, Inc., 1055 Westlakes Drive, Suite 300, Berwyn, PA 19312. 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.

Certain of our existing stockholders have indicated an interest in purchasing an aggregate of approximately $800,000 in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, fewer or no shares in this offering to any of these stockholders, and any of these stockholders may determine to purchase more, fewer or no shares

in this offering. The following table does not reflect any such purchases by these existing stockholders or their affiliated entities.

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	1,359,698(1)	30.5%	23.1%
Maria Maccecchini	1,112,889(2)	24.5%	18.7%
Ben Franklin Technology Partners	230,991(3)	5.3%	4.0%
Building 100 Innovation Center 4801 S Broad Street, Suite 200 The Navy Yard Philadelphia, PA 19112			
Named Executive Officers and Directors Other Than 5% or Greater Stockholders			
Robert Whelan	95,697(4)	2.2%	1.6%
Claudine Bruck	37,225(5)	*%	*%
Mark White	70,869(6)	1.6%	1.2%
Jeffrey McGroarty	—	*%	*%
All Executive Officers and Directors as a Group (6 persons)	2,676,378(7)	57.0%	43.7%

* Less than 1%.

(1) Includes (i) currently exercisable stock options to purchase 7,142 shares at an exercise price of $0.25 per share and (ii) 55,884 shares of our common stock that will be issued upon conversion of $250,000 principal amount of our convertible promissory notes plus accrued interest 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 85,714 shares at an exercise price of $0.14 per share and 50,000 shares at an exercise price of $0.25 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 17,855 shares at an exercise price of $0.14 per share and 7,142 shares at an exercise price of $0.25 per share and (ii) 11,176 shares of our common stock that will be issued upon conversion of $50,000 principal amount of our convertible promissory notes plus accrued interest 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 24,997 shares at an exercise price of $0.14 per share and 7,142 shares at an exercise price of $0.25 per share and (ii) 1,117 shares of our common stock that will be issued upon conversion of $5,000 principal amount of our convertible promissory notes plus accrued interest upon the closing of this offering into shares of our common stock at a 20% discount to the public offering price.

(6) Includes (i) currently exercisable stock options to purchase 14,284 shares at an exercise price of $0.14 per share and 7,142 shares at an exercise price of $0.25 per share and (ii) 3,252 shares of our common stock that will be issued upon conversion of $14,550 principal amount of our convertible promissory notes plus accrued interest upon the closing of this offering into shares of our common stock at a 20% discount to the public offering price.

(7) Includes (i) currently exercisable stock options to purchase 142,850 shares at an exercise price of $0.14 per share, 78,568 shares at an exercise price of $0.25 per share and (ii) 71,429 shares of our common stock that will be issued upon conversion of $319,550 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 35 million shares of common stock, par value $0.0001 per share, and two million shares of preferred stock, par value $0.0001 per share.

Common Stock

As of September 30, 2019, there were 282,614 shares of our common stock issued and outstanding and 4,117,089 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.

Registration Rights

Under our registration rights agreement dated as of December 19, 2014, following the closing of this offering, the holders of approximately 2,273,847 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 but 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.

Our amended and restated bylaws will not apply to suits brought to enforce a duty or liability created by the Securities Act or the Exchange Act, or any other claim for which federal courts have exclusive jurisdiction.

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

Our common stock has been approved for listing on NYSE American 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 6,518,173 shares of common stock, assuming the issuance of 2,000,000 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, the issuance of 118,470 shares of our common stock upon conversion of the $530,000 principal amount of our convertible promissory notes plus accrued interest as of January 31, 2020, the expected closing date of this offering, into shares of our common stock at a 20% discount to the public offering price and no exercise of options after September 30, 2019. 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 4,518,173 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 6,518,173 shares will be available for sale in the public market, subject in some cases to applicable limitations under Rule 144.

In addition, 353,565 shares of our common stock were subject to vested stock options outstanding as of September 30, 2019 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 does 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 65,182 shares immediately after this offering; or
- the average weekly trading volume in our common stock on NYSE American 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 NYSE American 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

Upon completion of this offering, the holders of 2,273,847 shares of common stock will be entitled to certain rights with respect to the registration of their shares under the Securities Act. Because these shares are held by affiliates of ours, registration of these shares under the Securities Act would result in the shares becoming tradable under the Securities Act 90 days after the effective date of the registration statement of which this prospectus is a part, subject to Rule 144 provisions regarding affiliate resales of restricted securities. 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 or arrangement 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 (including any entity or arrangement treated as 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 U.S. 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 U.S. 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 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 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 a U.S. real property interest, or USRPI, by reason of our status as a U.S. real property holding corporation, or USRPHC, for U.S. federal income tax purposes, at any time within the shorter of the five-year period preceding the disposition or the non-U.S. holder's holding period for our common stock.

