ANNOVIS BIO, INC.

FORM 10-K
(Annual Report)

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Industry	Biotechnology & Medical Research
Sector	Healthcare
Fiscal Year	12/31

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2019

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission file number 001-39202

Annovis Bio, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**26-2540421**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

1055 Westlakes Drive, Suite 300
Berwyn, PA 19312
(Address of principal executive offices including zip code)

(610) 727-3913
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Trading Symbol	Name of Each Exchange on Which Registered
Common Stock, par value $0.0001 per share	ANVS	NYSE American

Securities registered pursuant to Section 12(g) of the Act: None.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☐ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

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

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☑

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☑

As of June 30, 2019, the last business day of the registrant's most recently completed second fiscal quarter, the registrant did not have a public float because there was no established public market for the registrant's common stock.

The number of shares of the issuer's common stock outstanding as of March 23, 2020, was 6,845,459.

Documents Incorporated by Reference

Certain portions, as expressly described in this report, of the registrant's proxy statement for the 2020 Annual Meeting of the Stockholders to be held June 3, 2020 are incorporated by reference into Part III of this Annual Report on Form 10-K.

TABLE OF CONTENTS

Cautionary Note Regarding Forward-Looking Statements.

This Annual Report on Form 10-K contains forward-looking statements, within the meaning of the U.S. Private Securities Litigation Reform Act of 1995, that involve substantial risks and uncertainties. In some cases, you can identify forward-looking statements by the words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "objective," "ongoing," "plan," "predict," "project," "potential," "should," "will," or "would," and or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report on Form 10-K, we caution you that these statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain.

The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- our business strategies;
- the timing of regulatory submissions;
- our ability to obtain and maintain regulatory approval of our existing product candidates and any other product candidates we may develop, and the labeling under any approval we may obtain;
- risks relating to the timing and costs of clinical trials and the timing and costs of other expenses;
- risks related to market acceptance of products;
- risks associated with our reliance on third-party organizations;
- our competitive position;
- assumptions regarding the size of the available market, product pricing and timing of commercialization of our product candidates;
- our intellectual property position and our ability to maintain and protect our intellectual property rights;
- our results of operations, financial condition, liquidity, prospects, and growth strategies;
- our cash needs and financing plans;
- the industry in which we operate; and
- the trends that may affect the industry or us.

You should refer to Part I, Item 1A "Risk Factors" of this Annual Report on Form 10-K for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of the risks, uncertainties and assumptions described under "Risk Factors" and elsewhere, we cannot assure you that the forward-looking statements in this Annual Report on Form 10-K will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame or at all.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance, or events and circumstances reflected in the forward-looking statements will be achieved or occur. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this report to conform these statements to new information, actual results or changes in our expectations, except as required by law.

PART I

Item 1. Business.

Overview

Our Company

Annovis Bio, Inc. is a clinical stage, drug platform company addressing neurodegeneration, such as Alzheimer's disease (AD), Parkinson's disease (PD) and Alzheimer's disease in Down syndrome (AD-DS). 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, ANVS401, for chronic neurodegenerative diseases, such as AD, PD and AD-DS. In several studies, ANVS401 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. We have shown in four mildly cognitive impaired (MCI) patients that our lead compound, ANVS401, 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, PD and AD-DS 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 and AD-DS as well as body and brain function in PD.

We believe that ANVS401 has the potential to be the first drug to interfere with the underlying mechanism of neurodegeneration. ANVS401 is a small, once a day, orally administered, brain penetrant inhibitor of neurotoxic proteins. The biological activity of ANVS401 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 ANVS401 was well tolerated and we saw promising clinical signals: in all four patients, ANVS401 reduced the levels of APP, tau and αSYN (αSYN is an unpublished, not statistically significant observation) and lowered inflammatory factors.

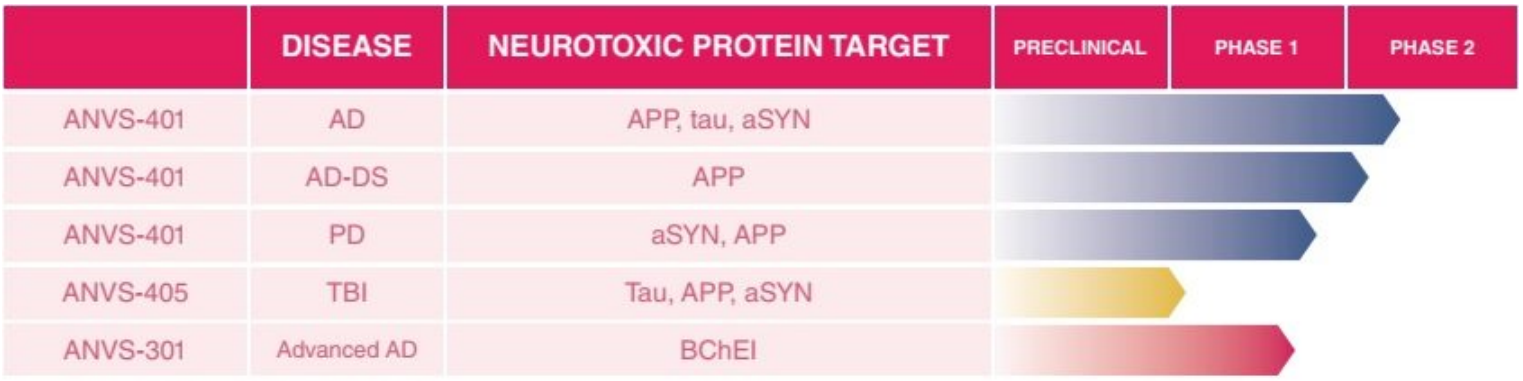
We are presently conducting a Phase 2a study in AD patients in collaboration with the Alzheimer Disease Cooperative Study (ADCS) and plan to initiate a second Phase 2a proof-of-concept study of ANVS401 in the first quarter of 2020 with 50 PD patients. The AD study being conducted by ADCS is expected 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 12 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 ANVS401'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 ANVS401, 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).

Innovation

Pipeline

Our pipeline consists of: ANVS401 for chronic neurodegeneration - including AD, its orphan indication AD-DS and PD; ANVS405 to treat acute neurodegeneration – including traumatic brain injury (TBI) and stroke; and ANVS301 for advanced AD.



ANVS401

Our lead compound, ANVS401, is an orally administered drug being developed for chronic indications such as AD, PD and AD-DS 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 ANVS401 for AD, PD, AD-DS and other chronic neurodegenerative disorders.

ANVS405

For acute indications, we are developing ANVS405, focused on protecting the brain after TBI and/or stroke. ANVS405 is the same compound as ANVS401 but it is given intravenously in cases of acute head and brain trauma. ANVS405 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 ANVS405 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 ANVS405 for acute indications of brain and nerve trauma. We plan to conduct a follow-on study to evaluate the effect of ANVS405 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.

ANVS301

We are developing our compound ANVS301 to increase cognitive capability in later stages of AD and dementia. ANVS301 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. ANVS301 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.

Clinical Human Data

Three clinical studies have been conducted with ANVS401. Clinical studies with single and repeated daily oral administration of ANVS401 tartrate showed ANVS401 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. ANVS401 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 ANVS401 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 ANVS401 in the brain, extrapolated from blood and CSF, were eight times higher than in plasma
  - ANVS401 lowered CSF levels of neurotoxic proteins and inflammatory markers. See pages 94 and 95.

In the four MCI patients, ANVS401 had a half-life of five hours in plasma and more than 12 hours in CSF. The longer concentration and persistence of ANVS401 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. ANVS401 is stable, orally available and enters the brain, therefore we are developing it as an oral drug candidate.

Summary of Safety in Humans

ANVS401'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 ANVS401 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 ANVS401 20-mg subject).

Adverse events seen in the first human SAD study conducted with ANVS401

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 ANVS401

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 ANVS401 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 ANVS401 and on Day 11 after the last administration of ANVS401. During each 12-hour period, a total of nine CSF samples were taken and levels of ANVS401 and metabolites were measured in plasma and CSF at all time points.

Pharmacokinetics

ANVS401 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, ANVS401 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 ANVS401 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, ANVS401 levels were found to be approximately six to eight times higher in brain than in plasma.

ANVS401'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 ANVS401 in the four human patients was consistent with the preclinical data in rodent brains.

The persistence of ANVS401 in the CSF and brain and the extended pharmacodynamic effect observed make ANVS401 a good candidate for once a day dosing. Extrapolated brain levels of ANVS401 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 ANVS401 needed to lower the levels of neurotoxic proteins are similar for the toxic proteins, suggesting similar dosing in AD, PD and AD-DS. We further compared ANVS401 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

ANVS401 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 ANVS401 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 ANVS401 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 ANVS401.

CSF Inflammatory Markers after 10 days of oral ANVS401 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. ANVS401 statistically significantly lowered the levels of three inflammatory markers in all four patients.

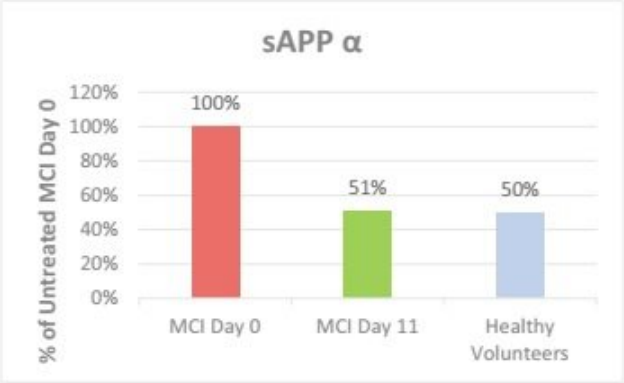
Comparison with Healthy Volunteers

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 ANVS401 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.

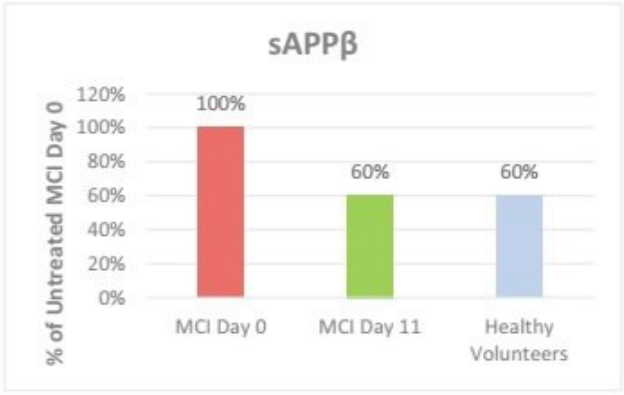
In order to make the comparison as accurate as possible, we used a single measurement from the same time point in each of the mornings of Day 0 and Day 11 for each MCI patient because this was similar to the timing for the healthy volunteers. In this very limited comparison, we were able to show that 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

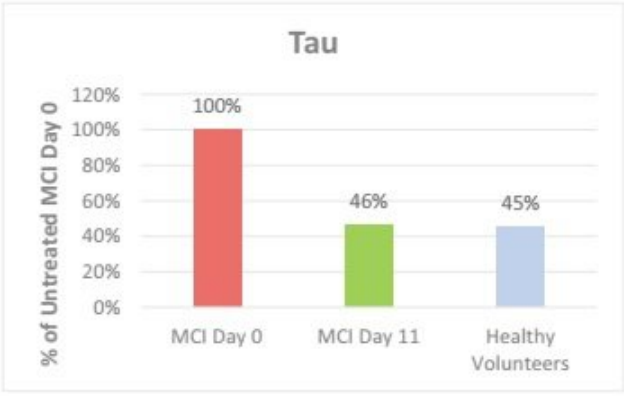
sAPPα					
MCI Patients				Healthy Volunteers	
ID	Day 0	Day 11	Decrease	ID	Single Sample
A	8,089	5,096	37%	1	4,450
B	11,517	5,700	51%	2	6,553
C	16,861	7,409	56%	3	6,876
D	11,137	6,093	46%	4	5,912
Avg.	11,901	6,075	49%		5,948



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



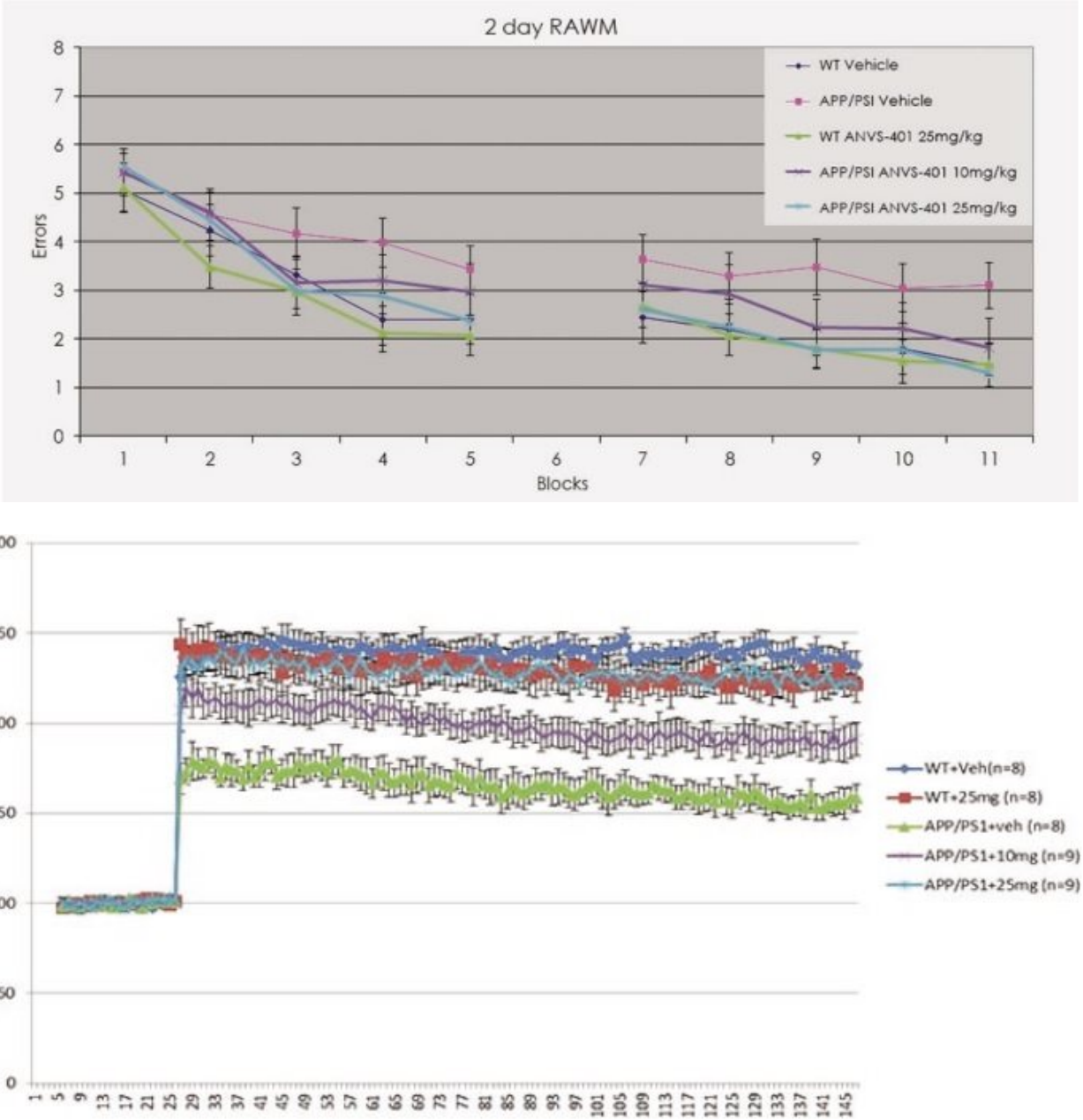
The tables above show the CSF levels of sAPPα, sAPPβ and tau in the four MCI patients and the four healthy volunteers. The percentages in the bar diagrams are derived from each of the tables, with red representing average of MCI patients at Day 0 before ANVS401 treatment; green representing average of MCI patients at day 11 after 10 days of ANVS401 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, ANVS401 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

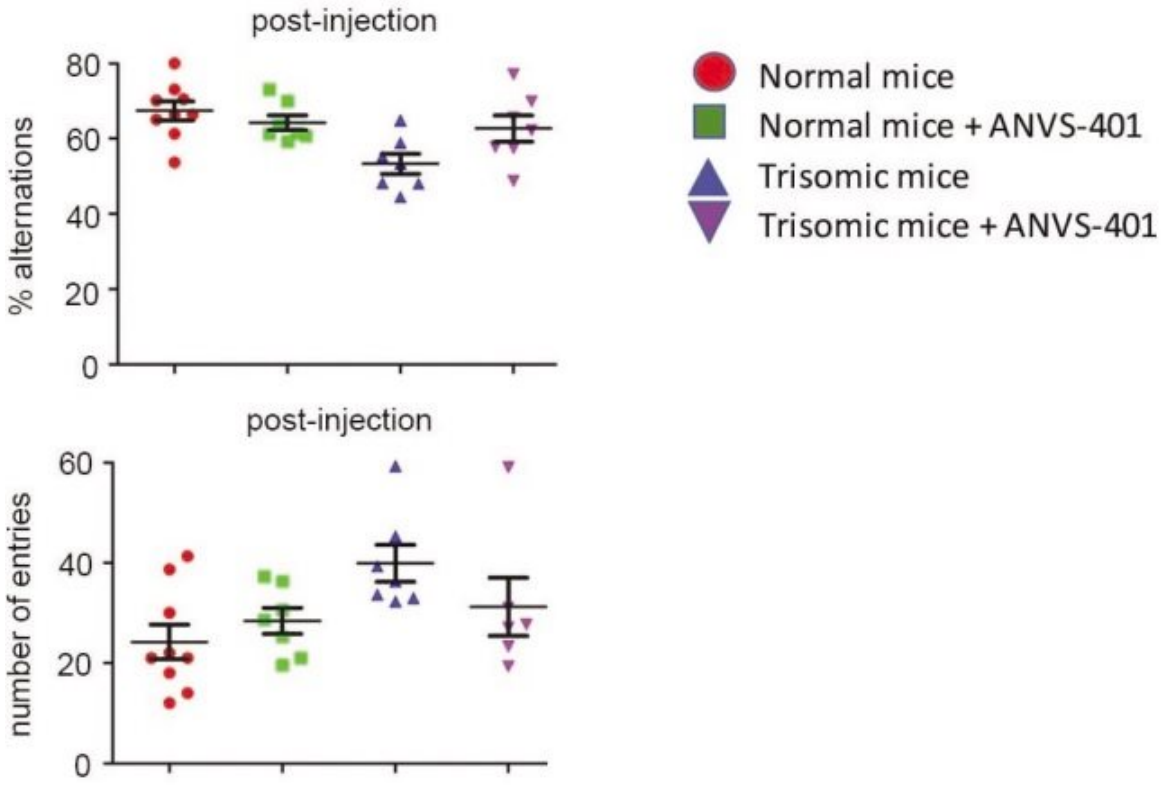
ANVS401 improved spatial-working memory as shown in a 2-day radial arm water maze test in this mouse AD model at a 25 mg/kg oral dose (p=0.0033, figure below-top) and showed a dose response at 10 mg/kg oral dose. In the same study ANVS401 improved synaptic function and long-term potentiation in hippocampal slices at both doses in a dose-dependent fashion (figure below-bottom). ANVS401 treatment did not affect wild-type (WT) mice.



APP/PS1 AD tg mice were treated for one month with ANVS401, 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

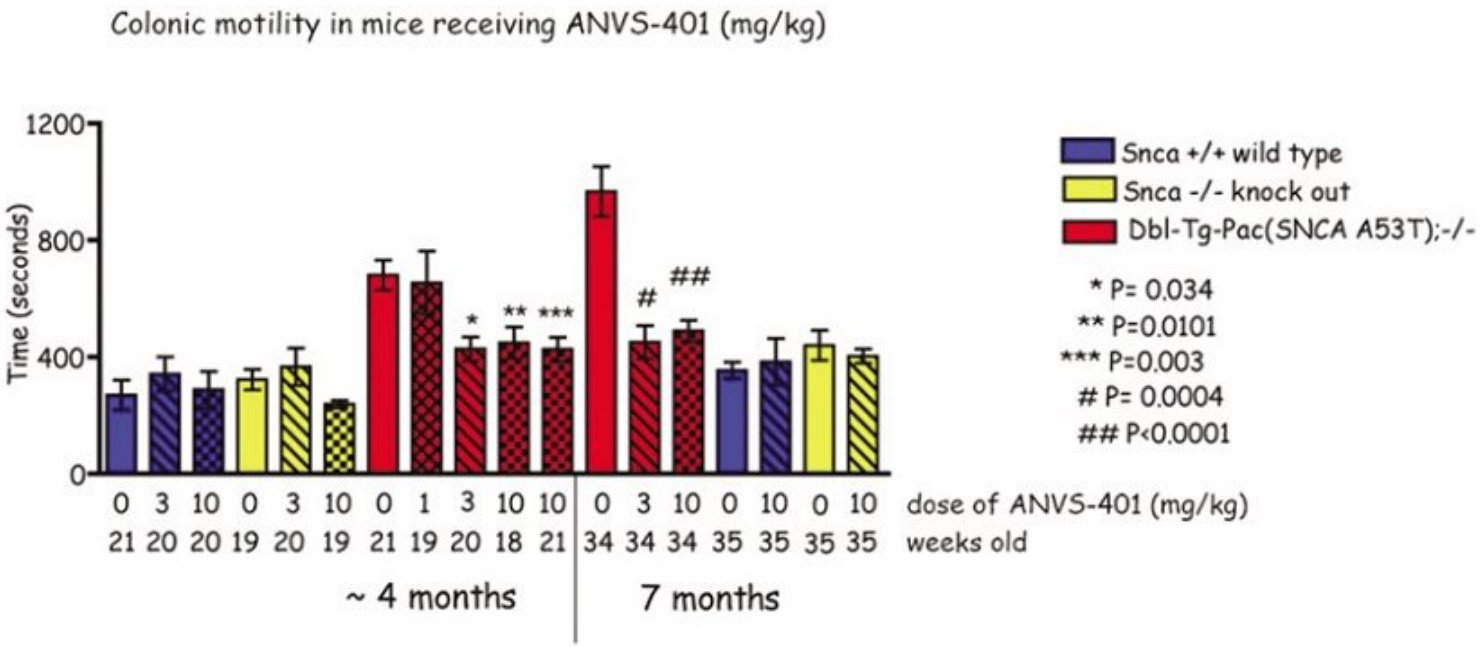
DS trisomic mice display several abnormal behaviors reminiscent of AD, including memory loss. They have elevated levels of APP that has been shown in mice to contribute to deficient memory and learning, cognitive impairment as well as dementia. DS trisomic mice are used as a model for AD, because they exhibit similar deficits as seen in AD. Thus, we considered whether ANVS401 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 ANVS401 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 ANVS401 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. ANVS401 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. ANVS401 statistically significantly (p=0.034 at four months and p=0.0001 at seven months) decreased the bead expulsion time between ANVS401 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). ANVS401 does not act as a laxative, since, when given to two different control mice breeds that do not develop constipation ($Snca^{+/+}$ and $Snca^{-/-}$), it does not affect their gut motility.