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 proceeds received on the disposition of shares will generally be subject to withholding at a rate of 15% and such non-U.S. holder's gain on the disposition of shares 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. 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, subject to the discussion of the proposed U.S. Treasury Regulations below, 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.

The U.S. Department of the Treasury has released proposed regulations which, if finalized in their present form, would eliminate the FATCA withholding tax of 30% applicable to the gross proceeds of a sale or disposition of our common stock. In its preamble to the proposed regulations, the U.S. Treasury stated that taxpayers may generally rely on the proposed regulations until final regulations are issued.

Prospective investors should consult their tax advisors regarding the potential application of these FATCA 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 January 29, 2020, 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.	2,000,000
Total	2,000,000

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 300,000 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 $13.8 million and the total net proceeds, before expenses, to us will be $12.8 million.

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	$ 6.00	$ 12,000,000	$ 13,800,000
Underwriting discount(1)	$ 0.42	$ 840,000	$ 966,000
Proceeds, before expense, to us	$ 5.58	$ 11,160,000	$ 12,834,000

(1) We have agreed to pay the underwriters a commission of 7.0% 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 $643,600.

Representative's Warrants

We have agreed to issue to the representative warrants to purchase up to a total of 100,000 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 $7.50 per share, which is 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 NYSE American, 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 NYSE American 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 was determined by negotiations among us and the representative of the underwriters. In addition to prevailing market conditions, among the factors considered in determining the initial public offering price of our common stock were:

- 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.

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.

Our common stock has been approved for listing on NYSE American under the trading symbol "ANVS." In order to meet one of the requirements for listing the common stock on NYSE American, the underwriters have undertaken to sell to a minimum of 400 beneficial holders.

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.

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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, and the reverse stock split described in Note 2(j), as to which the date is August 8, 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 282,614 and 268,328 shares issued and outstanding at December 31, 2018 and 2017, respectively	28	27
Additional paid-in capital	192,117	106,590
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	$ (2.57)	$ (2.66)
Weighted average number of common shares outstanding, basic and diluted	277,585	256,146

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	—	$ —	218,197	$ 22	$ 49,605	$ (6,389,828)	$ (6,340,201)
Proceeds from the issuance of preferred shares	—	—	360,000	324,000	—	—	—	—	—
Proceeds from the issuance of common shares	—	—	—	—	50,131	5	8,490	—	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	268,328	27	106,590	(7,072,177)	(6,965,560)
Proceeds from the issuance of preferred shares	—	—	270,722	243,649	—	—	—	—	—
Proceeds from the issuance of common shares	—	—	—	—	14,286	1	2,799	—	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	282,614	$ 28	$ 192,117	$ (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	(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 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.

(j) Reverse Stock Split

On July 31, 2019, the board of directors and shareholders of the Company approved a reverse stock split of the Company's common stock at a ratio of one share for every 1.4 shares previously held. All common stock share and per-share data and conversion or exercise price data for applicable common stock equivalents included in these financial statements have been retroactively adjusted to reflect the reverse stock split.

(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.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(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

(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.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(6) Commitments (Continued)

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.

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

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(6) Commitments (Continued)

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 amended on December 14, 2017 to authorize 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 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.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(7) Redeemable Convertible Preferred Stock and Stockholders' Equity (Continued)

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.

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 transactions of substantially all of the assets of the Company in which the holders of the Company's outstanding 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

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(7) Redeemable Convertible Preferred Stock and Stockholders' Equity (Continued)

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 equal to $1.26 and the Series A conversion price is equal to $0.70, as adjusted for the reverse stock split discussed in Note 2(j).

The conversion price shall be adjusted for diluting issues such as issuance of: any options or convertible 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 reorganization.

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 initial public offering ("IPO") with gross proceeds of at least $20,000,000 or upon the consent of the holders of a majority of the Preferred Stock, all outstanding shares 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.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(8) Share-Based Compensation

In 2008, the Board approved the QR Pharma, Inc. 2008 Equity Incentive Plan (the "2008 Plan") initially authorizing 357,143 options to be issued which was subsequently increased to 446,017. On April 12, 2018, the 2008 Plan was succeeded by the QR Pharma, Inc. 2018 Equity Incentive Plan (the "2018 Plan") authorizing 376,123 shares to be issued (the 18,980 shares remaining available for issuance under the prior plan as of the effective date plus 357,143 additional shares). If grants of stock options under the 2018 Plan or 2008 Plan are cancelled or forfeited, the shares subject to such grants will again be available under the 2018 Plan. The 2008 Plan had 373,006 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 by the Board. As of December 31, 2018, and 2017, 381,280 and 142,780 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	147,618	$ 0.20	8.2
Granted	154,754	0.14	—
Exercised	(50,122)	0.20	—
Forfeited	(3,044)	0.78	—
Outstanding at December 31, 2017	249,206	$ 0.16	8.5
Granted	123,800	0.25	—
Exercised	(14,284)	0.20	—
Forfeited	(5,157)	0.08	
Outstanding at December 31, 2018	353,565	$ 0.19	8.2
Vested and exercisable	341,070		
Vested and expected to vest at December 31, 2018	353,565		

The intrinsic value of the outstanding shares as of December 31, 2018 and 2017 was $235,299 and $54,704 respectively.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(8) Share-Based Compensation (Continued)

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 $0.71 and $0.29 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.

(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	277,585	256,146
Net loss per share attributable to common stockholders, basic and diluted	$ (2.57)	$ (2.66)

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(9) Net Loss Per Share (Continued)

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, as converted	4,117,089	3,923,686
Stock options	353,565	249,206

(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 statement of operations for the year ended December 31, 2017.

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%

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(10) Income Taxes (Continued)

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 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

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(10) Income Taxes (Continued)

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.

(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

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

December 31, 2018 and 2017

(13) Subsequent Events (Continued)

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.

In July 2019, the board of directors and shareholders of the Company approved a reverse stock split of the Company's common stock. See Note 2(j).

ANNOVIS BIO INC.

Balance Sheets

	September 30, 2019 (unaudited)	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 56,250	$ 35,312
Prepaid expenses and other current assets	42,294	15,680
Total current assets	98,544	50,992
Long-term assets:		
Deferred offering costs	281,331	—
Total long-term assets	281,331	—
Total assets	$ 379,875	$ 50,992
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 425,093	$ 68,425
Accrued expenses	701,325	499,518
Total current liabilities	1,126,418	567,943
Long-term liabilities:		
Derivative liability	53,000	—
Convertible debt, net of unamortized deferred financing fees of $7,809 and debt discount of $23,918	498,273	—
Total long-term liabilities	551,273	—
Total liabilities	1,677,691	567,943
Redeemable convertible preferred stock—$0.0001 par value		
Series A, –5,133,159 shares authorized, issued and outstanding at September 30, 2019 and December 31, 2018	6,509,303	6,509,303
Series A-1, –1,111,111 shares authorized at September 30, 2019 and December 31, 2018, and 630,722 shares issued and outstanding at September 30, 2019 and December 31, 2018	567,649	567,649
Stockholders' equity (deficit):		
Common stock—$0.0001 par value, 10,150,000 shares authorized at September 30, 2019 and December 31, 2018, and 282,614 shares issued and outstanding at September 30, 2019 and December 31, 2018	28	28
Additional paid-in capital	200,976	192,117
Accumulated deficit	(8,575,772)	(7,786,048)
Total stockholders' equity (deficit)	(8,374,768)	(7,593,903)
Total liabilities and stockholders' equity (deficit)	$ 379,875	$ 50,992

See accompanying notes to financial statements.

ANNOVIS BIO INC.

Statements of Operations

(Unaudited)

	For the Nine Months Ended September 30,	
	2019	**2018**
Operating expenses:		
Research and development	$ 14,074	$ 98,319
General and administrative	720,586	447,562
Total operating expenses	734,660	545,881
Operating loss	(734,660)	(545,881)
Other income (expense):		
Change in fair value of derivative liability	(26,500)	—
Interest income (expense), net	(28,564)	61
Total other income (expense)	(55,064)	61
Loss before income taxes	(789,724)	(545,820)
Income tax expense (benefit)	—	—
Net loss	$ (789,724)	$ (545,820)
Basic and Diluted loss per common share	$ (2.79)	$ (1.98)
Weighted average number of common shares outstanding, basic and diluted	282,614	275,890