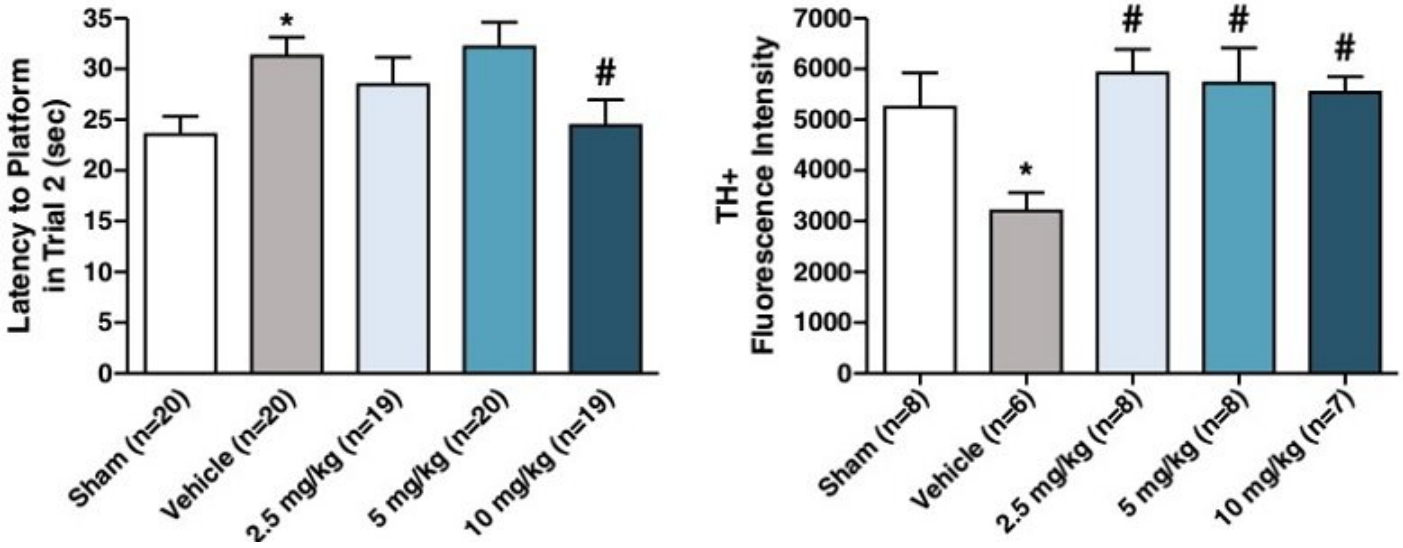
SNCA^{A53T} and SNCA^{A30P} mice (producing human mutant αSYN associated with familial PD) were treated intraperitoneally with vehicle or ANVS401 beginning at six weeks up to seven months of age. ANVS401 prevented the impaired gut motility of the SNCA^{A53T} and SNCA^{A30P} mice at 3 and 10 mg/kg. Older mice demonstrate a more severe phenotype that nonetheless responded to ANVS401.

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 ANVS405 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.

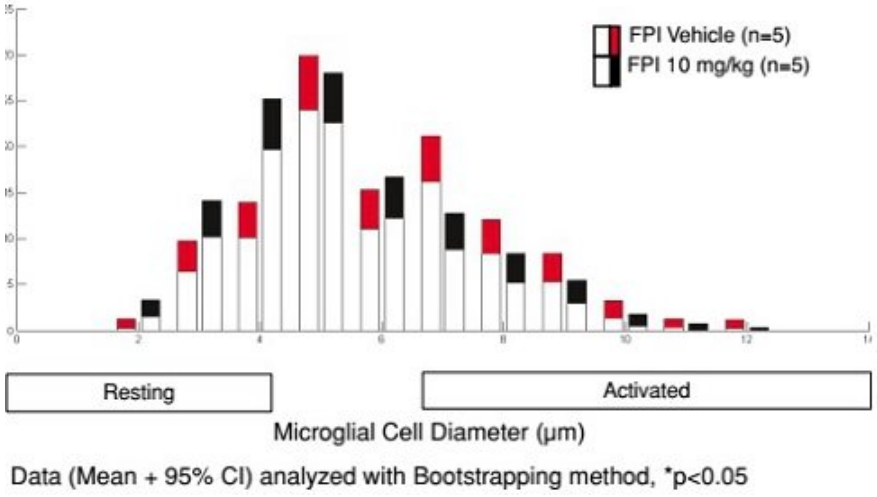
In our study (manuscript in preparation), rats were subjected to either fluid percussion injury (FPI) or sham operation to one side of the brain. Three different ANVS405 doses or saline were given intraperitoneally to rats subjected to FPI for four weeks, with the first dose administered one hour post-injury. 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 ANVS405 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 ANVS405 showed higher TH staining in the ipsilateral area of the brain than the vehicle treated animals (figure below-right). Thus, ANVS405 protects the striatum following FPI in rats.



Effects of ANVS405 treatment on rats subjected to FPI. Left: performance in a water maze-FPI-Vehicle vs. FPI-10mg/kg ANVS405#; *p=0.035 by one-way ANOVA, Bonferroni comparison. Right: TH immunoreactivity in the ipsilateral area of rats-FPI-Vehicle* vs. FPI-all ANVS405 doses#; #p<0.05 by one-way ANOVA, Bonferroni comparison.*

Because FPI can induce microglial activation, we next checked whether ANVS405 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. ANVS405 increases the number of resting microglia and reduces the number of activated microglia.

Effect of 10mg/kg ANVS405 on Microglial Activation



Effect of treatment with 10mg/kg ANVS405 on microglial activation following FPI in rats.

Collectively, these data show ANVS401 and ANVS405 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 ANVS401 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 ANVS405 in the TBI study.

Furthermore, reduced inflammation has been shown in spinal fluid of four humans treated with ANVS401 in the human POC study and in brains of rats treated with ANVS405 in the TBI study.

As discussed, ANVS401 and ANVS405 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, PD and AD-DS mouse models, and lowering of the toxic effects of neurotoxic proteins, leads us to believe that ANVS401 is a promising drug for the treatment of both AD and PD. 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 ANVS401 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.

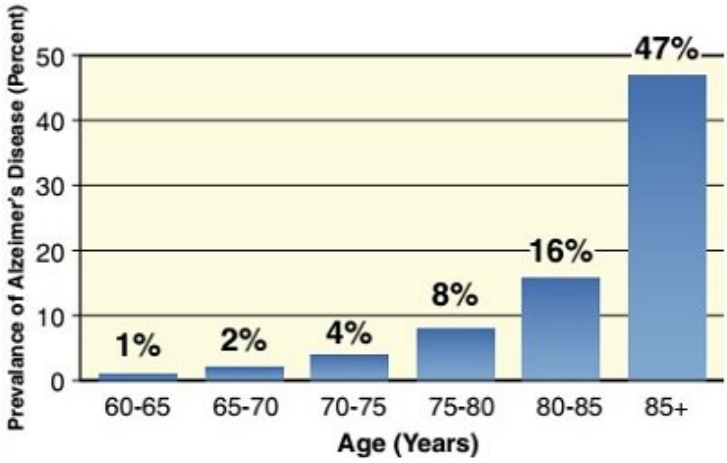
In the US AD-DS is an orphan indication, because about 50,000 DS people have AD and about 120,000 are at risk to develop AD in the next 5 to 10 years.

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 ANVS401 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-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. Among the DMTs in the pipeline as shown on clinicaltrials.gov, 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.

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 ANVS401 is the only drug that satisfies this criterion.

A concerning observation derived from a review of the AD pipeline is the lack of agents targeting the moderate to advanced stages of AD. 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. Although several 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 March 23, 2020, our portfolio of owned and licensed patents totaled 35 issued or pending patents consisting of eight issued U.S. patents, three pending U.S. patent applications, 14 issued foreign patents and 10 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 ANVS401; a process for producing phenserine and analogs thereof, including ANVS401; and a method of treating Down syndrome via the administration of (-) phenserine or (+) phenserine (ANVS401) 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 ANVS401. 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 ANVS401 includes three patent families and more specifically claims:

- The first of these patent families relates to a composition of matter for ANVS401 tartrate, a method of inhibiting production of amyloid precursor protein and a method of treating AD and dementia via the administration of ANVS401 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 = ANVS401 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 (ANVS401) 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 ANVS401 and ANVS405 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 ANVS401 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 and Canada. 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 issuance of our new patent gives us some comfort that the patent life of ANVS401 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 ANVS405. 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, Australia, Canada, China, Europe, Hong Kong and Japan. 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 ANVS401 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 ANVS401 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 ANVS401 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

ANVS401 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 ANVS401 and its analogs. We have a worldwide exclusive license to ANVS401 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, 2019, we had accrued $506,000 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 ANVS401 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

ANVS401 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 ANVS401 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 lead product candidate, ANVS401, 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 ANVS401 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 March 23, 2020, we had two employees. In addition to our employees, we contract with consultants and third parties for the conduct of certain clinical development, accounting and administrative activities.

Corporate Information

We were incorporated in Delaware in 2008. Our principal executive offices are located at 1055 Westlakes Drive, Suite 300, Berwyn, PA 19312 and our telephone number is (610)727-3913. Our website address is *www.annovisbio.com*. The inclusion of our website address is, in each case, intended to be an inactive textual reference only and not an active hyperlink to our website. The information contained in, or that can be accessed through, our website is not part of this Annual Report on Form 10-K.

Item 1A. Risk Factors

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 $990,980 and $713,871 for the years ended December 31, 2019 and 2018, respectively. As of December 31, 2019, we had an accumulated deficit of $8,777,028. 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 ANVS401 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 an NDA for ANVS401 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.

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 ANVS401.

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts to advance the clinical development of ANVS401 and launch and commercialize ANVS401, if we receive regulatory approval. We will require additional capital for the further development and potential commercialization of ANVS401 and may also need to raise additional funds sooner to pursue a more accelerated development of ANVS401. 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 our initial public offering that we completed on January 31, 2020 (the "IPO") 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 ANVS401 or any other future product candidates;
- clinical development plans we establish for ANVS401 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.

For the year ended December 31, 2018, we, as well as our independent registered public accounting firm expressed substantial doubt about our ability to continue as a going concern.

Our recurring losses from operations raised 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. We believe that the net proceeds from our IPO 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, 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 ANVS401 for treatment of AD, PD and AD-DS 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 ANVS401 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 December 31, 2019, we had net operating loss carryforwards, or NOLs, of $4,256,228 for federal income tax purposes, which may be available to offset our future taxable income, if any, and begin to expire in various amounts in 2032. NOLs of $1,491,988 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, 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 ANVS401, 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 ANVS401. 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 ANVS401 in a timely manner. We cannot commercialize ANVS401 in the United States without first obtaining regulatory approval from the FDA; similarly, we cannot commercialize ANVS401 outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of ANVS401 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 ANVS401 is safe and effective for use for that target indication and that the manufacturing facilities, processes and controls are adequate. Even if ANVS401 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 ANVS401 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 ANVS401, 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 ANVS401, we may not be able to earn sufficient revenue to continue our business

Disruptions associated with widespread health emergencies could harm our ability to complete or could materially delay our clinical trials.

The emergence of widespread health emergencies or pandemics, such as coronavirus disease (COVID-19), could lead to quarantines, business shutdowns, labor shortages, disruptions to the healthcare system, and overall economic instability. If the suppliers, CROs, hospitals, clinical trial sites, regulators, consultants and other third parties with whom we conduct business were to experience shutdowns or other business disruptions, our ability to enroll patients and conduct our clinical trials in the manner and on the timelines presently planned could be materially and negatively impacted. The clinical trial sites participating in our Phase 2a trial in AD patients have temporarily suspended enrollment of new patients because of the ongoing COVID-19 pandemic. Although we currently believe our clinical trials will be completed on time, the extent to which the COVID-19 pandemic could have a material impact on our clinical trials is dependent on the spread of the disease and government and healthcare system responses to such spread, which are presently highly uncertain.

the 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, ANVS401 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 (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 (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 ANVS401 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 ANVS401 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 an 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, PD and AD-DS, 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 ANVS401 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, ANVS401 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 ANVS401. This could result in a longer than expected regulatory review process, increased expected development costs or the delay or prevention of commercialization of ANVS401 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 ANVS401 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 ANVS401 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 ANVS401 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 ANVS401, if approved, may be smaller than we anticipate.

We expect to initially seek approval for ANVS401 for AD, PD and AD-DS 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 ANVS401 or any other product candidate in the United States, we may never obtain approval for or commercialize ANVS401 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 ANVS401 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 ANVS401 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 ANVS401 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 ANVS401 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 ANVS401 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 ANVS401 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 ANVS401. Our competitors may also obtain FDA or other regulatory approval for their product candidates more rapidly than we may obtain approval for ANVS401, which could result in our competitors establishing or strengthening their market position before we are able to enter the market.

The successful commercialization of ANVS401 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 ANVS401, 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 ANVS401 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 ANVS401 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 ANVS401, if approved.

We do not have any infrastructure for the sales, marketing or distribution of ANVS401, 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 collaborate with third parties to perform these services. We expect to build a focused sales, distribution and marketing infrastructure to market ANVS401, 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 ANVS401 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 ANVS401, 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 ANVS401, 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 ANVS401 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 ANVS401 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 organization (CMOs), for the production of clinical supply of ANVS401 and intend to rely on CMOs for the production of commercial supply of ANVS401, 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 ANVS401 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 ANVS401 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 ANVS401. 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 Annual Report on Form 10-K 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 ANVS401. We have an exclusive worldwide license, subject to standard reservation of rights under federal law, to ANVS401 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 ANVS401 for those indications. The agreement allows us to either pay license fees and royalties on sales to develop and sell ANVS401 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 ANVS401. 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 ANVS401 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 ANVS401 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 ANVS401. Unless these applications are approved by the U.S. and international patent offices, the patent life of using ANVS401 is limited. The first patent application family we filed, which would be expected to expire in 2031, covers the use of ANVS401 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 ANVS405'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 ANVS401 and ANVS405 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 ANVS401 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 ANVS401 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 ANVS401 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 ANVS401 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 ANVS401 and any future product candidates, and we expect to collaborate with third parties on the development of ANVS401 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 ANVS401 or our future product candidates. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize ANVS401 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 ANVS401.

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 ANVS401 or any other product candidate could be delayed.

Risks Related to Our Common Stock

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.

The market price of our common stock is 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 ANVS401;
- 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 ANVS401 or any future product candidate;
- inability to obtain additional funding;
- regulatory or legal developments in the United States and other countries applicable to ANVS401 or any other product candidate;
- adverse regulatory decisions;
- changes in the structure of healthcare payment systems;
- inability to obtain adequate product supply for ANVS401 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, 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.

Our directors, executive officers and certain shareholders 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.

Our directors, executive officers, and shareholders affiliated with our directors and executive officers beneficially own approximately 39.7% of the voting power of our outstanding common stock. Therefore, they 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 depends, 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.

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 our IPO, 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 our IPO are 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 our IPO are 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 closing of the IPO.

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 our IPO, (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 became effective upon the closing of our IPO 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 became effective upon the closing of our IPO 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

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our offices are in Berwyn, Pennsylvania, where we have leased and have access to 1,500 square feet of office space pursuant to a short-term lease agreement. We believe that our facilities are adequate to meet our current needs.

Item 3. Legal Proceedings.

From time to time, we may become subject to litigation and claims arising in the ordinary course of business. We are not currently a party to any material legal proceedings, and we are not aware of any pending or threatened legal proceedings against us that we believe could have a material adverse effect on our business, operating results or financial condition.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock is listed on the NYSE American under the symbol "ANVS" and began trading on January 29, 2020. Prior to that date, there was no public market for our stock.

Use of Proceeds from Registered Offering

On January 31, 2020, we completed our IPO pursuant to which we issued and sold 2,300,000 shares of our common stock at a price to the public of $6.00 per share. All of the shares of common stock issued and sold in our IPO were registered under the Securities Act pursuant to registration statements on Form S-1 (Registration Nos. 333-232529 and 333-236126), which were declared effective by the SEC on January 28, 2020. We received net proceeds of approximately $12.1 million, after deducting underwriting discounts and commissions and offering expenses borne by us. None of the expenses incurred by us were direct or indirect payments to any of (i) our directors or officers or their associates, (ii) persons owning 10% or more of our common stock, or (iii) our affiliates. There has been no material change in the planned use of proceeds from our IPO as described in our final prospectus filed with the SEC on January 30, 2020 pursuant to Rule 424(b)(4). ThinkEquity acted as sole book running manager for the offering. The offering commenced on January 28, 2020 and did not terminate before all securities registered in the registration statement were sold.

Holders of Record

As of March 23, 2020, there were approximately 79 holders of record of shares of our common stock. This number does not reflect the beneficial holders of our common stock who hold shares in street name through brokerage accounts or other nominees.

Dividend Policy

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future.

Securities Authorized for Issuance Under Equity Compensation Plans

The information called for by this item regarding equity compensation plans is incorporated by reference to Part III, Item 12 of this Annual Report on Form 10-K.

Issuer Purchases of Equity Securities

None.

Recent Sales of Unregistered Securities

Set forth below is information regarding shares of capital stock issued by us from January 1, 2019 to December 31, 2019. Also included is the consideration received by us for such shares and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

(a) We issued convertible promissory notes in the principal amount of $530,000.

The offers, sales and issuances of the securities described in paragraph (a) above were exempt from registration in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(a)(2) under the Securities Act and under Regulation D of the Securities Act, relative to transactions by an issuer not involving a public offering.

All purchasers of securities in transactions exempt from registration pursuant to Regulation D described above represented to us in connection with their purchase that they were "accredited investors" and were acquiring the securities for investment purposes only and not with a view to, or for sale in connection with, any distribution thereof and that they could bear the risks of the investment and could hold the securities for an indefinite period of time

Item 6. Selected Financial Data

This item is not required for smaller reporting companies.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes appearing at the end of this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. You should read "Cautionary Note Regarding Forward-Looking Statements" and Item 1A. Risk Factors of this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

Company Overview

We are a clinical stage, drug platform company addressing neurodegeneration such as Alzheimer's disease (AD), Parkinson's disease (PD) and Alzheimer's disease in Down Syndrome (AD-DS). Our lead compound, ANVS401, 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 ANVS401 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.

ANVS401 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. ANVS401 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, ANVS401 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 ANVS401 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 ANVS401 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 $990,980 and $713,871 for the years ended December 31, 2019 and 2018, respectively, and our accumulated deficit at December 31, 2019 was $8,777,028. 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 candidates. 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 candidates, 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 candidates are 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.

Our research and development expenses in 2019 primarily related to two long-term animal toxicology studies which began in November 2019—a six-month study in rats and a nine-month study in dogs. We expect that our research and development expenses in 2020 and for the next several years will be higher than in 2019 as a result of the continuation of our long-term toxicology studies, increased expenditures for our Phase 2a study in AD and our expected initiation of our Phase 2a study in PD in April 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 ANVS401. As a result of the difficulties of forecasting research and development costs of ANVS401 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 approved product candidates.

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 candidates.

We expect that our general and administrative expenses in 2020 and for the next several years will be higher than in 2019 as we increase our employee count. Following our IPO in January 2020, we also anticipate increased expenses relating to our operation 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 cash and cash equivalents and interest expense on our convertible promissory notes, including amortization of deferred financing fees and debt discount.

Grant Income

Grants received are recognized as grant income in the statements of operations as and when they are earned for the specific research and development projects for which these grants are designated. In September 2019, we received a Notice of Award for a $1.7 million grant from the National Institute on Aging of the NIH to cover the costs of long-term toxicology studies on ANVS401 in rats and dogs. We expect grant income to increase in 2020 as a result of the continuation of our long-term toxicology studies.

Income Taxes

As of December 31, 2019, the Company had U.S. federal net operating loss carryforwards of $4,256,228, 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 2032. The remaining $1,491,988 of federal net operating loss carryforwards generated in 2018 and later, do not expire but are limited 80% of taxable income in future years.

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 Annual Report on Form 10-K, 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. The Black-Scholes model requires us to make assumptions and judgments about the variables used in the calculations, including the expected term, the expected volatility of our common stock, the risk-free interest rate and the expected dividend rate.

Prior to our IPO, in the absence of a public trading market for our common stock, on each grant date, we developed an estimate of the fair value of our common stock underlying the option grants. 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. Following the closing of our IPO on January 31, 2020, 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.

Grant Income

Grants received are recognized as grant income in the statements of operations as and when they are earned for the specific research and development projects for which these grants are designated. Grants payments received in excess of grant income earned are recognized as deferred grant on the balance sheet and grant income earned in excess of grant payments received is recognized as grant receivable on the balance sheets.

Results of Operations

Operating expenses and other income (expense) were comprised of the following:

	Year Ended December 31,	
	2019	2018
	(in thousands)	
Research and development	$ 776.2	$ 111.6
General and administrative	829.4	602.3
Change in fair value of derivative liability	(79.5)	-
Interest income (expense), net	(40.9)	0.7
Grant income	735.1	-

Years Ended December 31, 2019 and 2018

Research and Development Expenses

Research and development expenses increased by $664.6 thousand for the year ended December 31, 2019 compared to the year ended December 31, 2018. The increase was primarily the result of contract research costs associated with our long-term toxicology studies in rats and dogs which began in November of 2019.

General and Administrative Expenses

General and administrative expenses increased by $227.1 thousand for the year ended December 31, 2019 compared to the year ended December 31, 2018. The increase was primarily the result of a $403.5 thousand increase in professional fees for accounting, audit, legal, technology and investor relations services, partially offset by a $83.3 thousand decrease in intellectual property legal costs and a $74.2 thousand decrease in stock-based compensation expense.

Change in Fair Value of Derivative Liability

The derivative liability represents an embedded derivative in our convertible promissory notes which were issued in March 2019. At each balance sheet date, we estimated the fair value of the derivative liability and recognized any change in our statements of operations. There was no derivative liability during the year ended December 31, 2018.

Interest Income (Expense), Net

Net interest expense increased $41.6 thousand for the year ended December 31, 2019 compared to the year ended December 31, 2018. The increase was primarily the result of interest recognized on our convertible promissory notes issued in March 2019.

Grant Income

Grant income increased $735.1 thousand for the year ended December 31, 2019 compared to the year ended December 31, 2018. The increase was the result of income recognized related to a grant from the NIH to reimburse the costs of our long-term toxicology studies in rats and dogs, which studies began in November 2019.

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 December 31, 2019, our principal source of liquidity was our cash, which totaled $56,250.

Equity Financings

For the years ended December 31, 2019 and 2018, we received net proceeds of $0 and $246,449, respectively, from the sale of common stock and redeemable convertible preferred stock.

We closed our IPO on January 31, 2020, raising gross proceeds of $13.8 million and net proceeds of $12.1 million, after deducting underwriting discounts and commissions and offering expenses.

Debt Financings

At December 31, 2019, we had outstanding $530,000 principal amount of convertible promissory notes, which were issued in March 2019. We had no debt outstanding during the year ended December 31, 2018. Upon the closing of our IPO on January 31, 2020, the outstanding convertible promissory notes plus accrued interest converted into 118,470 shares of our common stock at a 20% discount to the public offering price.

Future Capital Requirements

We expect that the net proceeds from our IPO 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 ANVS401 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.

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.

Cash Flows

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

	Year Ended December 31,	
	2019	2018
	(in thousands)	
Statement of Cash Flows Data:		
Total net cash provided by (used in):		
Operating activities	$ (476.5)	$ (558.6)
Financing activities	443.1	246.4
Increase (decrease) in cash and cash equivalents	$ (33.4)	$ (312.2)

Years ended December 31, 2019 and 2018

Operating Activities

For the year ended December 31, 2019, cash used in operations was $476.5 thousand compared to $558.6 thousand for the year ended December 31, 2018. The decrease in cash used in operations was primarily the result of the increase in accounts payable and accrued expense balances from 2018.