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			
Nine Months Ended September 30, 2019									
Balance, December 31, 2018	5,133,159	$ 6,509,303	630,722	$ 567,649	282,614	$ 28	$ 192,117	$ (7,786,048)	$ (7,593,903)
Share-based compensation expense	—	—	—	—	—	—	8,859	—	8,859
Net loss	—	—	—	—	—	—	—	(789,724)	(789,724)
Balance, September 30, 2019	5,133,159	$ 6,509,303	630,722	$ 567,649	282,614	$ 28	$ 200,976	$ (8,575,772)	$ (8,374,768)
Nine Months Ended September 30, 2018									
Balance, December 31, 2017	5,133,159	$ 6,509,303	360,000	$ 324,000	268,328	$ 27	$ 106,590	$ (7,072,177)	$ (6,965,560)
Proceeds from the issuance of preferred shares	—	—	270,722	243,649	—	—	—	—	—
Proceeds from the issuance of common shares	—	—	—	—	14,286	1	2,799	—	2,800
Share-based compensation expense	—	—	—	—	—	—	72,183	—	72,183
Net loss	—	—	—	—	—	—	—	(545,820)	(545,820)
Balance, September 30, 2018	5,133,159	$ 6,509,303	630,722	$ 567,649	282,614	$ 28	$ 181,572	$ (7,617,997)	$ (7,436,397)

See accompanying notes to financial statements.

ANNOVIS BIO INC.

Statements of Cash Flow

(Unaudited)

	For the Nine Months Ended September 30,	
	2019	**2018**
Cash flows from operating activities:		
Net loss	$ (789,724)	$ (545,820)
Adjustments to reconcile net loss to net cash used in operating activities:		
Amortization of deferred financing fees	813	—
Amortization of debt discount	2,582	—
Share-based compensation expense	8,859	72,183
Change in fair value of derivative liability	26,500	—
Changes in assets and liabilities:		
Prepaid expenses and other current assets	(26,614)	(14,071)
Accounts payable	215,282	(71,107)
Accrued expenses	138,288	76,366
Net cash used in operating activities	(424,014)	(482,449)
Cash flows from financing activities:		
Proceeds from issuance of common shares	—	2,800
Proceeds from issuance of convertible debt	530,000	—
Proceeds from issuance of preferred shares	—	243,649
Payment of deferred offering costs	(76,747)	—
Payment of deferred financing fees	(8,301)	—
Net cash provided by financing activities	444,952	246,449
Net increase (decrease) in cash	20,938	(236,000)
Cash and cash equivalents, beginning of period	35,312	347,472
Cash and cash equivalents, end of period	$ 56,250	$ 111,472
Supplemental disclosure of cash flow information		
Deferred offering costs in accounts payable and accrued expenses	$ 204,584	$ —
Deferred financing fees in accounts payable and accrued expenses	$ 321	$ —

See accompanying notes to financial statements.

Annovis Bio, Inc.

Notes to Financial Statements

September 30, 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 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 $789,724 and $545,820 for the nine months ended September 30, 2019 and 2018, respectively, and had an accumulated deficit of $8,575,772 as of September 30, 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 until the first quarter of 2020. 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 September 30, 2019, and its results of operations and its cash flows for the nine months ended September 30, 2019 and 2018. The interim

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

September 30, 2019 and 2018

(Unaudited)

(2) Summary of Significant Accounting Policies (Continued)

results of 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 $56,250 as of September 30, 2019 which does not exceed the FDIC coverage limit of $250,000.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

September 30, 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 September 30, 2019, the deferred offering costs amounted to $281,331. 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 September 30, 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)

September 30, 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 September 30, 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 September 30, 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)

September 30, 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)

September 30, 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)

September 30, 2019 and 2018

(Unaudited)

(2) Summary of Significant Accounting Policies (Continued)

(k) Reverse Stock Split

On July 31, 2019, the board of directors and shareholders of the Company approved a reverse stock split of the Company's common stock at a ratio of one share for every 1.4 shares previously held. All common stock share and per-share data and conversion or exercise price data for applicable common stock equivalents included in these financial statements have been retroactively adjusted to reflect the reverse stock split.

(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 September 30, 2019 and December 31, 2018:

		Fair Value Measurement at September 30, 2019		
	Carrying Value	Level 1	Level 2	Level 3
Cash and cash equivalents	$ 56,250	$ 56,250	$ —	$ —
Derivative liability	$ 53,000	$ —	$ —	$ 53,000

		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	$ —	$ —	$ —	$ —

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

September 30, 2019 and 2018

(Unaudited)

(3) Fair Value Measurements (Continued)

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 the fair value of the derivative liability at September 30, 2019 was $53,000. The change in the fair value of the derivative liability is reflected in the statement of operations for the nine months ended September 30, 2019.