We expect cash used in operating activities to increase in 2020 as compared to 2019 due to an expected increase in our operating losses associated with ongoing development of our product candidates and additional costs associated with being a public company.

Financing Activities

Cash provided by financing activities was $443.1 thousand during the year ended December 31, 2019, attributable to $530.0 thousand proceeds from the sale of convertible promissory notes partially offset by the payment of $78.6 thousand deferred offering costs associated with our IPO and $8.3 thousand of fees on the issuance of the convertible promissory notes. Cash provided by financing activities was $246.4 thousand during the year ended December 31, 2018, attributable to $243.6 thousand from the sale of 270,722 shares of our Series A-1 Preferred Stock and $2.8 thousand from the sale of 14,286 shares of our common stock.

We completed our IPO on January 31, 2020, raising gross proceeds of $13.8 million and net proceeds of $12.1 million, after deducting underwriting discounts and commissions and offering expenses.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements, except for short-term 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 Financial Accounting Standards Board ("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 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 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.

In December 2019, the FASB issued ASU No. 2019-12, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes. The amendments in ASU 2019-12 simplify the accounting for income taxes by removing certain exceptions to the general principles in Topic 740 and clarifying and amending existing guidance. The new standard is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2020, with early adoption permitted. We are currently evaluating ASU 2019-12 but do not believe the adoption of this standard will have a significant impact on our financial statements.

Significant Contractual Obligations and Commitments

We lease our office facilities under a month-to-month operating lease.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements, as defined by applicable SEC regulations.

JOBS Act

Section 107 of the JOBS Act also provides that an "emerging growth company" can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. In other words, an "emerging growth company" can delay the adoption of new or revised accounting standards until those standards would otherwise 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.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

This item is not required for smaller reporting companies.

Item 8. Financial Statements and Supplementary Data.

Our financial statements, accompanying notes and Report of Independent Registered Public Accounting Firm are included in this Annual Report on Form 10-K beginning on page F-1, which are incorporated in this Item 8 by reference.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of the end of the period covered by this Annual Report on Form 10-K. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost benefit relationship of possible controls and procedures. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of the end of the period covered by this report, our disclosure controls and procedures were effective to ensure that the information required to be disclosed by us in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in SEC rules and forms, and that information required to be disclosed in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as our principal financial and accounting officer, to allow timely decisions regarding required disclosures.

Management's Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

Changes in Internal Control Over Financial Reporting

There was no change in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(f) of the Exchange Act that occurred during the quarter ended December 31, 2019 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

Compensatory Arrangements of Certain Officers

We have entered into employment agreements with our Named Executive Officers, which include provisions regarding post termination compensation. We do not have a formal severance policy or plan applicable to our executive officers as a group. The following summaries of the employment agreements are qualified in their entirety by reference to the text of the employment agreements, as amended, which are filed as exhibits to this Annual Report on Form 10-K.

Maccecchini Employment Agreement

On March 24, 2020, we entered into a second amended and restated employment agreement with Maria L. Maccecchini, our President and Chief Executive Officer. The principal terms of Dr. Maccecchini's employment agreement are as follows:

- base salary of $420,000 per year, subject to annual review;
- annual performance bonus in an amount up to 50.0% of base salary based on the achievement of certain performance goals established by our board of directors (the "Board"), and such bonus may be paid in cash or equity as determined by the Board;
- on or before April 30, 2020, we will grant an equity incentive award of 300,000 shares of our common stock in such form as shall be determined by our Board, upon consultation with Dr. Maccecchini, of which all such shares vest in full upon grant;
- on or after January 1, 2021 and on or before April 30, 2021, we will grant an equity incentive award of 112,995 shares of our common stock in such form as shall be determined by our Board, upon consultation with Dr. Maccecchini, all of which shall vest in full upon grant; and
- Dr. Maccecchini is eligible to receive an additional equity incentive award for 165,199 shares of common stock in the Board's discretion upon completion of an additional capital raise prior to April 30, 2021, subject to the approval, if required, by stockholders of additional shares under our equity incentive plan. Such award will vest in two equal installments on March 31, 2022 and March 31, 2023.

The employment agreement has a term commencing on the date thereof and continuing until terminated (i) upon death or disability, (ii) for cause, (iii) with good reason or without cause, or (iv) voluntarily. Upon a termination of Dr. Maccecchini's employment by us without cause or a resignation by Dr. Maccecchini for good reason, Dr. Maccecchini is eligible to receive a continuation of her base salary for twelve months, with such amount payable in a lump sum payment upon a change in control, as defined in the employment agreement, subject to her execution and delivery of a general release of claims. If such termination occurs upon or within twelve months after a change of control, Dr. Maccecchini will also be entitled to receive an amount equal to the projected target amount of her annual bonus for the calendar year in which her employment termination occurs payable in a single lump sum. Upon such termination, Dr. Maccecchini is also eligible to receive reimbursement for the medical insurance premiums at the same level as was in effect on the termination date until the earlier of (1) the end of such 12-month period or (2) the date she becomes eligible for medical benefits through another employer.

McGroarty Employment Agreement

On March 24, 2020, we entered into an employment agreement with Jeffrey McGroarty, our Chief Financial Officer. The principal terms of Mr. McGroarty's employment agreement are as follows:

- base salary of $300,000 per year, subject to annual review;
- annual performance bonus in an amount up to 50.0% of base salary based on the achievement of certain performance goals established by our Board or the compensation committee of the Board, and such bonus may be paid in cash or equity as determined by the Board;
- on or before April 30, 2020, we will grant an equity incentive award of 300,000 shares of our common stock in such form as shall be determined by our Board, upon consultation with Mr. McGroarty, of which 250,000 vest in full upon grant and the remaining 50,000 shall vest on April 30, 2021;
- on or after January 1, 2021 and on or before April 30, 2021, we will grant an equity incentive award of 30,396 shares of our common stock in such form as shall be determined by our Board, upon consultation with Mr. McGroarty, all of which shall vest in full upon grant; and
- Mr. McGroarty is eligible to receive an additional equity incentive award for 165,199 shares of common stock in the Board's discretion upon completion of an additional capital raise prior to April 30, 2021, subject to the approval, if required, by stockholders of additional shares under our equity incentive plan. Such award will vest in two equal installments on March 31, 2022 and March 31, 2023.

The employment agreement has a term commencing on the date thereof and continuing until terminated (i) upon death or disability, (ii) for cause, (iii) with good reason or without cause, or (iv) voluntarily. Upon a termination of Mr. McGroarty's employment by us without cause or a resignation by Mr. McGroarty for good reason, Mr. McGroarty is eligible to receive a continuation of his base salary for twelve months, with such amount payable in a lump sum payment upon a change in control, as defined in the employment agreement, subject to his execution and delivery of a general release of claims. If such termination occurs upon or within twelve months after a change of control, Mr. McGroarty will also be entitled to receive an amount equal to seventy-five percent of the projected target amount of his annual bonus for the calendar year in which his employment termination occurs payable in a single lump sum. Upon such termination, Mr. McGroarty is also eligible to receive reimbursement for the medical insurance premiums at the same level as was in effect on the termination date until the earlier of (1) the end of such 12-month period or (2) the date he becomes eligible for medical benefits through another employer.

PART III

Item 10. Directors and Executive Officers and Corporate Governance.

We incorporate the information required by this Item 10 by reference to the definitive proxy statement for our 2020 annual meeting of shareholders, to be filed with the SEC.

Item 11. Executive Compensation.

We incorporate the information required by this Item 11 by reference to the definitive proxy statement for our 2020 annual meeting of shareholders, to be filed with the SEC.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

We incorporate the information required by this Item 12 by reference to the definitive proxy statement for our 2020 annual meeting of shareholders, to be filed with the SEC.

Item 13. Certain Relationships and Related Transactions and Director Independence.

We incorporate the information required by this Item 13 by reference to the definitive proxy statement for our 2020 annual meeting of shareholders, to be filed with the SEC.

Item 14. Principal Accountants Fees and Services.

We incorporate the information required by this Item 14 by reference to the definitive proxy statement for our 2020 annual meeting of shareholders, to be filed with the SEC.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a) Documents filed as part of this report:

1. Financial Statements. The financial statements as set forth under Item 8 of this Annual Report on Form 10-K are incorporated herein.

2. Financial Statement Schedules. All financial statement schedules have been omitted because they are not applicable, not required, or the information is shown in the financial statements or related notes.

3. Exhibits. See (b) below.

(b) Exhibits:

Exhibit Number	Description of Exhibit
3.1	Amended and Restated Certificate of Incorporation of the Registrant. (Incorporated by reference to Exhibit 3.1 to Form 8-K filed February 6, 2020.)
3.2	Amended and Restated Bylaws of the Registrant. (Incorporated by reference to Exhibit 3.2 to Form 8-K filed February 6, 2020.)
4.1	Specimen Certificate evidencing shares of the Registrant's common stock. (Incorporated by reference to Exhibit 4.1 to Amendment No. 3 to Form S-1 filed September 20, 2019.)
4.2	Form of Warrant to purchase common stock issued to ThinkEquity, a division of Fordham Financial Management, Inc. in connection with the closing of the IPO
4.3	Description of Registrant's Securities
10.1+	Second Amended and Restated Employment Agreement dated as of March 24, 2020 between the Registrant and Maria Maccecchini.
10.2+	Annovis Bio, Inc. 2018 Equity Incentive Plan. (Incorporated by reference to Exhibit 10.2 to Form S-1 filed July 3, 2019.)
10.3	License Agreement dated as of November 10, 2008 between TorreyPines Therapeutics, Inc. and the Registrant. (Incorporated by reference to Exhibit 10.3 to Form S-1 filed July 3, 2019.)
10.4	License Agreement Amendment dated November 29, 2011 between Raptor Therapeutics, Inc. and the Registrant. (Incorporated by reference to Exhibit 10.4 to Form S-1 filed July 3, 2019.)
10.5	Registration Rights Agreement dated as of December 19, 2014 among the Registrant and the signatories thereto. (Incorporated by reference to Exhibit 10.5 to Amendment No. 1 to Form S-1 filed August 8, 2019.)
10.6	License Agreement Amendment No. 2 effective as of May 2, 2012 between Raptor Therapeutics and the Registrant. (Incorporated by reference to Exhibit 10.6 to Form S-1 filed July 3, 2019.)
10.7	Investigator-Initiated Clinical Trial Agreement dated June 27, 2016 between The Regents of the University of California and the Registrant. (Incorporated by reference to Exhibit 10.7 to Form S-1 filed July 3, 2019.)
10.8+	Annovis Bio, Inc. 2019 Equity Incentive Plan. (Incorporated by reference to Exhibit 10.8 to Amendment No. 1 to Form S-1 filed August 8, 2019.)
10.9+	Employment Agreement dated as of March 24, 2020 between the Registrant and Jeffrey McGroarty.
23.1	Consent of WithumSmith+Brown, PC.
24.1	Power of Attorney. (Included on signature page to this Annual Report on Form 10-K.)
31.1	Certification Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2	Certification Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

+ Indicates management contract or compensatory plan.

(b) Financial Statement Schedules

See index to financial statements on page F-1. All schedules have been omitted because they are not required or are not applicable.

(c) None.

Item 16. Form 10-K Summary.

None.

ANNOVIS BIO, INC.

Table of Contents

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders of Annovis Bio, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Annovis Bio, Inc. (the "Company"), as of December 31, 2019 and 2018, 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, 2019 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, 2019 and 2018, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2019, in conformity with accounting principles generally accepted in the United States of America.

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.

/s/ WithumSmith+Brown, PC

We have served as the Company's auditor since 2019.

East Brunswick, New Jersey
March 25, 2020

ANNOVIS BIO, INC.

Balance Sheets

	As of December 31,	
	2019	**2018**
Assets		
Current assets:		
Cash and cash equivalents	$ 1,858	$ 35,312
Grant receivable	735,075	—
Prepaid expenses and other current assets	10,579	15,680
Total current assets	747,512	50,992
Long-term assets:		
Deferred offering costs	369,595	—
Total long-term assets	369,595	—
Total assets	$ 1,117,107	$ 50,992
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 1,233,877	$ 68,425
Accrued expenses	776,871	499,518
Total current liabilities	2,010,748	567,943
Long-term liabilities:		
Derivative liability	106,000	—
Convertible promissory notes, net of unamortized deferred financing fees of $7,431 and debt discount of $22,762	499,807	—
Total long-term liabilities	605,807	—
Total liabilities	2,616,555	567,943
Commitments and contingencies (Note 8)		
Redeemable convertible preferred stock—$0.0001 par value:		
Series A - 5,133,159 shares authorized, issued and outstanding at December 31, 2019 and 2018	6,509,303	6,509,303
Series A-1 - 1,111,111 shares authorized at December 31, 2019 and 2018, and 630,722 shares issued and outstanding at December 31, 2019 and 2018	567,649	567,649
Stockholders' equity (deficit):		
Common stock - $0.0001 par value, 10,150,000 shares authorized at December 31, 2019 and 2018, and 282,614 shares issued and outstanding at December 31, 2019 and 2018	28	28
Additional paid-in capital	200,600	192,117
Accumulated deficit	(8,777,028)	(7,786,048)
Total stockholders' equity (deficit)	(8,576,400)	(7,593,903)
Total liabilities and stockholders' equity (deficit)	$ 1,117,107	$ 50,992

See accompanying notes to financial statements.

ANNOVIS BIO, INC.

Statements of Operations

	Year Ended December 31,	
	2019	**2018**
Operating expenses:		
Research and development	$ 776,256	$ 111,608
General and administrative	829,366	602,329
Total operating expenses	1,605,622	713,937
Operating loss	(1,605,622)	(713,937)
Other income (expense):		
Change in fair value of derivative liability	(79,500)	—
Interest income (expense), net	(40,933)	66
Grant income	735,075	—
Total other income (expense)	614,642	66
Loss before income taxes	(990,980)	(713,871)
Income tax expense (benefit)	—	—
Net loss	$ (990,980)	$ (713,871)
Basic and Diluted loss per common share	$ (3.51)	$ (2.57)
Weighted average number of common shares outstanding, basic and diluted	282,614	277,585

See accompanying notes to financial statements.

ANNOVIS BIO, INC.

Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)

	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, 2017	5,133,159	$ 6,509,303	360,000	$ 324,000	268,328	$ 27	$ 106,590	$ (7,072,177)	$ (6,965,560)
Issuance of preferred shares	—	—	270,722	243,649	—	—	—	—	—
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)
Share-based compensation expense	—	—	—	—	—	—	8,483	—	8,483
Net loss	—	—	—	—	—	—	—	(990,980)	(990,980)
Balance, December 31, 2019	5,133,159	$ 6,509,303	630,722	$ 567,649	282,614	$ 28	$ 200,600	$ (8,777,028)	$ (8,576,400)

See accompanying notes to financial statements.

ANNOVIS BIO, INC.

Statements of Cash Flows

	Year Ended December 31,	
	2019	**2018**
Cash flows from operating activities:		
Net loss	$ (990,980)	$ (713,871)
Adjustments to reconcile net loss to net cash used in operating activities:		
Amortization of deferred financing fees	1,191	—
Amortization of debt discount	3,738	—
Share-based compensation expense	8,483	82,728
Change in fair value of derivative liability	79,500	—
Changes in assets and liabilities:		
Grant receivable	(735,075)	—
Prepaid expenses and other current assets	5,101	(5,189)
Accounts payable	969,091	(2,682)
Accrued expenses	182,409	80,405
Net cash used in operating activities	(476,542)	(558,609)
Cash flows from financing activities:		
Proceeds from issuance of common shares	—	2,800
Proceeds from issuance of convertible promissory notes	530,000	—
Proceeds from issuance of preferred shares	—	243,649
Payment of deferred offering costs	(78,611)	—
Payment of deferred financing fees	(8,301)	—
Net cash provided by financing activities	443,088	246,449
Net decrease in cash	(33,454)	(312,160)
Cash and cash equivalents, beginning of year	35,312	347,472
Cash and cash equivalents, end of year	$ 1,858	$ 35,312
Supplemental disclosure of cash flow information		
Deferred offering costs in accounts payable and accrued expenses	$ 290,984	$ —
Deferred financing fees in accounts payable and accrued expenses	$ 321	$ —

See accompanying notes to financial statements.

(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. Annovis is a clinical-stage drug platform company addressing neurodegeneration such as Alzheimer's disease ("AD"), Parkinson's disease ("PD") and Alzheimer's disease in Down syndrome ("AD-DS"). The Company's lead compound, ANVS401, is a small molecule administered orally that attacks neurodegeneration by entering the brain and inhibiting the translation of multiple neurotoxic proteins thereby improving axonal 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.

The Company incurred a net loss of $990,980 and $713,871for the years ended December 31, 2019 and 2018, respectively, and had an accumulated deficit of $8,777,028 as of December 31, 2019. The Company anticipates incurring additional losses until such time, if ever, that it can generate significant revenue from its product candidates currently in development. The Company's primary source of capital has been the issuance of equity securities.

On January 31, 2020, the Company completed its initial public offering (the "IPO") (see Note 14 – Subsequent Events). As of the date these financial statements are issued, management believes that the net proceeds from the Company's initial public offering, grant funding and the current cash and cash equivalents are sufficient to fund operations and capital requirements for at least the next 12 months. The Company will need to raise additional capital 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").

(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 share-based compensation expense, the valuation of the 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 Net Income (Loss) per Share

Basic net income (loss) per share is determined using the weighted average number of shares of common stock outstanding during each period. Diluted net income (loss) per share includes the effect, if any, from the potential exercise or conversion of securities, such as redeemable convertible preferred stock, convertible promissory notes and stock options, which would result in the issuance of incremental shares of common stock. The computation of diluted net income (loss) per shares does not include the conversion of securities that would have an anti-dilutive effect.

(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 $1,858 and $35,312 as of December 31, 2019 and 2018, respectively, which does not exceed the FDIC coverage limit of $250,000.

(e) Deferred Offering Costs

Included in long-term assets, are costs incurred in connection with our IPO and primarily consist of direct incremental legal, printing and accounting fees (see Note 14). These costs are capitalized as incurred and will be offset against proceeds in the period in which the IPO is completed. As of December 31, 2019, the deferred offering costs amounted to $369,595. 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 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.

(h) Grant Income

Grants received are recognized as grant income in the statements of operations as and when they are earned for the specific research and development projects for which these grants are designated. Grants payments received in excess of grant income earned are recognized as deferred grant on the balance sheet and grant income earned in excess of grant payments received is recognized as grant receivable on the balance sheets.

(i) 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. Forfeitures are recognized in compensation expense in the period when they occur.

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 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.

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.

Upon exercise of stock options, the Company issues shares first from treasury stock, if available, then from authorized but unissued shares.

(j) 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, 2019 and 2018, the Company had a full valuation allowance against deferred tax assets.

The Company is subject to the provisions of ASC 740, Income Taxes, which 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, 2019 or December 31, 2018.

(k) 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, 2020 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 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 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 Cuts and Jobs Act of 2107 (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 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.

In December 2019, the FASB issued ASU No. 2019-12, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes. The amendments in ASU 2019-12 simplify the accounting for income taxes by removing certain exceptions to the general principles in Topic 740 and clarifying and amending existing guidance. The new standard is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2020, with early adoption permitted. The Company is currently evaluating ASU 2019-12 but does not believe the adoption of this standard will have a significant impact on its financial statements.

(l) Reverse Stock Split

On July 31, 2019, the board of directors (the "Board") 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 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 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 December 31, 2019 and December 31, 2018:

		Fair Value Measurement at December 31, 2019		
	Carrying Value	Level 1	Level 2	Level 3
Cash and cash equivalents	$ 1,858	$ 1,858	$ —	$ —
Derivative liability	$ 106,000	$ —	$ —	$ 106,000

		Fair Value Measurement at December 31, 2018		
	Carrying Value	Level 1	Level 2	Level 3
Cash and cash equivalents	$ 35,312	$ 35,312	$ —	$ —

The derivative liability is associated with the March 2019 issuance of convertible promissory notes (see Note 7). The Company computed the 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 December 31, 2019 was $106,000. The change in the fair value of the derivative liability is reflected in the statement of operations for the year ended December 31, 2019.

(4) Grant Receivable

In September 2019, the Company received a Notice of Award for a $1.7 million grant from the National Institute on Aging of the National Institutes of Health (the "NIH") to cover costs of long-term chronic toxicology studies of ANVS401 in rats and dogs. The Company began the long-term chronic toxicology studies in November 2019 and recognized grant income of $735,075 for the year ended December 31, 2019 in connection with the NIH grant. The Company received no payments under the grant during the year ended December 31, 2019 and recorded a grant receivable of $735,075 as of December 31, 2019 to reflect unreimbursed, eligible costs incurred under the grant.

(5) Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following:

	As of December 31,	
	2019	2018
Prepaid rent	$ —	$ 1,904
Prepaid research and development	—	4,976
Prepaid expenses	4,135	5,000
Security deposit	6,444	3,800
Total prepaid expenses and other current assets	$ 10,579	$ 15,680

(6) Accrued Expenses

Accrued expenses consisted of the following:

	As of December 31,	
	2019	2018
Payroll and related benefits	$ 131,530	$ 21,640
Accrued interest expense	36,041	—
Accrued professional fees	103,300	17,878
Accrued license payments	506,000	460,000
	$ 776,871	$ 499,518

See Note 8 for further detail on the accrued license payments.

(7) 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) the sale of substantially all of the assets of the Company in which the Company's stockholders own less than 50% of the equity securities after the event; or (iii) a liquidation of the Company.

Effective upon the closing of a Qualified Financing, the principal and accrued interest of the notes will convert into the equity security issued by the Company at a 20% discount from the price of the security issued and on the same terms as the security. A Qualified Financing means an IPO with a total offering of at least $8.0 million or the issuance of at least $8.0 million of preferred stock of the Company for new money. Effective upon any other financing, each holder of the Notes has the right to convert into shares of the security at the same per share purchase price as the security issued. On January 31, 2020, the Company closed its IPO and the outstanding Notes plus accrued interest converted into 118,470 shares of Company common stock (see Note 14).

The Company incurred costs of $8,622 in connection with the issuance 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. The Company is amortizing the deferred financing fees and debt discount over the term of the Notes as additional interest expense using the effective interest method. For the year ended December 31, 2019, the Company recognized interest expense of $36,041 related to the contractual 8% coupon, $1,191 related to the amortization of deferred financing fees and $3,738 related to the amortization of the debt discount. The effective interest rate on the Notes was 9.8%. The Company made no cash payments for interest during the year ended December 31, 2019.

(8) Commitments and Contingencies

(a) Leases

The Company leases its office facilities under a month-to-month operating lease. Total rental expense was $34,351 and $22,372 for the years ended December 31, 2019 and 2018, respectively.

(b) License Agreements

In November 2008, the Company licensed the rights to certain chemical compounds, know-how and intellectual property rights that may be suitable for the development of human therapeutics. Currently, the intellectual property rights are owned by a subsidiary of Horizon Therapeutics, PLC ("Licensor"). Payments by the Company under the license agreement include a one-time non-refundable fee of $50,000, a minimum annual commitment of $40,000 commencing in 2009, milestone payments upon attainment of certain milestone events, royalties based on net sales of products covered by the patent-related rights and a portion of any sublicense income received by the Company. The Company is responsible for the development and commercialization of the licensed products.

In May 2012, such license agreement was amended. The minimum annual commitment was increased to $46,000 and may be deferred by the Company until the Company raises at least $2 million in equity financing, then the aggregate annual payments of all amounts will become payable.

At December 31, 2019 and December 31, 2018, the Company had accrued $506,000 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.

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, 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 agreements with its executive officers that provide for severance payments to the employee upon termination of the agreement by the Company for any reason other than for cause, death or disability or by the employee for good reason The maximum aggregate severance payments under the agreements were approximately $120,000 at December 31, 2019. In March 2020, the Company entered into new employment agreements with its executive officers. The maximum aggregate severance payments under the agreements are approximately $720,000.

(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, 2019 and December 31, 2018, the Company did not have any pending legal actions.

(9) 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 December 31, 2019 and 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 December 31, 2019 and 2018.

b) Common Stock:

a. Dividends:

Subject to the rights of holders of Preferred Stock, the holders of the Common Stock are entitled to receive dividends as declared from time to time by the Board.

b. Liquidation:

Subject to the rights of holders of Preferred Stock as to liquidation, upon the liquidation, dissolution or winding up of the Corporation, the remaining assets of the Corporation will be distributed to the holders of Common Stock.

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 are 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 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.

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 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. On January 31, 2020, the Company closed its IPO and the outstanding Preferred Stock converted into 4,117,089 shares of Company common stock (see Note 14).

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.

(10) Share-Based Compensation

In April 2018, the Board approved the 2018 Equity Incentive Plan (the "2018 Plan") as the successor to the Company's Amended and Restated 2008 Equity Incentive Plan (the "2008 Plan") authorizing 376,123 shares to be issued (18,980 shares remaining available for issuance under the 2008 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, 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, 2019, and 2018, 382,563 and 381,280 stock options were available for future grants.

Effective upon the closing of the Company's IPO on January 31, 2020, the Company's 2019 Equity Incentive Plan (the "2019 Plan") became effective, succeeding the 2018 Plan (see Note 14). Under the 2019 Plan, 1,000,000 shares are authorized to be issued and no new options may be issued under the 2018 Plan, although shares subject to grants which are cancelled or forfeited will again be available under the 2019 Plan.

As of December 31, 2019, and 2018, 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, 2017	249,206	$ 0.16	
Granted	123,800	0.25	
Exercised	(14,284)	0.20	
Forfeited	(5,157)	0.08	
Outstanding at December 31, 2018	353,565	0.19	
Granted	—	—	
Exercised	—	—	
Forfeited	(1,283)	0.14	
Outstanding at December 31, 2019	352,282	0.19	7.2
Exercisable at December 31, 2019	352,282	0.19	7.2

The aggregate intrinsic value of options outstanding and exercisable was $1,624,472 as of December 31, 2019.

There were no options issued during the year ended December 31, 2019 and 123,800 options were issued for the year ended December 31, 2018. The weighted average grant date fair value of options issued during the year ended December 31, 2018 was $0.71. The fair value was estimated using the Black Sholes option pricing model using the following weighted average assumptions:

	Year Ended December 31, 2018
Risk-free interest rate	2.58%
Expected life	5.15
Expected volatility	75%
Expected dividend yield	—

Share-based compensation expense for the years ended December, 2019 and 2018 was $8,483 and $82,728, respectively. As of December 31, 2019 there was no unrecognized compensation expense related to unvested options.

(11) Net Loss Per Share

The Company has reported a net loss for the years ended December 31, 2019 and 2018, 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, convertible promissory notes 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:

	Year Ended December 31,	
	2019	2018
Numerator		
Net loss	$ (990,980)	$ (713,871)
Denominator		
Weighted-average common shares outstanding, basic and diluted	282,614	277,585
Net loss per share attributable to common stockholders, basic and diluted	$ (3.51)	$ (2.57)

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:

	Year Ended December 31,	
	2019	2018
Redeemable convertible preferred stock, as converted	4,117,089	4,117,089
Stock options	352,282	353,565

(12) Income Taxes

The federal and state provision (benefit) for income taxes was $0 for the years ended December 31, 2019 and 2018.

A reconciliation of income tax benefit computed at the statutory federal income tax rate to income taxes as reflected in the financial statements for the years ended December 31, 2019 and 2018 is as follows:

	Year Ended December 31,	
	2019	**2018**
Federal income tax benefit at statutory rate	21.0%	21.0%
State and local tax, net of federal benefit	8.0%	7.5%
Permanent differences	0.4%	(1.3)%
Change in valuation allowance	(29.4)%	(27.1)%
Effective Income Tax rate	0.0%	0.0%

Deferred taxes are recognized for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. The significant components of the Company's deferred tax assets are comprised of the following:

	As of December 31,	
	2019	2018
Net operating loss carryforwards	$ 1,430,716	$ 1,181,738
Stock compensation	37,708	19,160
Convertible debt	24,049	—
R&D credit carryforward	137,826	137,826
Total deferred tax assets	1,630,299	1,338,724
Less valuation allowance	(1,630,299)	(1,338,724)
Net deferred taxes	$ —	$ —

As of December 31, 2019, the Company had U.S. federal net operating loss carryforwards of $4,256,228, 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 2032. The remaining $1,491,988 of federal net operating loss carryforwards generated in 2018 and later, do not expire but are limited 80% of taxable income in future years. As of December 31, 2019, the Company also had U.S. state net operating loss carryforwards of $6,803,111 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, 2019 and 2018 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 $291,575 and $188,205 in the years ended December 31, 2019 and 2018, respectively.

As of December 31, 2019, 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. On January 31, 2020, the Company closed its IPO and issued 2,300,000 new shares of common stock (see Note 14).

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 2016 to the present remain open for review. All open years may be examined to the extent that tax credits or net operating loss carryforwards are used in future periods. The Company will recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 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.

(13) Related-Party Transactions

As discussed in Note 7, 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. On January 31, 2020, the Company closed its IPO and the outstanding Notes plus accrued interest held by directors converted into 71,429 shares of Company common stock (see Note 14).

(14) Subsequent Events

On January 28, 2020, the Company announced the pricing of its IPO of 2,000,000 shares of its common stock at an initial offering price of $6.00 per share. In addition, the Company granted the underwriters a 45-day option to purchase up to an additional 300,000 shares of common stock at the public offering price. The Company's common stock commenced trading on the NYSE American on January 29, 2020 under the ticker symbol "ANVS". The IPO closed on January 31, 2020 at which time the underwriters exercised their option to purchase 300,000 additional shares of the Company's common stock bringing the total number of shares of common stock sold by the Company to 2,300,000 shares. The gross proceeds from the IPO, including proceeds from the exercise of the underwriters' option to purchase additional shares, were approximately $13.8 million. The net proceeds of the IPO were approximately $12.1 million after deducting underwriting discounts, commissions and offering expenses payable by the Company. In conjunction with the IPO, the Company granted the underwriters 100,000 warrants to purchase shares of Company common stock at an exercise price of $7.50 per share, which is 125% of initial public offering price. Upon the closing of the IPO, outstanding Preferred Stock and Notes converted into shares of Company common stock totaling 4,117,089 and 118,470, respectively.

Effective January 31, 2020, the Company's 2019 Plan became effective (see Note 10).

In March 2020, the Company entered into new employment agreements with its executive officers (see Note 8).

SIGNATURES

In accordance with the requirements Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ANNOVIS BIO, INC.

By: /s/ MARIA MACCECCHINI
Name: Maria Maccecchini
Title: *President and Chief Executive Officer*

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated. Each of the undersigned hereby constitute and appoint Maria Maccecchini and Jeffrey McGroarty, and each of them, his or her true and lawful attorneys-in-fact and agents, with full and several power of substitution and resubstitution, for him or her and in his or her name, place and stead in any and all capacities, to sign one or more amendments to this Annual Report on Form 10-K, each in such form as they or any one of them may approve, and to file the same with all exhibits thereto and other documents in connection therewith with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done so that this Annual Report and any amendments shall comply with the Securities Exchange Act of 1934, as amended, and the applicable rules and regulations adopted or issued pursuant thereto, as fully and to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them or their substitute or resubstitute, may lawfully do or cause to be done by virtue hereof.

Signature	Title	Date
/s/ MARIA MACCECCHINI Maria Maccecchini	President and Chief Executive Officer (principal executive officer)	March 25, 2020
/s/ JEFFREY MCGROARTY Jeffrey McGroarty	Chief Financial Officer (principal financial and accounting officer)	March 25, 2020
/s/ MICHAEL HOFFMAN Michael Hoffman	Chairman of the Board and Director	March 25, 2020
/s/ CLAUDINE BRUCK Claudine Bruck	Director	March 25, 2020
/s/ ROBERT WHELAN Robert Whelan	Director	March 25, 2020
/s/ MARK WHITE Mark White	Director	March 25, 2020

THE REGISTERED HOLDER OF THIS PURCHASE WARRANT BY ITS ACCEPTANCE HEREOF, AGREES THAT IT WILL NOT SELL, TRANSFER OR ASSIGN THIS PURCHASE WARRANT EXCEPT AS HEREIN PROVIDED AND THE REGISTERED HOLDER OF THIS PURCHASE WARRANT AGREES THAT IT WILL NOT SELL, TRANSFER, ASSIGN, PLEDGE OR HYPOTHECATE THIS PURCHASE WARRANT FOR A PERIOD OF ONE HUNDRED EIGHTY DAYS FOLLOWING THE DATE OF THE UNDERWRITING AGREEMENT (DEFINED BELOW) TO ANYONE OTHER THAN (I) THINKEQUITY, A DIVISION OF FORDHAM FINANCIAL MANAGEMENT, INC., OR AN UNDERWRITER OR A SELECTED DEALER IN CONNECTION WITH THE OFFERING, OR (II) A BONA FIDE OFFICER OR PARTNER OF THINKEQUITY, A DIVISION OF FORDHAM FINANCIAL MANAGEMENT, INC., OR OF ANY SUCH UNDERWRITER OR SELECTED DEALER.

THIS PURCHASE WARRANT IS NOT EXERCISABLE PRIOR TO JANUARY 29, 2021. VOID AFTER 5:00 P.M., EASTERN TIME, JANUARY 28, 2025.

WARRANT TO PURCHASE COMMON STOCK

ANNOVIS BIO, INC.

Warrant Shares: 100,000

Initial Exercise Date: January 29, 2021

THIS WARRANT TO PURCHASE COMMON STOCK (the "Warrant") certifies that, for value received, ThinkEquity, a division of Fordham Financial Management, Inc. or its assigns (the "Holder") is entitled, upon the terms and subject to the limitations on exercise and the conditions hereinafter set forth, at any time on or after January 29, 2021 (the "Initial Exercise Date") and, in accordance with FINRA Rule 5110(f)(2)(G)(i), prior to at 5:00 p.m. (New York time) on the date (such date, the "Termination Date") that is five (5) years following the effective date of the offering , but not thereafter, to subscribe for and purchase from Annovis Bio, Inc., a Delaware corporation (the "Company"), up to 100,000 shares of Common Stock, par value $0.0001 per share, of the Company (the "Warrant Shares"), as subject to adjustment hereunder. The purchase price of one share of Common Stock under this Warrant shall be equal to the Exercise Price, as defined in Section 2(b).

Section 1. Definitions. In addition to the terms defined elsewhere in this Agreement, the following terms have the meanings indicated in this Section 1:

"Affiliate" means any Person that, directly or indirectly through one or more intermediaries, controls or is controlled by or is under common control with a Person, as such terms are used in and construed under Rule 405 under the Securities Act.

"Business Day" means any day except any Saturday, any Sunday, any day which is a federal legal holiday in the United States or any day on which banking institutions in the State of New York are authorized or required by law or other governmental action to close.

"Commission" means the United States Securities and Exchange Commission.

"Exchange Act" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

"Person" means an individual or corporation, partnership, trust, incorporated or unincorporated association, joint venture, limited liability company, joint stock company, government (or an agency or subdivision thereof) or other entity of any kind.

"Rule 144" means Rule 144 promulgated by the Commission pursuant to the Securities Act, as such Rule may be amended or interpreted from time to time, or any similar rule or regulation hereafter adopted by the Commission having substantially the same purpose and effect as such Rule.

"Securities Act" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

"Trading Day" means a day on which the New York Stock Exchange is open for trading.

"Trading Market" means any of the following markets or exchanges on which the Common Stock is listed or quoted for trading on the date in question: the NYSE American, the Nasdaq Capital Market, the Nasdaq Global Market, the Nasdaq Global Select Market, or the New York Stock Exchange (or any successors to any of the foregoing).

"VWAP" means, for any date, the price determined by the first of the following clauses that applies: (a) if the Common Stock then listed or quoted on a Trading Market, the daily volume weighted average price of the Common Stock for such date (or the nearest preceding date) on the Trading Market on which the Common Stock is then listed or quoted as reported by Bloomberg L.P. (based on a Trading Day from 9:30 a.m. (New York City time) to 4:02 p.m. (New York City time)), (b) if OTCQB or OTCQX is not a Trading Market, the volume weighted average price of a share of Common Stock for such date (or the nearest preceding date) on the OTCQB or OTCQX as applicable, (c) if Common Stock is not then listed or quoted for trading on the OTCQB or OTCQX and if prices for Common Stock are then reported in the "Pink Sheets" published by OTC Markets Group, Inc. (or a similar organization or agency succeeding to its functions of reporting prices), the most recent bid price per share of Common Stock so reported, or (d) in all other cases, the fair market value of the Common Stock as determined by an independent appraiser selected in good faith by the Holder and reasonably acceptable to the Company, the fees and expenses of which shall be paid by the Company.

Section 2. Exercise.

a. Exercise of the purchase rights represented by this Warrant may be made, in whole or in part, at any time or times on or after the Initial Exercise Date and on or before the Termination Date by delivery to the Company (or such other office or agency of the Company as it may designate by notice in writing to the registered Holder at the address of the Holder appearing on the books of the Company) of a duly executed facsimile copy (or e-mail attachment) of the Notice of Exercise Form annexed hereto. Within two (2) Trading Days following the date of exercise as aforesaid, the Holder shall deliver the aggregate Exercise Price for the shares specified in the applicable Notice of Exercise by wire transfer or cashier's check drawn on a United States bank unless the cashless exercise procedure specified in Section 2(c) below is specified in the applicable Notice of Exercise. No ink-original Notice of Exercise shall be required, nor shall any medallion guarantee (or other type of guarantee or notarization) of any Notice of Exercise form be required. Notwithstanding anything herein to the contrary, the Holder shall not be required to physically surrender this Warrant to the Company until the Holder has purchased all of the Warrant Shares available hereunder and the Warrant has been exercised in full, in which case, the Holder shall surrender this Warrant to the Company for cancellation within five (5) Trading Days of the date the final Notice of Exercise is delivered to the Company. Partial exercises of this Warrant resulting in purchases of a portion of the total number of Warrant Shares available hereunder shall have the effect of lowering the outstanding number of Warrant Shares purchasable hereunder in an amount equal to the applicable number of Warrant Shares purchased. The Holder and the Company shall maintain records showing the number of Warrant Shares purchased and the date of such purchases. The Company shall deliver any objection to any Notice of Exercise Form within three (3) Business Days of receipt of such notice. **The Holder and any assignee, by acceptance of this Warrant, acknowledge and agree that, by reason of the provisions of this paragraph, following the purchase of a portion of the Warrant Shares hereunder, the number of Warrant Shares available for purchase hereunder at any given time may be less than the amount stated on the face hereof.**

b. Exercise Price. The exercise price per share of the Common Stock under this Warrant shall be **$7.50**, subject to adjustment hereunder (the "Exercise Price").

c. Cashless Exercise. If at any time on or after the Initial Exercise Date, there is no effective registration statement registering, or the prospectus contained therein is not available for the issuance of the Warrant Shares to the Holder, then this Warrant may also be exercised, in whole or in part, at such time by means of a "cashless exercise" in which the Holder shall be entitled to receive the number of Warrant Shares equal to the quotient obtained by dividing [(A-B) (X)] by (A), where:

(A) = the VWAP on the Trading Day immediately preceding the date on which Holder elects to exercise this Warrant by means of a "cashless exercise," as set forth in the applicable Notice of Exercise;

(B) = the Exercise Price of this Warrant, as adjusted hereunder; and

(X) = the number of Warrant Shares that would be issuable upon exercise of this Warrant in accordance with the terms of this Warrant if such exercise were by means of a cash exercise rather than a cashless exercise.

If Warrant Shares are issued in such a "cashless exercise," the parties acknowledge and agree that in accordance with Section 3(a)(9) of the Securities Act, the Warrant Shares shall take on the registered characteristics of the Warrants being exercised, and the holding period of the Warrants being exercised may be tacked on to the holding period of the Warrant Shares. The Company agrees not to take any position contrary to this Section 2(c).

Notwithstanding anything herein to the contrary, on the Termination Date, this Warrant shall be automatically exercised via cashless exercise pursuant to this Section 2(c).

d. Mechanics of Exercise.

i. Delivery of Warrant Shares Upon Exercise. The Company shall cause the Warrant Shares purchased hereunder to be transmitted by its transfer agent to the Holder by crediting the account of the Holder's or its designee's balance account with The Depository Trust Company through its Deposit or Withdrawal at Custodian system ("DWAC") if the Company is then a participant in such system and either (A) there is an effective registration statement permitting the issuance of the Warrant Shares to or resale of the Warrant Shares by Holder, or (B) the Warrant Shares are eligible for resale by the Holder without volume or manner-of-sale limitations pursuant to Rule 144 and, in either case, the Warrant Shares have been sold by the Holder prior to the Warrant Share Delivery Date (as defined below), and otherwise by physical delivery of a certificate, registered in the Company's share register in the name of the Holder or its designee, for the number of Warrant Shares to which the Holder is entitled pursuant to such exercise to the address specified by the Holder in the Notice of Exercise by the date that is two (2) Trading Days after the delivery to the Company of the Notice of Exercise (such date, the "Warrant Share Delivery Date"). If the Warrant Shares can be delivered via DWAC, the transfer agent shall have received from the Company, at the expense of the Company, any legal opinions or other documentation required by it to deliver such Warrant Shares without legend (subject to receipt by the Company of reasonable back up documentation from the Holder, including with respect to affiliate status) and, if applicable and requested by the Company prior to the Warrant Share Delivery Date, the transfer agent shall have received from the Holder a confirmation of sale of the Warrant Shares (provided the requirement of the Holder to provide a confirmation as to the sale of Warrant Shares shall not be applicable to the issuance of unlegended Warrant Shares upon a cashless exercise of this Warrant if the Warrant Shares are then eligible for resale pursuant to Rule 144(b)(1)). The Warrant Shares shall be deemed to have been issued, and Holder or any other person so designated to be named therein shall be deemed to have become a holder of record of such shares for all purposes, as of the date the Warrant has been exercised, with payment to the Company of the Exercise Price (or by cashless exercise, if permitted) and all taxes required to be paid by the Holder, if any, pursuant to Section 2(d)(vi) prior to the issuance of such shares, having been paid. If the Company fails for any reason to deliver to the Holder the Warrant Shares subject to a Notice of Exercise by the second Trading Day following the Warrant Share Delivery Date, the Company shall pay to the Holder, in cash, as liquidated damages and not as a penalty, for each $1,000 of Warrant Shares subject to such exercise (based on the VWAP of the Common Stock on the date of the applicable Notice of Exercise), $10 per Trading Day (increasing to $20 per Trading Day on the fifth Trading Day after such liquidated damages begin to accrue) for each Trading Day after the second Trading Day following such Warrant Share Delivery Date until such Warrant Shares are delivered or Holder rescinds such exercise.

ii. Delivery of New Warrants Upon Exercise. If this Warrant shall have been exercised in part, the Company shall, at the request of a Holder and upon surrender of this Warrant certificate, at the time of delivery of the Warrant Shares, deliver to the Holder a new Warrant evidencing the rights of the Holder to purchase the unpurchased Warrant Shares called for by this Warrant, which new Warrant shall in all other respects be identical with this Warrant.

iii. Rescission Rights. If the Company fails to cause its transfer agent to deliver to the Holder the Warrant Shares pursuant to Section 2(d)(i) by the Warrant Share Delivery Date, then the Holder will have the right to rescind such exercise; provided, however, that the Holder shall be required to return any Warrant Shares or Common Stock subject to any such rescinded exercise notice concurrently with the return to Holder of the aggregate Exercise Price paid to the Company for such Warrant Shares and the restoration of Holder's right to acquire such Warrant Shares pursuant to this Warrant (including, issuance of a replacement warrant certificate evidencing such restored right).

iv. Compensation for Buy-In on Failure to Timely Deliver Warrant Shares Upon Exercise. In addition to any other rights available to the Holder, if the Company fails to cause its transfer agent to transmit to the Holder the Warrant Shares pursuant to an exercise on or before the Warrant Share Delivery Date, and if after such date the Holder is required by its broker to purchase (in an open market transaction or otherwise) or the Holder's brokerage firm otherwise purchases, shares of Common Stock to deliver in satisfaction of a sale by the Holder of the Warrant Shares which the Holder anticipated receiving upon such exercise (a "Buy-In"), then the Company shall (A) pay in cash to the Holder the amount, if any, by which (x) the Holder's total purchase price (including brokerage commissions, if any) for the shares of Common Stock so purchased exceeds (y) the amount obtained by multiplying (1) the number of Warrant Shares that the Company was required to deliver to the Holder in connection with the exercise at issue times (2) the price at which the sell order giving rise to such purchase obligation was executed, and (B) at the option of the Holder, either reinstate the portion of the Warrant and equivalent number of Warrant Shares for which such exercise was not honored (in which case such exercise shall be deemed rescinded) or deliver to the Holder the number of shares of Common Stock that would have been issued had the Company timely complied with its exercise and delivery obligations hereunder. For example, if the Holder purchases Common Stock having a total purchase price of $11,000 to cover a Buy-In with respect to an attempted exercise of shares of Common Stock with an aggregate sale price giving rise to such purchase obligation of $10,000, under clause (A) of the immediately preceding sentence the Company shall be required to pay the Holder $1,000. The Holder shall provide the Company written notice indicating the amounts payable to the Holder in respect of the Buy-In and, upon request of the Company, evidence of the amount of such loss. Nothing herein shall limit a Holder's right to pursue any other remedies available to it hereunder, at law or in equity including, without limitation, a decree of specific performance and/or injunctive relief with respect to the Company's failure to timely deliver shares of Common Stock upon exercise of the Warrant as required pursuant to the terms hereof.

v. No Fractional Shares or Scrip. No fractional shares or scrip representing fractional shares shall be issued upon the exercise of this Warrant. As to any fraction of a share which the Holder would otherwise be entitled to purchase upon such exercise, the Company shall, at its election, either pay a cash adjustment in respect of such final fraction in an amount equal to such fraction multiplied by the Exercise Price or round up to the next whole share.

vi. Charges, Taxes and Expenses. Issuance of Warrant Shares shall be made without charge to the Holder for any issue or transfer tax or other incidental expense in respect of the issuance of such Warrant Shares, all of which taxes and expenses shall be paid by the Company, and such Warrant Shares shall be issued in the name of the Holder or in such name or names as may be directed by the Holder; provided, however, that in the event that Warrant Shares are to be issued in a name other than the name of the Holder, this Warrant when surrendered for exercise shall be accompanied by the Assignment Form attached hereto duly executed by the Holder and the Company may require, as a condition thereto, the payment of a sum sufficient to reimburse it for any transfer tax incidental thereto. The Company shall pay all transfer agent fees required for same-day processing of any Notice of Exercise and all fees to the Depository Trust Company (or another established clearing corporation performing similar functions) required for same-day electronic delivery of the Warrant Shares.