(4) Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following:

	September 30, 2019	December 31, 2018
Prepaid rent	$ —	$ 1,904
Prepaid research and development	—	4,976
Prepaid expenses	850	5,000
Prepaid professional fees	35,000	—
Security deposit	6,444	3,800
Total prepaid expenses and other current assets	$ 42,294	$ 15,680

(5) Accrued Expenses

Accrued expenses consisted of the following:

	September 30, 2019	December 31, 2018
Accrued interest	$ 25,205	$ —
Payroll and related benefits	101,530	21,640
Accrued professional fees	80,090	17,878
Accrued license payments	494,500	460,000
	$ 701,325	$ 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.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

September 30, 2019 and 2018

(Unaudited)

(6) Convertible Promissory Notes (Continued)

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 $8,622 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 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 $24,344 and $16,768 for the nine months ended September 30, 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 September 30, 2019 and December 31, 2018, the Company had accrued $494,500 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. Expenses related to the license agreement are recognized in general and administrative expense in the Statements of Operations.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

September 30, 2019 and 2018

(Unaudited)

(7) Commitments (Continued)

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 September 30, 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 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.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

September 30, 2019 and 2018

(Unaudited)

(7) Commitments (Continued)

(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 September 30, 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 was amended on December 14, 2017 to authorize 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 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 September 30, 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 September 30, 2019 and December 31, 2018.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

September 30, 2019 and 2018

(Unaudited)

(8) Redeemable Convertible Preferred Stock and Stockholders' Equity (Continued)

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.

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 transactions of substantially all of the assets of the Company in which the holders of the Company's outstanding 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

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

September 30, 2019 and 2018

(Unaudited)

(8) Redeemable Convertible Preferred Stock and Stockholders' Equity (Continued)

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 equal to $1.26 and the Series A conversion price is equal to $0.70, as adjusted for the reverse stock split discussed in Note 2(k).

The conversion price shall be adjusted for diluting issues such as issuance of: any options or convertible 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 reorganization.

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 initial IPO with gross proceeds of at least $20,000,000 or upon the consent of the holders of a majority of the Preferred Stock, all outstanding shares 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.

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

September 30, 2019 and 2018

(Unaudited)

(9) Share-Based Compensation

Share-based compensation expense for the nine months ended September 30, 2019 and 2018 was $8,859 and $72,183, respectively.

As of September 30, 2019 and December 31, 2018, 381,280 stock options were available for future grants.

As of September 30, 2019, there were 353,565 options outstanding, all of which were vested and exercisable. As of December 31, 2018, there were 353,565 options outstanding, of which 341,070 were vested and exercisable. The intrinsic value of outstanding options was $235,299 as of September 30, 2019.

There were no options issued during the nine months ended September 30, 2019 and 123,800 options were issued for the nine months ended September 30, 2018. The options granted during the nine months ended September 30, 2018 were valued using the Black Sholes option pricing model using the following weighted average assumptions:

	Nine Months Ended September 30, 2018
Risk-free interest rate	2.58%
Expected life	5.15
Expected volatility	75%
Expected dividend yield	—

(10) Net Loss Per Share

The Company has reported a net loss for the nine months ended September 30, 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:

	Nine Months Ended September 30,	
	2019	2018
Numerator		
Net loss	$ (789,724)	$ (545,820)
Denominator		
Weighted-average common shares outstanding, basic and diluted	282,614	275,890
Net loss per share attributable to common stockholders, basic and diluted	$ (2.79)	$ (1.98)

Annovis Bio, Inc.

Notes to Financial Statements (Continued)

September 30, 2019 and 2018

(Unaudited)

(10) Net Loss Per Share (Continued)

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:

	Nine Months Ended September 30,	
	2019	2018
Redeemable convertible preferred stock, as converted	4,117,089	4,117,089
Stock options	353,565	353,565

(11) Income Taxes

The Company's income tax benefit (expense) was $0.0 million for the nine months ended September 30, 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 nine months ended September 30, 2019 and 2018 was offset by changes in the valuation allowance.

As of September 30, 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.

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2,000,000 Shares of Common Stock

ANNOVIS BIO, INC.

PROSPECTUS

ThinkEquity

a division of Fordham Financial Management, Inc.

January 29, 2020

Through and including February 23, 2020 (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.