vii. Closing of Books. The Company will not close its stockholder books or records in any manner which prevents the timely exercise of this Warrant, pursuant to the terms hereof.

viii. Signature. This Section 2 and the exercise form attached hereto set forth the totality of the procedures required of the Holder in order to exercise this Purchase Warrant. Without limiting the preceding sentences, no ink-original exercise form shall be required, nor shall any medallion guarantee (or other type of guarantee or notarization) of any exercise form be required in order to exercise this Purchase Warrant. No additional legal opinion, other information or instructions shall be required of the Holder to exercise this Purchase Warrant. The Company shall honor exercises of this Purchase Warrant and shall deliver Shares underlying this Purchase Warrant in accordance with the terms, conditions and time periods set forth herein.

e. Holder's Exercise Limitations. The Company shall not effect any exercise of this Warrant, and a Holder shall not have the right to exercise any portion of this Warrant, pursuant to Section 2 or otherwise, to the extent that after giving effect to such issuance after exercise as set forth on the applicable Notice of Exercise, the Holder (together with the Holder's Affiliates, and any other Persons acting as a group together with the Holder or any of the Holder's Affiliates), would beneficially own in excess of the Beneficial Ownership Limitation (as defined below). For purposes of the foregoing sentence, the number of shares of Common Stock beneficially owned by the Holder and its Affiliates shall include the number of shares of Common Stock issuable upon exercise of this Warrant with respect to which such determination is being made, but shall exclude the number of shares of Common Stock which would be issuable upon (i) exercise of the remaining, nonexercised portion of this Warrant beneficially owned by the Holder or any of its Affiliates and (ii) exercise or conversion of the unexercised or nonconverted portion of any other securities of the Company (including, without limitation, any other Common Stock Equivalents) subject to a limitation on conversion or exercise analogous to the limitation contained herein beneficially owned by the Holder or any of its Affiliates. Except as set forth in the preceding sentence, for purposes of this Section 2(e), beneficial ownership shall be calculated in accordance with Section 13(d) of the Exchange Act and the rules and regulations promulgated thereunder, it being acknowledged by the Holder that the Company is not representing to the Holder that such calculation is in compliance with Section 13(d) of the Exchange Act and the Holder is solely responsible for any schedules required to be filed in accordance therewith. To the extent that the limitation contained in this Section 2(e) applies, the determination of whether this Warrant is exercisable (in relation to other securities owned by the Holder together with any Affiliates) and of which portion of this Warrant is exercisable shall be in the sole discretion of the Holder, and the submission of a Notice of Exercise shall be deemed to be the Holder's determination of whether this Warrant is exercisable (in relation to other securities owned by the Holder together with any Affiliates) and of which portion of this Warrant is exercisable, in each case subject to the Beneficial Ownership Limitation, and the Company shall have no obligation to verify or confirm the accuracy of such determination. In addition, a determination as to any group status as contemplated above shall be determined in accordance with Section 13(d) of the Exchange Act and the rules and regulations promulgated thereunder. For purposes of this Section 2(e), in determining the number of outstanding shares of Common Stock, a Holder may rely on the number of outstanding shares of Common Stock as reflected in (A) the Company's most recent periodic or annual report filed with the Commission, as the case may be, (B) a more recent public announcement by the Company or (C) a more recent written notice by the Company or the Company's transfer agent setting forth the number of shares of Common Stock outstanding. Upon the written or oral request of a Holder, the Company shall within two Trading Days confirm orally and in writing to the Holder the number of shares of Common Stock then outstanding. In any case, the number of outstanding shares of Common Stock shall be determined after giving effect to the conversion or exercise of securities of the Company, including this Warrant, by the Holder or its Affiliates since the date as of which such number of outstanding shares of Common Stock was reported. The "Beneficial Ownership Limitation" shall be 9.99% of the number of shares of the Common Stock outstanding immediately after giving effect to the issuance of shares of Common Stock issuable upon exercise of this Warrant. The Holder, upon notice to the Company, may increase or decrease the Beneficial Ownership Limitation provisions of this Section 2(e), provided that the Beneficial Ownership Limitation in no event exceeds 9.99% of the number of shares of the Common Stock outstanding immediately after giving effect to the issuance of shares of Common Stock upon exercise of this Warrant held by the Holder and the provisions of this Section 2(e) shall continue to apply. Any increase in the Beneficial Ownership Limitation will not be effective until the 61st day after such notice is delivered to the Company. The provisions of this paragraph shall be construed and implemented in a manner otherwise than in strict conformity with the terms of this Section 2(e) to correct this paragraph (or any portion hereof) which may be defective or inconsistent with the intended Beneficial Ownership Limitation herein contained or to make changes or supplements necessary or desirable to properly give effect to such limitation. The limitations contained in this paragraph shall apply to a successor holder of this Warrant.

Section 3. Certain Adjustments.

a. Stock Dividends and Splits. If the Company, at any time while this Warrant is outstanding: (i) pays a stock dividend or otherwise makes a distribution or distributions on shares of its Common Stock or any other equity or equity equivalent securities payable in shares of Common Stock (which, for avoidance of doubt, shall not include any shares of Common Stock issued by the Company upon exercise of this Warrant), (ii) subdivides outstanding shares of Common Stock into a larger number of shares, (iii) combines (including by way of reverse stock split) outstanding shares of Common Stock into a smaller number of shares, or (iv) issues by reclassification of shares of the Common Stock any shares of capital stock of the Company, then in each case the Exercise Price shall be multiplied by a fraction of which the numerator shall be the number of shares of Common Stock (excluding treasury shares, if any) outstanding immediately before such event and of which the denominator shall be the number of shares of Common Stock outstanding immediately after such event, and the number of shares issuable upon exercise of this Warrant shall be proportionately adjusted such that the aggregate Exercise Price of this Warrant shall remain unchanged. Any adjustment made pursuant to this Section 3(a) shall become effective immediately after the record date for the determination of stockholders entitled to receive such dividend or distribution and shall become effective immediately after the effective date in the case of a subdivision, combination or re-classification. For the purposes of clarification, the Exercise Price of this Warrant will not be adjusted in the event that the Company or any subsidiary thereof, as applicable, sells or grants any option to purchase, or sell or grant any right to reprice, or otherwise dispose of or issue (or announce any offer, sale, grant or any option to purchase or other disposition) any Common Stock or Common Stock Equivalents, at an effective price per share less than the Exercise Price then in effect.

b. [RESERVED]

c. Subsequent Rights Offerings. In addition to any adjustments pursuant to Section 3(a) above, if at any time the Company grants, issues or sells any Common Stock Equivalents or rights to purchase stock, warrants, securities or other property pro rata to the record holders of any class of shares of Common Stock (the "Purchase Rights"), then the Holder will be entitled to acquire, upon the terms applicable to such Purchase Rights, the aggregate Purchase Rights which the Holder could have acquired if the Holder had held the number of shares of Common Stock acquirable upon complete exercise of this Warrant (without regard to any limitations on exercise hereof, including without limitation, the Beneficial Ownership Limitation) immediately before the date on which a record is taken for the grant, issuance or sale of such Purchase Rights, or, if no such record is taken, the date as of which the record holders of shares of Common Stock are to be determined for the grant, issue or sale of such Purchase Rights (provided, however, to the extent that the Holder's right to participate in any such Purchase Right would result in the Holder exceeding the Beneficial Ownership Limitation, then the Holder shall not be entitled to participate in such Purchase Right to such extent (or beneficial ownership of such shares of Common Stock as a result of such Purchase Right to such extent) and such Purchase Right to such extent shall be held in abeyance for the Holder until such time, if ever, as its right thereto would not result in the Holder exceeding the Beneficial Ownership Limitation).

d. Pro Rata Distributions. During such time as this Warrant is outstanding, if the Company shall declare or make any dividend (other than cash dividends) or other distribution of its assets (or rights to acquire its assets) to holders of shares of Common Stock, by way of return of capital or otherwise (including, without limitation, any distribution of shares or other securities, property or options by way of a dividend, spin off, reclassification, corporate rearrangement, scheme of arrangement or other similar transaction) (a "Distribution"), at any time after the issuance of this Warrant, then, in each such case, the Holder shall be entitled to participate in such Distribution to the same extent that the Holder would have participated therein if the Holder had held the number of shares of Common Stock acquirable upon complete exercise of this Warrant (without regard to any limitations on exercise hereof, including without limitation, the Beneficial Ownership Limitation) immediately before the date of which a record is taken for such Distribution, or, if no such record is taken, the date as of which the record holders of shares of Common Stock are to be determined for the participation in such Distribution (provided, however, to the extent that the Holder's right to participate in any such Distribution would result in the Holder exceeding the Beneficial Ownership Limitation, then the Holder shall not be entitled to participate in such Distribution to such extent (or in the beneficial ownership of any shares of Common Stock as a result of such Distribution to such extent) and the portion of such Distribution shall be held in abeyance for the benefit of the Holder until such time, if ever, as its right thereto would not result in the Holder exceeding the Beneficial Ownership Limitation). To the extent that this Warrant has not been partially or completely exercised at the time of such Distribution, such portion of the Distribution shall be held in abeyance for the benefit of the Holder until the Holder has exercised this Warrant.

e. Fundamental Transaction. If, at any time while this Warrant is outstanding, (i) the Company, directly or indirectly, in one or more related transactions effects any merger or consolidation of the Company with or into another Person, (ii) the Company, directly or indirectly, effects any sale, lease, license, assignment, transfer, conveyance or other disposition of all or substantially all of its assets in one or a series of related transactions, (iii) any, direct or indirect, purchase offer, tender offer or exchange offer (whether by the Company or another Person) is completed pursuant to which holders of Common Stock are permitted to sell, tender or exchange their shares for other securities, cash or property and has been accepted by the holders of 50% or more of the outstanding Common Stock, (iv) the Company, directly or indirectly, in one or more related transactions effects any reclassification, reorganization or recapitalization of the Common Stock or any compulsory share exchange pursuant to which the Common Stock is effectively converted into or exchanged for other securities, cash or property, or (v) the Company, directly or indirectly, in one or more related transactions consummates a stock or share purchase agreement or other business combination (including, without limitation, a reorganization, recapitalization, spin-off or scheme of arrangement) with another Person or group of Persons whereby such other Person or group acquires more than 50% of the outstanding shares of Common Stock (not including any shares of Common Stock held by the other Person or other Persons making or party to, or associated or affiliated with the other Persons making or party to, such stock or share purchase agreement or other business combination) (each a "Fundamental Transaction"), then, upon any subsequent exercise of this Warrant, the Holder shall have the right to receive, for each Warrant Share that would have been issuable upon such exercise immediately prior to the occurrence of such Fundamental Transaction, at the option of the Holder (without regard to any limitation in Section 2(e) on the exercise of this Warrant), the number of shares of Common Stock of the successor or acquiring corporation or of the Company, if it is the surviving corporation, and any additional consideration (the "Alternate Consideration") receivable by holders of Common Stock as a result of such Fundamental Transaction for each share of Common Stock for which this Warrant is exercisable immediately prior to such Fundamental Transaction (without regard to any limitation in Section 2(e) on the exercise of this Warrant). For purposes of any such exercise, the determination of the Exercise Price shall be appropriately adjusted to apply to such Alternate Consideration based on the amount of Alternate Consideration issuable in respect of one share of Common Stock in such Fundamental Transaction, and the Company shall apportion the Exercise Price among the Alternate Consideration in a reasonable manner reflecting the relative value of any different components of the Alternate Consideration. If holders of Common Stock are given any choice as to the securities, cash or property to be received in a Fundamental Transaction, then the Holder shall be given the same choice as to the Alternate Consideration it receives upon any exercise of this Warrant following such Fundamental Transaction. The Company shall cause any successor entity in a Fundamental Transaction in which the Company is not the survivor (the "Successor Entity") to assume in writing all of the obligations of the Company under this Warrant in accordance with the provisions of this Section 3(e) pursuant to written agreements in form and substance reasonably satisfactory to the Holder and approved by the Holder (without unreasonable delay) prior to such Fundamental Transaction and shall, at the option of the Holder, deliver to the Holder in exchange for this Warrant a security of the Successor Entity evidenced by a written instrument substantially similar in form and substance to this Warrant which is exercisable for a corresponding number of shares of capital stock of such Successor Entity (or its parent entity) equivalent to the shares of Common Stock acquirable and receivable upon exercise of this Warrant (without regard to any limitations on the exercise of this Warrant) prior to such Fundamental Transaction, and with an exercise price which applies the exercise price hereunder to such shares of capital stock (but taking into account the relative value of the shares of Common Stock pursuant to such Fundamental Transaction and the value of such shares of capital stock, such number of shares of capital stock and such exercise price being for the purpose of protecting the economic value of this Warrant immediately prior to the consummation of such Fundamental Transaction), and which is reasonably satisfactory in form and substance to the Holder. Upon the occurrence of any such Fundamental Transaction, the Successor Entity shall succeed to, and be substituted for (so that from and after the date of such Fundamental Transaction, the provisions of this Warrant referring to the "Company" shall refer instead to the Successor Entity), and may exercise every right and power of the Company and shall assume all of the obligations of the Company under this Warrant with the same effect as if such Successor Entity had been named as the Company herein.

f. Calculations. All calculations under this Section 3 shall be made to the nearest cent or the nearest 1/100th of a share, as the case may be. For purposes of this Section 3, the number of shares of Common Stock deemed to be issued and outstanding as of a given date shall be the sum of the number of shares of Common Stock (excluding treasury shares, if any) issued and outstanding.

g. Notice to Holder.

i. Adjustment to Exercise Price. Whenever the Exercise Price is adjusted pursuant to any provision of this Section 3, the Company shall promptly mail to the Holder a notice setting forth the Exercise Price after such adjustment and any resulting adjustment to the number of Warrant Shares and setting forth a brief statement of the facts requiring such adjustment.

ii. Notice to Allow Exercise by Holder. If (A) the Company shall declare a dividend (or any other distribution in whatever form) on the Common Stock, (B) the Company shall declare a special nonrecurring cash dividend on or a redemption of the Common Stock, (C) the Company shall authorize the granting to all holders of the Common Stock rights or warrants to subscribe for or purchase any shares of capital stock of any class or of any rights, (D) the approval of any stockholders of the Company shall be required in connection with any reclassification of the Common Stock, any consolidation or merger to which the Company is a party, any sale or transfer of all or substantially all of the assets of the Company, or any compulsory share exchange whereby the Common Stock is converted into other securities, cash or property, or (E) the Company shall authorize the voluntary or involuntary dissolution, liquidation or winding up of the affairs of the Company, then, in each case, the Company shall cause to be mailed a notice to the Holder at its last address as it shall appear upon the Warrant Register of the Company, at least 20 calendar days prior to the applicable record or effective date hereinafter specified, stating (x) the date on which a record is to be taken for the purpose of such dividend, distribution, redemption, rights or warrants, or if a record is not to be taken, the date as of which the holders of the Common Stock of record to be entitled to such dividend, distributions, redemption, rights or warrants are to be determined or (y) the date on which such reclassification, consolidation, merger, sale, transfer or share exchange is expected to become effective or close, and the date as of which it is expected that holders of the Common Stock of record shall be entitled to exchange their shares of the Common Stock for securities, cash or other property deliverable upon such reclassification, consolidation, merger, sale, transfer or share exchange; provided that the failure to provide such notice or any defect therein shall not affect the validity of the corporate action required to be specified in such notice. To the extent that any notice provided hereunder constitutes, or contains, material, non-public information regarding the Company or any of its subsidiaries, the Company shall simultaneously file such notice with the Commission pursuant to a Current Report on Form 8-K. The Holder shall remain entitled to exercise this Warrant during the period commencing on the date of such notice to the effective date of the event triggering such notice except as may otherwise be expressly set forth herein.

Section 4. Transfer of Warrant.

a. Transferability. Pursuant to FINRA Rule 5110(g)(1), neither this Warrant nor any Warrant Shares issued upon exercise of this Warrant shall be sold, transferred, assigned, pledged, or hypothecated, or be the subject of any hedging, short sale, derivative, put, or call transaction that would result in the effective economic disposition of the securities by any person for a period of 180 days immediately following the date of effectiveness or commencement of sales of the offering pursuant to which this Warrant is being issued, except the transfer of any security:

i. by operation of law or by reason of reorganization of the Company;

ii. to any FINRA member firm participating in the offering and the officers or partners thereof, if all securities so transferred remain subject to the lock-up restriction in this Section 4(a) for the remainder of the time period;

iii. if the aggregate amount of securities of the Company held by the Holder or related person do not exceed 1% of the securities being offered;

iv. that is beneficially owned on a pro-rata basis by all equity owners of an investment fund, provided that no participating member manages or otherwise directs investments by the fund, and participating members in the aggregate do not own more than 10% of the equity in the fund; or

v. the exercise or conversion of any security, if all securities received remain subject to the lock-up restriction in this Section 4(a) for the remainder of the time period.

Subject to the foregoing restriction, any applicable securities laws and the conditions set forth in Section 4(d), this Warrant and all rights hereunder (including, without limitation, any registration rights) are transferable, in whole or in part, upon surrender of this Warrant at the principal office of the Company or its designated agent, together with a written assignment of this Warrant substantially in the form attached hereto duly executed by the Holder or its agent or attorney and funds sufficient to pay any transfer taxes payable upon the making of such transfer. Upon such surrender and, if required, such payment, the Company shall execute and deliver a new Warrant or Warrants in the name of the assignee or assignees, as applicable, and in the denomination or denominations specified in such instrument of assignment, and shall issue to the assignor a new Warrant evidencing the portion of this Warrant not so assigned, and this Warrant shall promptly be cancelled. Notwithstanding anything herein to the contrary, the Holder shall not be required to physically surrender this Warrant to the Company unless the Holder has assigned this Warrant in full, in which case, the Holder shall surrender this Warrant to the Company within three (3) Trading Days of the date the Holder delivers an assignment form to the Company assigning this Warrant full. The Warrant, if properly assigned in accordance herewith, may be exercised by a new holder for the purchase of Warrant Shares without having a new Warrant issued.

b. New Warrants. This Warrant may be divided or combined with other Warrants upon presentation hereof at the aforesaid office of the Company, together with a written notice specifying the names and denominations in which new Warrants are to be issued, signed by the Holder or its agent or attorney. Subject to compliance with Section 4(a), as to any transfer which may be involved in such division or combination, the Company shall execute and deliver a new Warrant or Warrants in exchange for the Warrant or Warrants to be divided or combined in accordance with such notice. All Warrants issued on transfers or exchanges shall be dated the initial issuance date of this Warrant and shall be identical with this Warrant except as to the number of Warrant Shares issuable pursuant thereto.

c. Warrant Register. The Company shall register this Warrant, upon records to be maintained by the Company for that purpose (the "Warrant Register"), in the name of the record Holder hereof from time to time. The Company may deem and treat the registered Holder of this Warrant as the absolute owner hereof for the purpose of any exercise hereof or any distribution to the Holder, and for all other purposes, absent actual notice to the contrary.

d. Representation by the Holder. The Holder, by the acceptance hereof, represents and warrants that it is acquiring this Warrant and, upon any exercise hereof, will acquire the Warrant Shares issuable upon such exercise, for its own account and not with a view to or for distributing or reselling such Warrant Shares or any part thereof in violation of the Securities Act or any applicable state securities law, except pursuant to sales registered or exempted under the Securities Act.

Section 5. Registration Rights.

a. Demand Registration.

i. Grant of Right. The Company, upon written demand (a "Demand Notice") of the Holder(s) of at least 51% of the Warrants ("Majority Holders"), agrees to register on Form S-3, on one occasion, all or any portion of the shares of Common Stock underlying the Warrants (collectively, the "Registrable Securities"). On such occasion, the Company will file a registration statement with the Commission covering the Registrable Securities within sixty (60) days after receipt of a Demand Notice and use its best efforts to have the registration statement declared effective promptly thereafter, subject to compliance with review by the Commission; provided, however, that the Company shall not be required to comply with a Demand Notice if the Company has filed a registration statement with respect to which the Holder is entitled to piggyback registration rights pursuant to Section 5.b hereof and either: (i) the Holder has elected to participate in the offering covered by such registration statement or (ii) if such registration statement relates to an underwritten primary offering of securities of the Company, until the offering covered by such registration statement has been withdrawn or until thirty (30) days after such offering is consummated. The demand for registration may be made at any time during a period of four (4) years beginning on the Initial Exercise Date. The Company covenants and agrees to give written notice of its receipt of any Demand Notice by any Holder(s) to all other registered Holders of the Warrants and/or the Registrable Securities within ten (10) days after the date of the receipt of any such Demand Notice.

ii. Terms. The Company shall bear all fees and expenses, except that the Holders included in such registration statement shall bear expense of up to $10,000 pro rata for their portion of the Registrable Securities included in such registration statement, attendant to the registration of the Registrable Securities pursuant to Section 5.a.i, but the Holders shall pay any and all underwriting commissions and the expenses of any legal counsel selected by the Holders to represent them in connection with the sale of the Registrable Securities. The Company agrees to use its best efforts to cause the filing required herein to become effective promptly and to qualify or register the Registrable Securities in such States as are reasonably requested by the Holder(s); provided, however, that in no event shall the Company be required to register the Registrable Securities in a State in which such registration would cause: (i) the Company to be obligated to register or license to do business in such State or submit to general service of process in such State or (ii) the principal shareholders of the Company to be obligated to escrow their shares of capital stock of the Company. The Company shall cause any registration statement filed pursuant to the demand right granted under Section 5.a.i to remain effective for a period of at least twelve (12) consecutive months after the date that the Holders of the Registrable Securities covered by such registration statement are first given the opportunity to sell all of such securities. The Holders shall only use the prospectuses provided by the Company to sell the shares of Common Stock covered by such registration statement, and will immediately cease to use any prospectus furnished by the Company if the Company advises the Holder that such prospectus may no longer be used due to a material misstatement or omission. Notwithstanding the provisions of this Section 5.a.ii, the Holder shall be entitled to a demand registration under this Section 5.a.ii on only one (1) occasion and such demand registration right shall terminate on the fifth anniversary of the effective date of the offering in accordance with FINRA Rule 5110(f)(2)(G)(iv).

b. "Piggy-Back" Registration.

i. Grant of Right. The Holder shall have the right, for a period of no more than two (2) years from the Initial Exercise Date in accordance with FINRA Rule 5110(f)(2)(G)(v), to include the Registrable Securities as part of any other registration of securities filed by the Company (other than in connection with a transaction contemplated by Rule 145(a) promulgated under the Securities Act or pursuant to Form S-8 or any equivalent form); provided, however, that if, solely in connection with any primary underwritten public offering for the account of the Company, the managing underwriter(s) thereof shall, in its reasonable discretion, impose a limitation on the number of shares of Common Stock which may be included in the Registration Statement because, in such underwriter(s)' judgment, marketing or other factors dictate such limitation is necessary to facilitate public distribution, then the Company shall be obligated to include in such Registration Statement only such limited portion of the Registrable Securities with respect to which the Holder requested inclusion hereunder as the underwriter shall reasonably permit. Any exclusion of Registrable Securities shall be made pro rata among the Holders seeking to include Registrable Securities in proportion to the number of Registrable Securities sought to be included by such Holders; provided, however, that the Company shall not exclude any Registrable Securities unless the Company has first excluded all outstanding securities, the holders of which are not entitled to inclusion of such securities in such Registration Statement or are not entitled to pro rata inclusion with the Registrable Securities.

ii. Terms. The Company shall bear all fees and expenses attendant to registering the Registrable Securities pursuant to Section 5.a.i hereof, but the Holders shall pay any and all underwriting commissions and the expenses of any legal counsel selected by the Holders to represent them in connection with the sale of the Registrable Securities. In the event of such a proposed registration, the Company shall furnish the then Holders of outstanding Registrable Securities with not less than thirty (30) days written notice prior to the proposed date of filing of such registration statement. Such notice to the Holders shall continue to be given for each registration statement filed by the Company during the two (2) year period following the Initial Exercise Date until such time as all of the Registrable Securities have been sold by the Holder. The holders of the Registrable Securities shall exercise the "piggy-back" rights provided for herein by giving written notice within ten (10) days of the receipt of the Company's notice of its intention to file a registration statement. Except as otherwise provided in this Warrant, there shall be no limit on the number of times the Holder may request registration under this Section 5.a.ii; provided, however, that such registration rights shall terminate on the second anniversary of the Initial Exercise Date.

c. General Terms.

i. Indemnification. The Company shall indemnify the Holder(s) of the Registrable Securities to be sold pursuant to any registration statement hereunder and each person, if any, who controls such Holders within the meaning of Section 15 of the Securities Act or Section 20(a) of the Exchange Act against all loss, claim, damage, expense or liability (including all reasonable attorneys' fees and other expenses reasonably incurred in investigating, preparing or defending against any claim whatsoever) to which any of them may become subject under the Securities Act, the Exchange Act or otherwise, arising from such registration statement but only to the same extent and with the same effect as the provisions pursuant to which the Company has agreed to indemnify the Underwriters contained in Section 5.a of the Underwriting Agreement (as defined below). The Holder(s) of the Registrable Securities to be sold pursuant to such registration statement, and their successors and assigns, shall severally, and not jointly, indemnify the Company, against all loss, claim, damage, expense or liability (including all reasonable attorneys' fees and other expenses reasonably incurred in investigating, preparing or defending against any claim whatsoever) to which they may become subject under the Securities Act, the Exchange Act or otherwise, arising from information furnished by or on behalf of such Holders, or their successors or assigns, in writing, for specific inclusion in such registration statement to the same extent and with the same effect as the foregoing provisions.

ii. Exercise of Warrants. Nothing contained in this Warrant shall be construed as requiring the Holder(s) to exercise their Warrants prior to or after the initial filing of any registration statement or the effectiveness thereof.

iii. Documents Delivered to Holders. The Company shall furnish to each Holder participating in any of the foregoing offerings and to each underwriter of any such offering, if any, a signed counterpart, addressed to such Holder or underwriter, of: (i) an opinion of counsel to the Company, dated the effective date of such registration statement (and, if such registration includes an underwritten public offering, an opinion dated the date of the closing under any underwriting agreement related thereto), and (ii) a "cold comfort" letter dated the effective date of such registration statement (and, if such registration includes an underwritten public offering, a letter dated the date of the closing under the underwriting agreement) signed by the independent registered public accounting firm which has issued a report on the Company's financial statements included in such registration statement, in each case covering substantially the same matters with respect to such registration statement (and the prospectus included therein) and, in the case of such accountants' letter, with respect to events subsequent to the date of such financial statements, as are customarily covered in opinions of issuer's counsel and in accountants' letters delivered to underwriters in underwritten public offerings of securities. The Company shall also deliver promptly to each Holder participating in the offering requesting the correspondence and memoranda described below and to the managing underwriter, if any, copies of all correspondence between the Commission and the Company, its counsel or auditors and all memoranda relating to discussions with the Commission or its staff with respect to the registration statement and permit each Holder and underwriter to do such investigation, upon reasonable advance notice, with respect to information contained in or omitted from the registration statement as it deems reasonably necessary to comply with applicable securities laws or rules of FINRA. Such investigation shall include access to books, records and properties and opportunities to discuss the business of the Company with its officers and independent auditors, all to such reasonable extent and at such reasonable times as any such Holder shall reasonably request.

iv. Underwriting Agreement. The Holders shall be parties to any underwriting agreement relating to an underwritten sale of their Registrable Securities and may, at their option, require that any or all the representations, warranties and covenants of the Company to or for the benefit of such underwriters shall also be made to and for the benefit of such Holders. Such Holders shall not be required to make any representations or warranties to or agreements with the Company or the underwriters except as they may relate to such Holders, their Warrant ADSs and their intended methods of distribution.

v. Documents to be Delivered by Holder(s). Each of the Holder(s) participating in any of the foregoing offerings shall furnish to the Company a completed and executed questionnaire provided by the Company requesting information customarily sought of selling security holders.

vi. Damages. Should the registration or the effectiveness thereof required by Sections 5.a hereof be delayed by the Company or the Company otherwise fails to comply with such provisions, the Holder(s) shall, in addition to any other legal or other relief available to the Holder(s), be entitled to obtain specific performance or other equitable (including injunctive) relief against the threatened breach of such provisions or the continuation of any such breach, without the necessity of proving actual damages and without the necessity of posting bond or other security.

Section 6. Miscellaneous.

a. No Rights as Stockholder Until Exercise. This Warrant does not entitle the Holder to any voting rights, dividends or other rights as a stockholder of the Company prior to the exercise hereof as set forth in Section 2(d)(i).

b. Loss, Theft, Destruction or Mutilation of Warrant. The Company covenants that upon receipt by the Company of evidence reasonably satisfactory to it of the loss, theft, destruction or mutilation of this Warrant or any certificate relating to the Warrant Shares, and in case of loss, theft or destruction, of indemnity or security reasonably satisfactory to it (which, in the case of the Warrant, shall not include the posting of any bond), and upon surrender and cancellation of such Warrant or stock certificate, if mutilated, the Company will make and deliver a new Warrant or stock certificate of like tenor and dated as of such cancellation, in lieu of such Warrant or stock certificate.

c. Saturdays, Sundays, Holidays, etc. If the last or appointed day for the taking of any action or the expiration of any right required or granted herein shall not be a Trading Day, then, such action may be taken or such right may be exercised on the next succeeding Trading Day.

d. Authorized Shares. The Company covenants that, during the period the Warrant is outstanding, it will reserve from its authorized and unissued Common Stock a sufficient number of shares to provide for the issuance of the Warrant Shares upon the exercise of any purchase rights under this Warrant. The Company further covenants that its issuance of this Warrant shall constitute full authority to its officers who are charged with the duty of issuing the necessary Warrant Shares upon the exercise of the purchase rights under this Warrant. The Company will take all such reasonable action as may be necessary to assure that such Warrant Shares may be issued as provided herein without violation of any applicable law or regulation, or of any requirements of the Trading Market upon which the Common Stock may be listed. The Company covenants that all Warrant Shares which may be issued upon the exercise of the purchase rights represented by this Warrant will, upon exercise of the purchase rights represented by this Warrant and payment for such Warrant Shares in accordance herewith, be duly authorized, validly issued, fully paid and nonassessable and free from all taxes, liens and charges created by the Company in respect of the issue thereof (other than taxes in respect of any transfer occurring contemporaneously with such issue).

Except and to the extent as waived or consented to by the Holder, the Company shall not by any action, including, without limitation, amending its certificate of incorporation or through any reorganization, transfer of assets, consolidation, merger, dissolution, issue or sale of securities or any other voluntary action, avoid or seek to avoid the observance or performance of any of the terms of this Warrant, but will at all times in good faith assist in the carrying out of all such terms and in the taking of all such actions as may be necessary or appropriate to protect the rights of Holder as set forth in this Warrant against impairment. Without limiting the generality of the foregoing, the Company will (i) not increase the par value of any Warrant Shares above the amount payable therefor upon such exercise immediately prior to such increase in par value, (ii) take all such action as may be necessary or appropriate in order that the Company may validly and legally issue fully paid and nonassessable Warrant Shares upon the exercise of this Warrant and (iii) use commercially reasonable efforts to obtain all such authorizations, exemptions or consents from any public regulatory body having jurisdiction thereof, as may be, necessary to enable the Company to perform its obligations under this Warrant.

Before taking any action which would result in an adjustment in the number of Warrant Shares for which this Warrant is exercisable or in the Exercise Price, the Company shall obtain all such authorizations or exemptions thereof, or consents thereto, as may be necessary from any public regulatory body or bodies having jurisdiction thereof.

e. Jurisdiction. All questions concerning the construction, validity, enforcement and interpretation of this Warrant shall be determined in accordance with the provisions of the underwriting agreement, dated January 29, 2020, by and between the Company and ThinkEquity, a division of Fordham Financial Management, Inc., as representatives of the underwriters set forth therein (the "Underwriting Agreement").

f. Restrictions. The Holder acknowledges that the Warrant Shares acquired upon the exercise of this Warrant, if not registered, and the Holder does not utilize cashless exercise, will have restrictions upon resale imposed by state and federal securities laws.

g. Nonwaiver and Expenses. No course of dealing or any delay or failure to exercise any right hereunder on the part of Holder shall operate as a waiver of such right or otherwise prejudice the Holder's rights, powers or remedies. Without limiting any other provision of this Warrant or the Underwriting Agreement, if the Company willfully and knowingly fails to comply with any provision of this Warrant, which results in any material damages to the Holder, the Company shall pay to the Holder such amounts as shall be sufficient to cover any costs and expenses including, but not limited to, reasonable attorneys' fees, including those of appellate proceedings, incurred by the Holder in collecting any amounts due pursuant hereto or in otherwise enforcing any of its rights, powers or remedies hereunder.

h. Notices. Any notice, request or other document required or permitted to be given or delivered to the Holder by the Company shall be delivered in accordance with the notice provisions of the Underwriting Agreement.

i. Limitation of Liability. No provision hereof, in the absence of any affirmative action by the Holder to exercise this Warrant to purchase Warrant Shares, and no enumeration herein of the rights or privileges of the Holder, shall give rise to any liability of the Holder for the purchase price of any Common Stock or as a stockholder of the Company, whether such liability is asserted by the Company or by creditors of the Company.

j. Remedies. The Holder, in addition to being entitled to exercise all rights granted by law, including recovery of damages, will be entitled to specific performance of its rights under this Warrant. The Company agrees that monetary damages would not be adequate compensation for any loss incurred by reason of a breach by it of the provisions of this Warrant and hereby agrees to waive and not to assert the defense in any action for specific performance that a remedy at law would be adequate.

k. Successors and Assigns. Subject to applicable securities laws, this Warrant and the rights and obligations evidenced hereby shall inure to the benefit of and be binding upon the successors and permitted assigns of the Company and the successors and permitted assigns of Holder. The provisions of this Warrant are intended to be for the benefit of any Holder from time to time of this Warrant and shall be enforceable by the Holder or holder of Warrant Shares.

l. Amendment. This Warrant may be modified or amended or the provisions hereof waived with the written consent of the Company and the Majority Holders.

m. Severability. Wherever possible, each provision of this Warrant shall be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Warrant shall be prohibited by or invalid under applicable law, such provision shall be ineffective to the extent of such prohibition or invalidity, without invalidating the remainder of such provisions or the remaining provisions of this Warrant.

n. Headings. The headings used in this Warrant are for the convenience of reference only and shall not, for any purpose, be deemed a part of this Warrant.

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(Signature Page Follows)

IN WITNESS WHEREOF, the Company has caused this Warrant to be executed by its officer thereunto duly authorized as of the date first above indicated.

ANNOVIS BIO, INC.

By:_____
Name:
Title:

Exhibit 4.3

DESCRIPTION OF REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The following description of our capital stock is intended as a summary only and therefore is not a complete description of our capital stock. This description is based upon, and is qualified by reference to, our amended and restated certificate of incorporation (the "Amended Certificate"), our amended and restated bylaws (the "Amended Bylaws") and applicable provisions of Delaware corporate law. You should read our Amended Certificate and Amended Bylaws, which are filed as exhibits to our Annual Report on Form 10-K, to which this exhibit is also appended.

Our authorized capital stock consists of 35,000,000 shares of common stock, par value $0.0001 per share, and 2,000,000 shares of preferred stock, par value $0.0001 per share.

Our common stock is the only class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act").

Common Stock

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 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 Certificate 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.

Registration Rights

Under our registration rights agreement dated as of December 19, 2014, holders of 2,273,847 shares of common stock, or their transferees, have the right to require us to register their shares under the Securities Act of 1933, as amended (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

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 stockholders and blue sky fees and expenses.

Warrant to Purchase Common Stock

In connection with the initial public offering of our common stock (the "IPO"), we issued to ThinkEquity, a division of Fordham Financial Management, Inc. (the "Representative"), a warrant (the "Representative's Warrants") to purchase 100,000 shares of our common stock at an exercise price of $7.50 per share (125% of our IPO price per share). 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. The Warrant is 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 January 28, 2020. Additionally, the Representative's Warrants may not be sold, transferred, assigned, pledged, or hypothecated for a 180-day period following January 28, 2020, 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 Representative's Warrants other than underwriting commissions incurred and payable by the holders.

Anti-Takeover Effects of Delaware Law and Our Amended Certificate and Amended Bylaws

Some provisions of Delaware law, our Amended Certificate and Amended Bylaws 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 Certificate, or our Amended Bylaws; or
- any action asserting a claim against us that is governed by the internal affairs doctrine.

Our Amended Bylaws do 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 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 Amended 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 Amended 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 Amended 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 listed on NYSE American under the symbol “ANVS.”

Exhibit 10.1

SECOND AMENDED AND RESTATED
EMPLOYMENT AGREEMENT

EMPLOYMENT AGREEMENT effective as of March 24, 2020 (this "Agreement") between Annovis Bio, Inc. (the "Company"), a Delaware corporation, and Maria L. Maccecchini (the "Executive").

Background:

The parties desire to enter into this Agreement to provide for the employment of the Executive by the Company from and after the Commencement Date and for certain other matters in connection with such employment, all as set forth more fully in this Agreement. Certain capitalized terms used in this Agreement have the respective meanings given to them in Exhibit A hereto.

Terms:

NOW, THEREFORE, in consideration of the premises and covenants set forth herein, and intending to be legally bound hereby, the parties to this Agreement hereby agree as follows:

1. Position and Duties; Board Seat.

(a) Position and Duties. The Company agrees that the Executive shall be employed by the Company to serve as Chief Executive Officer and President of the Company. The Executive shall report to the Board of Directors of the Company (the "Board"). The Executive agrees to be so employed by the Company and agrees to devote substantially all of her business time, attention, skill and efforts to perform services for the Company and to faithfully and diligently discharge and fulfill the Executive's duties hereunder to the best of her abilities. In so doing, the Executive shall perform such executive, managerial, administrative and financial functions as are required to develop the Company's business and to perform other duties assigned to the Executive by the Board that are consistent with the Executive's title as Chief Executive Officer and President. The Executive shall perform her duties hereunder primarily at the Company's principal offices. In the performance of her duties, the Executive shall travel to such other places at such times as the needs of the Company may from time-to-time dictate or be desirable.

(b) Other Activities. Notwithstanding Section 1(a), the Executive may engage in other business and professional activities to the extent that they do not interfere with the Executive's obligations under this Agreement, provided that each of those activities is first disclosed to and approved by the Board. The parties acknowledge that activities in which the Executive is currently engaged have been disclosed to and approved by the Board.

(c) Board Seat. The Executive serves as a member of the Board. The Executive agrees to resign as a member of the Board if the Executive resigns or is terminated as the Chief Executive Officer of the Company for any reason.

2. Term. The Executive's employment under this Agreement shall commence on the Commencement Date and shall end when terminated pursuant to Section 4.

3. Compensation.

(a) Base Salary. During the term of the Executive's employment under this Agreement, the Executive shall be paid an annual salary at the rate of $420,000 (the "Base Salary"), retroactive to January 1, 2020, payable in accordance with the Company's payroll practices and policies in effect from time to time and subject to applicable withholding of income taxes, social security taxes and other such other payroll deductions as are required by law or applicable employee benefit programs. The Board shall review the Executive's Base Salary for annual increases, commencing with the Base Salary for the 2021 calendar year.

(b) Annual Bonus. With respect to each fiscal year of the Company during the continued full-time employment of the Executive hereunder, commencing with the 2020 fiscal year, the Executive will be eligible to be considered for an annual performance bonus (the "Annual Bonus") in an amount of up to 50% of the Executive's Base Salary. The Annual Bonus, if any, will be awarded by the Board in its sole discretion based on the achievement of Company and personal performance goals established by the Board on an annual basis, following consultation with the Executive and shall take into account the stock options and any other equity incentive awards that vest in the year the bonus is paid. Any Annual Bonus awarded to the Executive hereunder may be paid in cash or in equity of the Company, as determined by the Board in its sole discretion, and will be payable or issuable, less applicable taxes and withholdings, not later than two and one-half months after the end of the fiscal year to which the Annual Bonus relates in accordance with the Company's customary practices for annual bonus payments.

(c) Equity Incentives. Subject to the approval of the Board, the Executive shall be granted stock options under the Equity Incentive Plan and shall be considered for future stock option awards as specified on Exhibit B hereto. In addition, the Executive shall be eligible to participate in future equity incentive programs established by the Company from time to time in the future in accordance with the terms of those programs.

(d) Vacation and Fringe Benefits. The Executive shall be entitled to participate in all vacation and other fringe benefit programs of the Company to the extent and on the same terms and conditions as are accorded to other senior management employees of the Company.

(e) Reimbursement of Other Expenses. The Company shall reimburse the Executive for the reasonable and necessary out-of-pocket business expenses incurred by the Executive for or on behalf of the Company in furtherance of the performance of the Executive's duties hereunder in accordance with the Company's policies as approved by the Board from time to time, subject in all cases to the Company's requirements with respect to reporting and documentation of such expenses.

(f) Section 409A. If any reimbursement under this Section 3 is not exempt from Section 409A of the Internal Revenue Code of 1986, as amended (the "Code") then (i) any reimbursement in one calendar year shall not affect the amount that may be reimbursed in any other calendar year; (ii) a reimbursement (or right thereto) may not be exchanged or liquidated for another benefit or payment; and (iii) a reimbursement shall be made no later than the end of the calendar year following the calendar year in which the Executive incurred the related expense.

4. Termination.

(a) Death or Disability. The Executive's employment with the Company shall automatically terminate effective as of the date of the Executive's death, and the Company may terminate the employment of the Executive immediately upon written notice to the Executive in the event of the Disability of the Executive. In the event of termination of the Executive's employment due to death or Disability, the Company shall not have any further obligation or liability under this Agreement except that the Company shall pay to the Executive or the Executive's estate (as applicable): (i) any portion of the Executive's Base Salary for the period up to the date of employment termination that has been earned but remains unpaid; (ii) any expenses properly incurred but not yet reimbursed, including, without limitation, the reimbursements provided for in Section 3(e); (iii) any benefits that have accrued to the Executive under the terms of the employee benefit plans of the Company, which benefits shall be paid in accordance with the terms of those plans (the payments in clauses (i) through (iii) collectively, the "Accrued Obligations"); and (iv) in the event of a termination of employment due to the Executive's death, the Annual Bonus awarded pursuant to Section 3(b), if any, with respect to the fiscal year prior to the fiscal year of termination, to the extend unpaid (the "Earned Bonus"). The Accrued Obligations shall be paid on the first payroll date following the last date of employment to the extent administratively feasible and, if not, then on the second payroll date following the last date of employment. The Earned Bonus, if any, will be paid when it would have been paid had Executive remained employed with the Company.

(b) Termination of the Executive's Employment for Cause. The Company may terminate the employment of the Executive for Cause immediately upon written notice of such termination to the Executive. If the Executive's employment with the Company is terminated by the Company for Cause, the Company shall not have any further obligation or liability under this Agreement except for the Accrued Obligations. The Accrued Obligations shall be paid on the first payroll date following the last date of employment to the extent administratively feasible and, if not, then on the second payroll date following the last date of employment.

(c) Involuntary Termination.

(i) The Company may terminate the employment of the Executive for any reason other than one specified in Section 4(a) or Section 4(b) immediately upon written notice of termination to the Executive, and the Executive may terminate her employment with the Company for Good Reason immediately upon providing written notice of such termination to the Company. Either of such terminations shall be deemed an "Involuntary Termination" for purposes of this Agreement.

(ii) Upon the occurrence of an Involuntary Termination, in addition to the Accrued Obligations, and subject to the execution by the Executive of a release in the form of Exhibit C hereto (the "Release") and the compliance by the Executive with the Release and all terms and provisions of this Agreement and the Confidentiality and Invention Assignment Agreement (as defined in Section 5) that survive the termination of the Executive's employment by the Company the Executive shall be entitled to receive (A) severance payments in an amount equal to the Base Salary in effect on the termination date for a period of 12 months; plus (B) monthly reimbursement (upon presentation of proof of payment) for the medical insurance premiums at the same level as was in effect on the termination date until the earlier of (1) the end of such 12-month period or (2) the date the Executive becomes eligible for medical benefits through another employer; provided, however, that if such Involuntary Termination shall occur upon the closing of a Change of Control or within 12 months thereafter: (A) the severance shall be payable in a single lump sum and (B) the Executive shall also be entitled to receive an amount equal to the projected target amount of the Executive's Annual Bonus for the calendar year in which the Executive's employment termination occurs payable in a single lump sum, such lump sum payments to be made in each case on the first regularly scheduled payroll date that occurs on or after 60 days after the effective date of such employment termination. Any payments due pursuant to this Section 4(c), other than the Accrued Obligations, shall commence as soon as administratively feasible within 60 days after the date of the Executive's termination of employment provided the Executive has timely executed and returned the Release and, if a revocation period is applicable, the Executive has not revoked the Release; provided, however, that if the 60-day period begins in one calendar year and ends in a second calendar year, the severance payments shall begin to be paid in the second calendar year. On the date that payments pursuant to clauses (A) and (B) commence, the Company will pay the Executive in a single lump sum payment, less applicable taxes and withholding, the payments that the Executive would have received on or prior to such date but for the delay imposed by the immediately preceding sentence, with the balance of the payments to be paid as originally scheduled. The Accrued Obligations will be paid on the first payroll date following last date of employment to the extent administratively feasible and, if not, then on the second payroll date following the last date of employment.

(iii) Notwithstanding anything to the contrary set forth elsewhere in this Agreement, the Executive may not terminate her employment with the Company for Good Reason pursuant to this Section 4(c), and shall not be considered to have done so for any purpose of this Agreement, unless (A) the Executive, within 60 days after the initial existence of the act or failure to act by the Company that constitutes "Good Reason" within the meaning of this Agreement, provides the Company with written notice that describes, in particular detail, the act or failure to act that the Executive believes to constitute "Good Reason" and identifies the particular event specified in the definition of "Good Reason" on Exhibit A that the Executive contends is applicable to such act or failure to act; (B) the Company, within 30 days after its receipt of such notice, fails or refuses to rescind such act or remedy such failure to act so as to eliminate "Good Reason" for the termination by the Executive of the Executive's employment relationship with the Company; and (C) the Executive actually resigns from the employ of the Company on or before that date that is 12 months after the initial existence of the act or failure to act by the Company that constitutes "Good Reason." If the requirements of the immediately preceding sentence are not fully satisfied on a timely basis, then the resignation by the Executive from the employ of the Company shall not be deemed to have been for "Good Reason," the Executive shall not be entitled to any of the benefits to which the Executive would have been entitled if the Executive had resigned from the employ of the Company for "Good Reason," and the Company shall not be required to pay any amount or provide any benefit that would otherwise have been due to the Executive under this Section 4(c) had the Executive resigned with "Good Reason."

(d) Other Termination by the Executive. The Executive may terminate the Executive's employment for any reason other than for Good Reason upon 30 days' prior written notice of termination to the Company. In the event the Executive shall terminate the Executive's employment pursuant to this Section 4(d), the Company shall not have any further obligation or liability under this Agreement, except for the Accrued Obligations, which shall be paid on the first payroll date following last date of employment to the extent administratively feasible and if not, then on the second payroll date following the last date of employment. The Company shall not have the right following Executive's provision of notice to terminate the Executive's employment prior to the end of the notice period unless the Company pays the Executive for the full notice period.

(e) Base Salary Continuation. The Base Salary continuation set forth in Section 4(c) above shall be intended either (i) to satisfy the safe harbor set forth in the Treas. Regs. 1.409A-1(b)(9)(iii), or (ii) be treated as a Short-term Deferral as that term is defined Treas. Regs. 1.409A-1(b)(4). To the extent such continuation payments exceed the applicable safe harbor amount or do not constitute a Short-term Deferral, the excess amount shall be treated as deferred compensation under Code section 409A and as such shall be payable pursuant to the following schedule: such excess amount shall be paid via standard payroll in periodic installments in accordance with the Company's usual practice for its senior executives. Solely for purposes of Code section 409A, each installment payment is considered a separate payment. Notwithstanding any provision in this Agreement to the contrary, in the event that the Executive is a "specified employee" as defined in Code section 409A, any continuation payment, continuation benefits or other amounts payable under this Agreement that would be subject to the special rule regarding payments to "specified employees" under Section 409A(a)(2)(B) of the Code shall not be paid before the expiration of a period of six months following the date of the Executive's termination of employment or before the date of the Executive's death, if earlier.

(f) Parachute Provisions. In the event a Change of Control occurs, the Company will engage an independent accounting firm (the "Accounting Firm") at its expense to determine whether the Executive received, is entitled to receive or will become entitled to receive any benefits or payments in the nature of compensation (within the meaning of Section 280G(b)(2) of the Code) (the "Total Payments"), and whether the Total Payments will be subject to the tax (the "Excise Tax") imposed by Section 4999 of the Code. If the Total Payments will be subject to the Excise Tax, the aggregate present value of the Total Payments shall be reduced (but not below $1) if reducing the Total Payments will provide the Executive with a greater net after-tax amount than would be the case if no reduction was made. Any reduction shall be effected in accordance with Section 409A of the Code.

5. Restrictive Covenants. Concurrently with the execution hereof, and as a condition of employment, the Executive shall execute and deliver an Employee Confidential Disclosure, Invention Assignment, Non-Competition, Non-Solicitation and Non-Interference Agreement (the "Confidentiality and Invention Assignment Agreement").

6. No Conflicts. The Executive represents and warrants that the Executive is not party to any agreement, contract or understanding, whether of employment, consultancy or otherwise, in conflict with this Agreement or which would in any way restrict or prohibit the Executive from undertaking or performing services for the Company or otherwise from entering into or performing this Agreement or the Confidentiality and Invention Assignment Agreement.

7. Full Agreement. This Agreement and the Confidentiality and Invention Assignment Agreement (including the Exhibits hereto), constitute the entire agreement of the parties concerning its subject matter and supersedes all other oral or written understandings, discussions, and agreements, including but not limited to the Amended and Restated Employment Agreement dated as of May 10, 2019 between the Executive and the Company, but shall not supersede, or otherwise be deemed to terminate, any confidentiality agreements, non-disclosure obligations or restrictive covenants in favor of the Company in effect immediately prior to the Commencement Date. This Agreement may be modified only in a writing signed by both parties. The Executive acknowledges that she has read and fully understand the contents of this Agreement and the Confidentiality and Invention Assignment Agreement and is executing it after having an opportunity to consult with legal counsel.

8. Amendments. Any amendment to this Agreement shall be made in writing and signed by the parties hereto.

9. Enforceability. If any provision of this Agreement shall be invalid or unenforceable, in whole or in part, then such provision shall be deemed to be modified or restricted to the extent and in the manner necessary to render the same valid and enforceable, or shall be deemed excised from this Agreement, as the case may require, and this Agreement shall be construed and enforced to the maximum extent permitted by law as if such provision had been originally incorporated herein as so modified or restricted or as if such provision had not been originally incorporated herein, as the case may be.

10. Construction. This Agreement shall be construed and interpreted in accordance with the internal laws of the Commonwealth of Pennsylvania.

11. Assignment.

(a) By the Company. The rights and obligations of the Company under this Agreement shall inure to the benefit of, and shall be binding upon, the successors and assigns of the Company. This Agreement may be assigned by the Company without the consent of the Executive.

(b) By the Executive. This Agreement and the obligations created hereunder may not be assigned by the Executive, but all rights of the Executive hereunder shall inure to the benefit of and be enforceable by the Executive's heirs, devisees, legatees, executors, administrators and personal representatives. Any attempted assignment in violation of this Section 11(b) shall be null and void.

12. **Notices.** All notices required or permitted to be given hereunder shall be in writing and shall be deemed to have been given when mailed by certified mail, return receipt requested, or delivered by a national overnight delivery service addressed to the intended recipient as follows:

If to the Company:

Annovis Bio, Inc.
1055 Westlakes Drive
Berwyn, PA 19312
Attention: Chairman of the Board

If to the Executive:

Maria L. Maccecchini
1223 Foxglove Lane
West Chester, PA 19380-5854

Any party may from time to time change its address for the purpose of notices to that party by a similar notice specifying a new address, but no such change shall be deemed to have been given until it is actually received by the party sought to be charged with its contents.

13. **Waivers.** No claim or right arising out of a breach or default under this Agreement shall be discharged in whole or in part by a waiver of that claim or right unless the waiver is supported by consideration and is in writing and executed by the aggrieved party hereto or such party's duly authorized agent. A waiver by any party hereto of a breach or default by the other party hereto of any provision of this Agreement shall not be deemed a waiver of future compliance therewith, and such provisions shall remain in full force and effect.

14. **Survival of Covenants.** The provisions of Section 4 through this Section 14 shall survive the termination of the Executive's employment shall continue in effect thereafter.

(Signature page follows.)

IN WITNESS WHEREOF, this Agreement has been executed by the parties as of the date first above written.

ANNOVIS BIO, INC.

By: /s/ Michael Hoffman
Name: Michael Hoffman
Title: Chairman of the Board

/s/ Maria L Maccecchini
Maria L. Maccecchini

EXHIBIT A

Certain Definitions

The following terms have the meaning set forth below wherever they are used in this Agreement:

"Cause" for the Company (or a successor, if appropriate) to terminate the Executive's employment will exist upon the occurrence of any of the following events: (i) the Executive's continued failure to substantially perform the Executive's duties and obligations to the Company, including but not limited to any material breach of this Agreement or any material violation of the Company's written policies or rules, and failure to cure the same within ten business days after being notified by the Board; (ii) the Executive's having committed willful fraud or willful misconduct, in any such case which is materially injurious to the Company; (iii) the Executive's having been convicted of a felony involving moral turpitude that results in material harm to the standing or reputation of the Company; or (iv) the Executive's material breach of the terms of the Confidentiality and Invention Assignment Agreement.

"Change of Control" shall have the meaning set forth in the Equity Incentive Plan.

"Code" means the Internal Revenue Code of 1986, as amended.

"Commencement Date" means March 24, 2020.

"Disability" means an illness, incapacity or a mental or physical condition that renders the Executive unable or incompetent, with or without a reasonable accommodation, to carry out the job responsibilities that the Executive held or the tasks that the Executive was assigned at the time the disability commenced for a period of 90 consecutive days, or 180 non-consecutive days in any rolling 12-month period.

"Equity Incentive Plan" shall mean the Company's 2020 Equity Incentive Plan, as amended and then in effect.

"Fully Diluted Equity" means the issued and outstanding shares of the Company's Common Stock, determined on a fully-diluted, as-converted basis as of the date of grant of the applicable stock options, inclusive of all allocated and unallocated shares authorized to be issued under the Equity Incentive Plan.

"Good Reason" for the Executive to resign from the employ of the Company will exist upon the occurrence of any of the following events, subject to compliance with the other provisions of Section 4(c): (a) a material reduction in the Base Salary, as then in effect; (b) a material reduction of the Executive's authority, position, responsibilities or duties; (c) the Company's material breach of this Agreement; or (d) a relocation at the request of the Board of the Executive's principal workplace by more than 50 miles from the Company's principal offices as of the Commencement Date; provided, however, that (i) clause (a) shall not apply if such reduction is part of a Company-wide reduction in compensation and/or benefits for all of its senior executives, and (ii) following a Change of Control, a reduction in authority, position, responsibilities or duties solely by virtue of the Company being acquired and becoming part of a larger entity or operated as a subsidiary shall not constitute Good Reason.

EXHIBIT B

Equity Incentive Awards

Pursuant to the terms and conditions of the Equity Incentive Plan and an appropriate grant agreement to be executed by the Executive and the Company, the Executive shall be granted the following equity incentive awards in such forms as shall be determined by the Board, upon consultation with the Executive: (a) on or before April 30, 2020, an equity incentive award of 300,000 shares of the Company's Common Stock, all of which shares shall be vested in full upon grant and (b) on or after January 1, 2021 and on or before April 30, 2021, an equity incentive award of 112,995 shares of the Company's Common Stock, which shall be vested in full upon grant.

In the event the Company raises additional capital prior to April 30, 2021 through the sale of its securities and the Board determines in its sole discretion that the Executive's performance warrants the grant of additional equity incentive awards, the Board shall grant to the Executive an additional equity incentive award of 165,199 shares of the Company's Common Stock, subject to approval by the stockholders of the Company of an increase in the shares available under the Equity Incentive Plan. Such additional equity incentive award shall: (a) be granted in accordance with the terms and conditions of the Equity Incentive Plan and an appropriate grant agreement to be executed by the Executive and the Company, and (b) vest in two equal installments on March 30, 2022 and March 30, 2023, respectively, subject to accelerated vesting of such additional award upon a Change of Control of the Company.

EXHIBIT C

Release of Claims

1. Termination of Employment. _____ ("Executive") hereby agrees and recognizes that, as of _____, 20__, Executive's employment relationship with Annovis Bio, Inc., a Delaware corporation (the "Company"), will be permanently and irrevocably severed.

2. Release of Claims. In consideration of the payments and benefits described in Section 4(d) and Section 4(e) of the employment agreement (the "Employment Agreement"), effective _____, 2020, by and between Executive and the Company, to which Executive agrees Executive is not entitled until and unless Executive executes and does not revoke this Release, Executive, for and on behalf of herself and her heirs, executors, administrators and assigns, hereby waives and releases any and all complaints, claims, suits, controversies, and actions, whether known or unknown, suspected or claimed, which Executive, or any of the Executive's heirs, executors, administrators or assigns ever had, now has or may have against the Company and/or its respective predecessors, successors, past or present parents or subsidiaries, affiliates, investors, branches or related entities (collectively, including the Company, the "Entities") and/or the Entities' past or present stockholders, insurers, assigns, trustees, directors, officers, limited and general partners, managers, joint venturers, members, employees or agents in their respective capacities as such (collectively with the Entities, the "Releasees") by reason of circumstances, acts or omissions which have occurred on or prior to the date that this Release becomes effective, including, without limitation, (a) any complaint, charge or cause of action arising under (i) federal, state or local laws pertaining to employment or termination of employment, including the Age Discrimination in Employment Act of 1967 (the "ADEA," a law which prohibits discrimination on the basis of age), the National Labor Relations Act, as amended, the Civil Rights Act of 1991, as amended, the Americans with Disabilities Act of 1990, as amended, Title VII of the Civil Rights Act of 1964, as amended, the Equal Pay Act of 1963, as amended, the Family and Medical Leave Act of 1993, as amended, the Worker Adjustment Retraining and Notification Act, as amended, the Executive Retirement Income Security Act of 1974, as amended, any applicable Executive Order Programs, the Fair Labor Standards Act, or their state or local counterparts (including, but not limited to, the Pennsylvania Human Relations Act); (ii) any other federal, state or local civil or human rights law; (iii) any other local, state, or federal law, regulation or ordinance; (iv) any public policy, contract and/or quasi-contract or tort (including, but not limited to, claims of breach of the Employment Agreement, an expressed or implied contract, tortious interference with contract or prospective business advantage, breach of the covenant of good faith and fair dealing, promissory estoppel, detrimental reliance, invasion of privacy, nonphysical injury, personal injury or sickness or any other harm, wrongful or retaliatory discharge, fraud, defamation, slander, libel, false imprisonment, negligent or intentional infliction of emotional distress); (v) common law; or (vi) any policies, practices or procedures of the Company; or (b) any claim for costs, fees, or other expenses, including attorneys' fees incurred in these matters (the "Released Claims"). By signing this Release, Executive acknowledges that she intends to waive and release any rights known or unknown that she may have against the Releasees under these and any other laws. Notwithstanding the foregoing, Executive does not release, discharge or waive: any rights to indemnification that she may have under the certificate of incorporation, the by-laws or equivalent governing documents of the Company or its subsidiaries or affiliates, the laws of the State of Delaware or any other state of which any such subsidiary or affiliate is a domiciliary, the Employment Agreement or any indemnification agreement between Executive and the Company; any rights to insurance coverage under any directors' and officers' personal liability insurance or fiduciary insurance policy; any rights she may have in her capacity as a stockholder of the Company; any rights she may have to enforce the vested terms of any equity or other incentive agreement previously provided to her; any rights she may have to severance benefits and payment of Accrued Obligations under the Employment Agreement (the "Excluded Claims"). The Executive acknowledges that she has made no assignment or transfer of any right, claim, demand, cause of action, or other matter covered by this Section 1.

3. Proceedings. Executive acknowledges that she has not filed any complaint, charge, claim or proceeding, if any, or assigned to any other person the right to bring any such complaint, charge, claim, or proceeding, relating to the Released Claims against any of the Releasees before any local, state or federal agency, court or other body (each individually a "Proceeding"). Executive (i) acknowledges that she will not initiate or cause to be initiated on her behalf any Proceeding and will not participate in any Proceeding, in each case, except as required by law and (ii) waives any right she may have to benefit in any manner from any relief (whether monetary or otherwise) arising out of any Proceeding, including any Proceeding conducted by the Equal Employment Opportunity Commission (the "EEOC"). Further, Executive understands that, by executing this Release, she will be limiting the availability of certain remedies that she may have against the Releasees and limiting also her ability to pursue certain claims against the Releasees. Notwithstanding the above, nothing in Section 1 of this Release shall prevent Executive from (i) initiating or causing to be initiated on the Executive's behalf any complaint, charge, claim or proceeding against any Releasee before any local, state or federal agency, court or other body challenging the validity of the waiver of the Executive's claims under the ADEA contained in Section 1 of this Release (but no other portion of such waiver), (ii) initiating or participating in an investigation or proceeding conducted by the EEOC or (iii) reporting possible violations of federal, state or local law, ordinance or regulation to any governmental agency or entity, including, but not limited to, the Department of Justice, the U.S. Securities and Exchange Commission (the "SEC"), the Congress and any agency Inspector General, or otherwise taking action or making disclosures that are protected under the whistleblower provisions of any federal, state or local law, ordinance or regulation, including, but not limited to, Rule 21F-17 promulgated under the Securities Exchange Act of 1934, as amended; or (iv) receiving a monetary award for information provided to the SEC pursuant to Rule 21F-17 promulgated under the Securities Exchange Act of 1934, as amended. The Executive acknowledges and agrees that the Executive's separation from employment with the Company in compliance with the terms of the Employment Agreement shall not serve as the basis for any claim or action (including, without limitation, any claim under the Age Discrimination in Employment Act of 1967).

4. Time to Consider. Executive acknowledges that she has been advised that she has [twenty-one (21)]/[forty-five (45)][1] days from the date of receipt of this Release to consider all the provisions of this Release and, further, that if Executive signs this Release prior to the expiration of such [twenty-one (21)]/[forty-five (45)] day period, she does hereby knowingly and voluntarily waive said given [twenty-one (21)]/[forty-five (45)] day period. EXECUTIVE FURTHER ACKNOWLEDGES THAT SHE HAS READ THIS RELEASE CAREFULLY, HAS BEEN ADVISED BY THE COMPANY TO, AND HAS IN FACT, CONSULTED AN ATTORNEY, AND FULLY UNDERSTANDS THAT BY SIGNING BELOW SHE IS GIVING UP CERTAIN RIGHTS WHICH SHE MAY HAVE TO SUE OR ASSERT A CLAIM AGAINST ANY OF THE RELEASEES, AS DESCRIBED IN SECTION 1 OF THIS RELEASE AND THE OTHER PROVISIONS HEREOF. EXECUTIVE ACKNOWLEDGES THAT SHE HAS NOT BEEN FORCED OR PRESSURED IN ANY MANNER WHATSOEVER TO SIGN THIS RELEASE, AND EXECUTIVE AGREES TO ALL OF ITS TERMS VOLUNTARILY. [EXECUTIVE ALSO ACKNOWLEDGES THAT SHE HAS RECEIVED ALL INFORMATION REQUIRED TO BE DISCLOSED IN CONNECTION WITH AN EXIT INCENTIVE OR OTHER EMPLOYMENT TERMINATION PROGRAM.]

5. Revocation. Executive hereby acknowledges and understands that Executive shall have seven (7) days from the date of her execution of this Release to revoke this Release (including, without limitation, any and all claims arising under the ADEA) and that neither the Company nor any other person is obligated to provide any benefits to Executive pursuant to Section 4(d) or Section 4(e) of the Employment Agreement until eight (8) days have passed since Executive's signing of this Release without Executive having revoked this Release, in which event the Company immediately shall arrange and/or pay for any such benefits otherwise attributable to said eight-(8) day period, consistent with the terms of the Employment Agreement. If Executive revokes this Release, Executive will be deemed not to have accepted the terms of this Release, no action or forbearance of action will be required of the Company under any section of this Release, and Executive shall not be entitled to receive any portion of the severance compensation and benefits which are conditioned on the delivery of this Release.

[1] NTD: To be selected based on whether applicable termination was "in connection with an exit incentive or other employment termination program" (as such phrase is defined in the Age Discrimination in Employment Act of 1967).

6. No Admission. This Release does not constitute an admission of liability or wrongdoing of any kind by Executive or the Company.

7. Confidentiality. Executive agrees that Executive will not communicate or disclose the terms of this Release to any persons with the exception of members of Executive's immediate family and Executive's attorney and financial advisor, or as permitted by Section 3 above.

8. Return of Company Property. Executive represents that all equipment and other property of the Company, including any documents and files, whether electronically stored or maintained in hard copy, have been returned to the Company, and that Executive has not retained any copies of the same.

9. Non-Disparagement. Executive will not disparage any Releasee or otherwise take any action which could reasonably be expected to adversely affect the personal or professional reputation of any Releasee. The Company's directors, officers and senior executives shall not disparage or otherwise take any action which could reasonably be expected to adversely affect the personal or professional reputation of the Executive.

10. Post-Employment Obligations. Executive reaffirms that she will comply with all of her post-employment obligations as set forth in Section 5 of the Employment Agreement.

11. Entire Agreement. This Agreement constitutes the entire agreement between the parties and supersedes any and all prior representations, agreements, written or oral, expressed or implied, except for Section 5 of the Employment Agreement, which survives the termination of Executive's employment and is incorporated herein by reference, and except for any agreements with respect to Executive's options to acquire Common Stock of the Company. This Agreement may not be modified or amended other than by an agreement in writing signed by an officer of the Company.

12. Acknowledgement. Executive acknowledges and agrees that, subsequent to the termination of Executive's employment, Executive shall not be eligible for any payments from the Company or Company-paid benefits, except as expressly set forth in this Agreement. Executive also acknowledges and agrees that Executive has been paid for all time worked and has received all other compensation owed to her.

13. Assignment. This Agreement shall be binding upon and be for the benefit of the parties as well as Executive's heirs and the Company's successors and assigns.

14. General Provisions. A failure of any of the Releasees to insist on strict compliance with any provision of this Release shall not be deemed a waiver of such provision or any other provision hereof. If any provision of this Release is determined to be so broad as to be unenforceable, such provision shall be interpreted to be only so broad as is enforceable, and in the event that any provision is determined to be entirely unenforceable, such provision shall be deemed severable, such that all other provisions of this Release shall remain valid and binding upon Executive and the Releasees.

15. Governing Law. The validity, interpretations, construction and performance of this Release shall be governed by the laws of the Commonwealth of Pennsylvania without giving effect to conflict of laws principles.

IN WITNESS WHEREOF, Executive has hereunto set Executive's hand as of the day and year set forth opposite her signature below.

Date	Maria L. Maccecchini

Exhibit 10.9

EMPLOYMENT AGREEMENT

EMPLOYMENT AGREEMENT effective as of March 24, 2020 (this "Agreement") between Annovis Bio, Inc. (the "Company"), a Delaware corporation, and Jeffrey B. McGroarty (the "Executive").

Background:

The parties desire to enter into this Agreement to provide for the employment of the Executive by the Company and for certain other matters in connection with such employment, all as set forth more fully in this Agreement. Certain capitalized terms used in this Agreement have the respective meanings given to them in Exhibit A hereto.

Terms:

NOW, THEREFORE, in consideration of the premises and covenants set forth herein, and intending to be legally bound hereby, the parties to this Agreement hereby agree as follows:

1. Position and Duties.

(a) Position and Duties. The Company agrees that the Executive shall be employed by the Company to serve as Chief Financial Officer of the Company. The Executive shall report to the Board of Directors of the Company (the "Board"). The Executive agrees to be so employed by the Company and agrees to devote substantially all of his business time, attention, skill and efforts to perform services for the Company and to faithfully and diligently discharge and fulfill the Executive's duties hereunder to the best of his abilities. In so doing, the Executive shall perform such executive, managerial, administrative and financial functions as are required to develop the Company's business and to perform other duties assigned to the Executive by the Board that are consistent with the Executive's title as Chief Financial Officer. The Executive shall perform his duties hereunder primarily at the Company's principal offices. In the performance of his duties, the Executive shall travel to such other places at such times as the needs of the Company may from time-to-time dictate or be desirable.

(b) Other Activities. Notwithstanding Section 1(a), the Executive may engage in other business and professional activities to the extent that they do not interfere with the Executive's obligations under this Agreement, provided that each of those activities is first disclosed to and approved by the Board. The parties acknowledge that activities in which the Executive is currently engaged have been disclosed to and approved by the Board.

2. Term. The Executive's employment under this Agreement shall commence on the Commencement Date and shall end when terminated pursuant to Section 4.

3. Compensation.

(a) Base Salary. During the term of the Executive's employment under this Agreement, the Executive shall be paid an annual salary at the rate of $300,000 (the "Base Salary"), retroactive to January 1, 2020, payable in accordance with the Company's payroll practices and policies in effect from time to time and subject to applicable withholding of income taxes, social security taxes and other such other payroll deductions as are required by law or applicable employee benefit programs. The Board shall review the Executive's Base Salary for annual increases, commencing with the Base Salary for the 2021 calendar year.

(b) Annual Bonus. With respect to each fiscal year of the Company during the continued full-time employment of the Executive hereunder, commencing with the 2020 fiscal year, the Executive will be eligible to be considered for an annual performance bonus (the "Annual Bonus") in an amount of up to 50% of the Executive's Base Salary. The Annual Bonus, if any, will be awarded by the Board in its sole discretion based on the achievement of Company and personal performance goals established by the Board on an annual basis, following consultation with the Executive and shall take into account the stock options and any other equity incentive awards that vest in the year the bonus is paid. Any Annual Bonus awarded to the Executive hereunder may be paid in cash or in equity of the Company, as determined by the Board in its sole discretion, and will be payable or issuable, less applicable taxes and withholdings, not later than two and one-half months after the end of the fiscal year to which the Annual Bonus relates in accordance with the Company's customary practices for annual bonus payments.

(c) Equity Incentives. Subject to the approval of the Board, the Executive shall be granted equity incentives under the Equity Incentive Plan and shall be considered for future equity incentive awards as specified on Exhibit B hereto. In addition, the Executive shall be eligible to participate in future equity incentive programs established by the Company from time to time in the future in accordance with the terms of those programs.

(d) Vacation and Fringe Benefits. The Executive shall be entitled to participate in all vacation and other fringe benefit programs of the Company to the extent and on the same terms and conditions as are accorded to other senior management employees of the Company.

(e) Reimbursement of Other Expenses. The Company shall reimburse the Executive for the reasonable and necessary out-of-pocket business expenses incurred by the Executive for or on behalf of the Company in furtherance of the performance of the Executive's duties hereunder in accordance with the Company's policies as approved by the Board from time to time, subject in all cases to the Company's requirements with respect to reporting and documentation of such expenses.

(f) Section 409A. If any reimbursement under this Section 3 is not exempt from Section 409A of the Internal Revenue Code of 1986, as amended (the "Code") then (i) any reimbursement in one calendar year shall not affect the amount that may be reimbursed in any other calendar year; (ii) a reimbursement (or right thereto) may not be exchanged or liquidated for another benefit or payment; and (iii) a reimbursement shall be made no later than the end of the calendar year following the calendar year in which the Executive incurred the related expense.

4. Termination.

(a) Death or Disability. The Executive's employment with the Company shall automatically terminate effective as of the date of the Executive's death, and the Company may terminate the employment of the Executive immediately upon written notice to the Executive in the event of the Disability of the Executive. In the event of termination of the Executive's employment due to death or Disability, the Company shall not have any further obligation or liability under this Agreement except that the Company shall pay to the Executive or the Executive's estate (as applicable): (i) any portion of the Executive's Base Salary for the period up to the date of employment termination that has been earned but remains unpaid; (ii) any expenses properly incurred but not yet reimbursed, including, without limitation, the reimbursements provided for in Section 3(e); (iii) any benefits that have accrued to the Executive under the terms of the employee benefit plans of the Company, which benefits shall be paid in accordance with the terms of those plans (the payments in clauses (i) through (iii) collectively, the "Accrued Obligations"); and (iv) in the event of a termination of employment due to the Executive's death, the Annual Bonus awarded pursuant to Section 3(b), if any, with respect to the fiscal year prior to the fiscal year of termination, to the extend unpaid (the "Earned Bonus"). The Accrued Obligations shall be paid on the first payroll date following the last date of employment to the extent administratively feasible and, if not, then on the second payroll date following the last date of employment. The Earned Bonus, if any, will be paid when it would have been paid had Executive remained employed with the Company.

(b) Termination of the Executive's Employment for Cause. The Company may terminate the employment of the Executive for Cause immediately upon written notice of such termination to the Executive. If the Executive's employment with the Company is terminated by the Company for Cause, the Company shall not have any further obligation or liability under this Agreement except for the Accrued Obligations. The Accrued Obligations shall be paid on the first payroll date following the last date of employment to the extent administratively feasible and, if not, then on the second payroll date following the last date of employment.

(c) Involuntary Termination.

(i) The Company may terminate the employment of the Executive for any reason other than one specified in Section 4(a) or Section 4(b) immediately upon written notice of termination to the Executive, and the Executive may terminate his employment with the Company for Good Reason immediately upon providing written notice of such termination to the Company. Either of such terminations shall be deemed an "Involuntary Termination" for purposes of this Agreement.

(ii) Upon the occurrence of an Involuntary Termination, in addition to the Accrued Obligations, and subject to the execution by the Executive of a release in the form of Exhibit C hereto (the "Release") and the compliance by the Executive with the Release and all terms and provisions of this Agreement and the Confidentiality and Invention Assignment Agreement (as defined in Section 5) that survive the termination of the Executive's employment by the Company the Executive shall be entitled to receive (A) severance payments in an amount equal to the Base Salary in effect on the termination date for a period of 12 months; plus (B) monthly reimbursement (upon presentation of proof of payment) for the medical insurance premiums at the same level as was in effect on the termination date until the earlier of (1) the end of such 12-month period or (2) the date the Executive becomes eligible for medical benefits through another employer; provided, however, that if such Involuntary Termination shall occur upon the closing of a Change of Control or within 12 months thereafter: (A) the severance shall be payable in a single lump sum and (B) the Executive shall also be entitled to receive an amount equal to 75% of the projected target amount of the Executive's Annual Bonus for the calendar year in which the Executive's employment termination occurs payable in a single lump sum, such lump sum payments to be made in each case on the first regularly scheduled payroll date that occurs on or after 60 days after the effective date of such employment termination. Any payments due pursuant to this Section 4(c), other than the Accrued Obligations, shall commence as soon as administratively feasible within 60 days after the date of the Executive's termination of employment provided the Executive has timely executed and returned the Release and, if a revocation period is applicable, the Executive has not revoked the Release; provided, however, that if the 60-day period begins in one calendar year and ends in a second calendar year, the severance payments shall begin to be paid in the second calendar year. On the date that payments pursuant to clauses (A) and (B) commence, the Company will pay the Executive in a single lump sum payment, less applicable taxes and withholding, the payments that the Executive would have received on or prior to such date but for the delay imposed by the immediately preceding sentence, with the balance of the payments to be paid as originally scheduled. The Accrued Obligations will be paid on the first payroll date following last date of employment to the extent administratively feasible and, if not, then on the second payroll date following the last date of employment.

(iii) Notwithstanding anything to the contrary set forth elsewhere in this Agreement, the Executive may not terminate his employment with the Company for Good Reason pursuant to this Section 4(c), and shall not be considered to have done so for any purpose of this Agreement, unless (A) the Executive, within 60 days after the initial existence of the act or failure to act by the Company that constitutes "Good Reason" within the meaning of this Agreement, provides the Company with written notice that describes, in particular detail, the act or failure to act that the Executive believes to constitute "Good Reason" and identifies the particular event specified in the definition of "Good Reason" on Exhibit A that the Executive contends is applicable to such act or failure to act; (B) the Company, within 30 days after its receipt of such notice, fails or refuses to rescind such act or remedy such failure to act so as to eliminate "Good Reason" for the termination by the Executive of the Executive's employment relationship with the Company; and (C) the Executive actually resigns from the employ of the Company on or before that date that is 12 months after the initial existence of the act or failure to act by the Company that constitutes "Good Reason." If the requirements of the immediately preceding sentence are not fully satisfied on a timely basis, then the resignation by the Executive from the employ of the Company shall not be deemed to have been for "Good Reason," the Executive shall not be entitled to any of the benefits to which the Executive would have been entitled if the Executive had resigned from the employ of the Company for "Good Reason," and the Company shall not be required to pay any amount or provide any benefit that would otherwise have been due to the Executive under this Section 4(c) had the Executive resigned with "Good Reason."

(d) Other Termination by the Executive. The Executive may terminate the Executive's employment for any reason other than for Good Reason upon 30 days' prior written notice of termination to the Company. In the event the Executive shall terminate the Executive's employment pursuant to this Section 4(d), the Company shall not have any further obligation or liability under this Agreement, except for the Accrued Obligations, which shall be paid on the first payroll date following last date of employment to the extent administratively feasible and if not, then on the second payroll date following the last date of employment. The Company shall not have the right following Executive's provision of notice to terminate the Executive's employment prior to the end of the notice period unless the Company pays the Executive for the full notice period.

(e) Base Salary Continuation. The Base Salary continuation set forth in Section 4(c) above shall be intended either (i) to satisfy the safe harbor set forth in the Treas. Regs. 1.409A-1(b)(9)(iii), or (ii) be treated as a Short-term Deferral as that term is defined Treas. Regs. 1.409A-1(b)(4). To the extent such continuation payments exceed the applicable safe harbor amount or do not constitute a Short-term Deferral, the excess amount shall be treated as deferred compensation under Code section 409A and as such shall be payable pursuant to the following schedule: such excess amount shall be paid via standard payroll in periodic installments in accordance with the Company's usual practice for its senior executives. Solely for purposes of Code section 409A, each installment payment is considered a separate payment. Notwithstanding any provision in this Agreement to the contrary, in the event that the Executive is a "specified employee" as defined in Code section 409A, any continuation payment, continuation benefits or other amounts payable under this Agreement that would be subject to the special rule regarding payments to "specified employees" under Section 409A(a)(2)(B) of the Code shall not be paid before the expiration of a period of six months following the date of the Executive's termination of employment or before the date of the Executive's death, if earlier.

(f) Parachute Provisions. In the event a Change of Control occurs, the Company will engage an independent accounting firm (the "Accounting Firm") at its expense to determine whether the Executive received, is entitled to receive or will become entitled to receive any benefits or payments in the nature of compensation (within the meaning of Section 280G(b)(2) of the Code) (the "Total Payments"), and whether the Total Payments will be subject to the tax (the "Excise Tax") imposed by Section 4999 of the Code. If the Total Payments will be subject to the Excise Tax, the aggregate present value of the Total Payments shall be reduced (but not below $1) if reducing the Total Payments will provide the Executive with a greater net after-tax amount than would be the case if no reduction was made. Any reduction shall be effected in accordance with Section 409A of the Code.

5. **Restrictive Covenants.** Concurrently with the execution hereof, and as a condition of employment, the Executive shall execute and deliver an Employee Confidential Disclosure, Invention Assignment, Non-Competition, Non-Solicitation and Non-Interference Agreement (the "Confidentiality and Invention Assignment Agreement").

6. **No Conflicts.** The Executive represents and warrants that the Executive is not party to any agreement, contract or understanding, whether of employment, consultancy or otherwise, in conflict with this Agreement or which would in any way restrict or prohibit the Executive from undertaking or performing services for the Company or otherwise from entering into or performing this Agreement or the Confidentiality and Invention Assignment Agreement.

7. **Full Agreement.** This Agreement and the Confidentiality and Invention Assignment Agreement (including the Exhibits hereto), constitute the entire agreement of the parties concerning its subject matter and supersedes all other oral or written understandings, discussions, and agreements, but shall not supersede, or otherwise be deemed to terminate, any confidentiality agreements, non-disclosure obligations or restrictive covenants in favor of the Company in effect immediately prior to the Commencement Date. This Agreement may be modified only in a writing signed by both parties. The Executive acknowledges that she has read and fully understand the contents of this Agreement and the Confidentiality and Invention Assignment Agreement and is executing it after having an opportunity to consult with legal counsel.

8. **Amendments.** Any amendment to this Agreement shall be made in writing and signed by the parties hereto.

9. **Enforceability.** If any provision of this Agreement shall be invalid or unenforceable, in whole or in part, then such provision shall be deemed to be modified or restricted to the extent and in the manner necessary to render the same valid and enforceable, or shall be deemed excised from this Agreement, as the case may require, and this Agreement shall be construed and enforced to the maximum extent permitted by law as if such provision had been originally incorporated herein as so modified or restricted or as if such provision had not been originally incorporated herein, as the case may be.

10. **Construction.** This Agreement shall be construed and interpreted in accordance with the internal laws of the Commonwealth of Pennsylvania.

11. **Assignment.**

(a) **By the Company.** The rights and obligations of the Company under this Agreement shall inure to the benefit of, and shall be binding upon, the successors and assigns of the Company. This Agreement may be assigned by the Company without the consent of the Executive.

(b) **By the Executive.** This Agreement and the obligations created hereunder may not be assigned by the Executive, but all rights of the Executive hereunder shall inure to the benefit of and be enforceable by the Executive's heirs, devisees, legatees, executors, administrators and personal representatives. Any attempted assignment in violation of this Section 11(b) shall be null and void.

12. **Notices.** All notices required or permitted to be given hereunder shall be in writing and shall be deemed to have been given when mailed by certified mail, return receipt requested, or delivered by a national overnight delivery service addressed to the intended recipient as follows:

If to the Company:

Annovis Bio, Inc.
1055 Westlakes Drive
Berwyn, PA 19312
Attention: Chairman of the Board

If to the Executive:

Jeffrey B. McGroarty
360 Hilltop Road
Paoli, PA 19301

Any party may from time to time change its address for the purpose of notices to that party by a similar notice specifying a new address, but no such change shall be deemed to have been given until it is actually received by the party sought to be charged with its contents.

13. **Waivers.** No claim or right arising out of a breach or default under this Agreement shall be discharged in whole or in part by a waiver of that claim or right unless the waiver is supported by consideration and is in writing and executed by the aggrieved party hereto or such party's duly authorized agent. A waiver by any party hereto of a breach or default by the other party hereto of any provision of this Agreement shall not be deemed a waiver of future compliance therewith, and such provisions shall remain in full force and effect.

14. **Survival of Covenants.** The provisions of Section 4 through this Section 14 shall survive the termination of the Executive's employment shall continue in effect thereafter.

(Signature page follows.)

IN WITNESS WHEREOF, this Agreement has been executed by the parties as of the date first above written.

ANNOVIS BIO, INC.

By: /s/ Maria L. Maccecchini
Name: Maria L. Maccecchini
Title: President and CEO

/s/ Jeffrey B. McGroarty
Jeffrey B. McGroarty

EXHIBIT A

Certain Definitions

The following terms have the meaning set forth below wherever they are used in this Agreement:

"Cause" for the Company (or a successor, if appropriate) to terminate the Executive's employment will exist upon the occurrence of any of the following events: (i) the Executive's continued failure to substantially perform the Executive's duties and obligations to the Company, including but not limited to any material breach of this Agreement or any material violation of the Company's written policies or rules, and failure to cure the same within ten business days after being notified by the Board; (ii) the Executive's having committed willful fraud or willful misconduct, in any such case which is materially injurious to the Company; (iii) the Executive's having been convicted of a felony involving moral turpitude that results in material harm to the standing or reputation of the Company; or (iv) the Executive's material breach of the terms of the Confidentiality and Invention Assignment Agreement.

"Change of Control" shall have the meaning set forth in the Equity Incentive Plan.

"Code" means the Internal Revenue Code of 1986, as amended.

"Commencement Date" means March 24, 2020.

"Disability" means an illness, incapacity or a mental or physical condition that renders the Executive unable or incompetent, with or without a reasonable accommodation, to carry out the job responsibilities that the Executive held or the tasks that the Executive was assigned at the time the disability commenced for a period of 90 consecutive days, or 180 non-consecutive days in any rolling 12-month period.

"Equity Incentive Plan" shall mean the Company's 2020 Equity Incentive Plan, as amended and then in effect.

"Fully Diluted Equity" means the issued and outstanding shares of the Company's Common Stock, determined on a fully-diluted, as-converted basis as of the date of grant of the applicable stock options, inclusive of all allocated and unallocated shares authorized to be issued under the Equity Incentive Plan.

"Good Reason" for the Executive to resign from the employ of the Company will exist upon the occurrence of any of the following events, subject to compliance with the other provisions of Section 4(c): (a) a material reduction in the Base Salary, as then in effect; (b) a material reduction of the Executive's authority, position, responsibilities or duties; (c) the Company's material breach of this Agreement; or (d) a relocation at the request of the Board of the Executive's principal workplace by more than 50 miles from the Company's principal offices as of the Commencement Date; provided, however, that (i) clause (a) shall not apply if such reduction is part of a Company-wide reduction in compensation and/or benefits for all of its senior executives, and (ii) following a Change of Control, a reduction in authority, position, responsibilities or duties solely by virtue of the Company being acquired and becoming part of a larger entity or operated as a subsidiary shall not constitute Good Reason.

EXHIBIT B

Equity Incentive Awards

Pursuant to the terms and conditions of the Equity Incentive Plan and an appropriate grant agreement to be executed by the Executive and the Company, the Executive shall be granted the following equity incentive awards in such forms as shall be determined by the Board, upon consultation with the Executive: (a) on or before April 30, 2020, an equity incentive award of 300,000 shares of the Company's Common Stock, of which 250,000 shares shall be vested in full upon grant and the remaining 50,000 shares shall vest on April 30, 2021 (the "2021 Vesting Date"); provided, however, that if a Change of Control shall occur prior to the 2021 Vesting Date, such award shall vest in full upon the closing of the Change of Control. Such grant shall be made on or before April 30, 2020; and (b) on or after January 1, 2021 and on or before April 30, 2021, an equity incentive award of 30,396 shares of the Company's Common Stock, all of which shall be vested in full upon grant.

In the event the Company raises additional capital prior to the 2021 Vesting Date through the sale of its securities and the Board determines in its sole discretion that the Executive's performance warrants the grant of additional equity incentive awards, the Board shall grant to the Executive an additional equity incentive award of 165,199 shares of the Company's Common Stock, subject to approval by the stockholders of the Company of an increase in the shares available under the Equity Incentive Plan. Such additional equity incentive award shall: (a) be granted in accordance with the terms and conditions of the Equity Incentive Plan and an appropriate grant agreement to be executed by the Executive and the Company, and (b) vest in two equal installments on March 31, 2022 and March 31, 2023, respectively, subject to accelerated vesting of such additional award upon a Change of Control of the Company.

EXHIBIT C

Release of Claims

1. Termination of Employment. _____ ("Executive") hereby agrees and recognizes that, as of _____, 20__, Executive's employment relationship with Annovis Bio, Inc., a Delaware corporation (the "Company"), will be permanently and irrevocably severed.

2. Release of Claims. In consideration of the payments and benefits described in Section 4(d) and Section 4(e) of the employment agreement (the "Employment Agreement"), effective _____, 2020, by and between Executive and the Company, to which Executive agrees Executive is not entitled until and unless Executive executes and does not revoke this Release, Executive, for and on behalf of himself and his heirs, executors, administrators and assigns, hereby waives and releases any and all complaints, claims, suits, controversies, and actions, whether known or unknown, suspected or claimed, which Executive, or any of the Executive's heirs, executors, administrators or assigns ever had, now has or may have against the Company and/or its respective predecessors, successors, past or present parents or subsidiaries, affiliates, investors, branches or related entities (collectively, including the Company, the "Entities") and/or the Entities' past or present stockholders, insurers, assigns, trustees, directors, officers, limited and general partners, managers, joint venturers, members, employees or agents in their respective capacities as such (collectively with the Entities, the "Releasees") by reason of circumstances, acts or omissions which have occurred on or prior to the date that this Release becomes effective, including, without limitation, (a) any complaint, charge or cause of action arising under (i) federal, state or local laws pertaining to employment or termination of employment, including the Age Discrimination in Employment Act of 1967 (the "ADEA," a law which prohibits discrimination on the basis of age), the National Labor Relations Act, as amended, the Civil Rights Act of 1991, as amended, the Americans with Disabilities Act of 1990, as amended, Title VII of the Civil Rights Act of 1964, as amended, the Equal Pay Act of 1963, as amended, the Family and Medical Leave Act of 1993, as amended, the Worker Adjustment Retraining and Notification Act, as amended, the Executive Retirement Income Security Act of 1974, as amended, any applicable Executive Order Programs, the Fair Labor Standards Act, or their state or local counterparts (including, but not limited to, the Pennsylvania Human Relations Act); (ii) any other federal, state or local civil or human rights law; (iii) any other local, state, or federal law, regulation or ordinance; (iv) any public policy, contract and/or quasi-contract or tort (including, but not limited to, claims of breach of the Employment Agreement, an expressed or implied contract, tortious interference with contract or prospective business advantage, breach of the covenant of good faith and fair dealing, promissory estoppel, detrimental reliance, invasion of privacy, nonphysical injury, personal injury or sickness or any other harm, wrongful or retaliatory discharge, fraud, defamation, slander, libel, false imprisonment, negligent or intentional infliction of emotional distress); (v) common law; or (vi) any policies, practices or procedures of the Company; or (b) any claim for costs, fees, or other expenses, including attorneys' fees incurred in these matters (the "Released Claims"). By signing this Release, Executive acknowledges that she intends to waive and release any rights known or unknown that she may have against the Releasees under these and any other laws. Notwithstanding the foregoing, Executive does not release, discharge or waive: any rights to indemnification that she may have under the certificate of incorporation, the by-laws or equivalent governing documents of the Company or its subsidiaries or affiliates, the laws of the State of Delaware or any other state of which any such subsidiary or affiliate is a domiciliary, the Employment Agreement or any indemnification agreement between Executive and the Company; any rights to insurance coverage under any directors' and officers' personal liability insurance or fiduciary insurance policy; any rights she may have in his capacity as a stockholder of the Company; any rights she may have to enforce the vested terms of any equity or other incentive agreement previously provided to her; any rights she may have to severance benefits and payment of Accrued Obligations under the Employment Agreement (the "Excluded Claims"). The Executive acknowledges that she has made no assignment or transfer of any right, claim, demand, cause of action, or other matter covered by this Section 1.

3. Proceedings. Executive acknowledges that she has not filed any complaint, charge, claim or proceeding, if any, or assigned to any other person the right to bring any such complaint, charge, claim, or proceeding, relating to the Released Claims against any of the Releasees before any local, state or federal agency, court or other body (each individually a "Proceeding"). Executive (i) acknowledges that she will not initiate or cause to be initiated on his behalf any Proceeding and will not participate in any Proceeding, in each case, except as required by law and (ii) waives any right she may have to benefit in any manner from any relief (whether monetary or otherwise) arising out of any Proceeding, including any Proceeding conducted by the Equal Employment Opportunity Commission (the "EEOC"). Further, Executive understands that, by executing this Release, she will be limiting the availability of certain remedies that she may have against the Releasees and limiting also his ability to pursue certain claims against the Releasees. Notwithstanding the above, nothing in Section 1 of this Release shall prevent Executive from (i) initiating or causing to be initiated on the Executive's behalf any complaint, charge, claim or proceeding against any Releasee before any local, state or federal agency, court or other body challenging the validity of the waiver of the Executive's claims under the ADEA contained in Section 1 of this Release (but no other portion of such waiver), (ii) initiating or participating in an investigation or proceeding conducted by the EEOC or (iii) reporting possible violations of federal, state or local law, ordinance or regulation to any governmental agency or entity, including, but not limited to, the Department of Justice, the U.S. Securities and Exchange Commission (the "SEC"), the Congress and any agency Inspector General, or otherwise taking action or making disclosures that are protected under the whistleblower provisions of any federal, state or local law, ordinance or regulation, including, but not limited to, Rule 21F-17 promulgated under the Securities Exchange Act of 1934, as amended; or (iv) receiving a monetary award for information provided to the SEC pursuant to Rule 21F-17 promulgated under the Securities Exchange Act of 1934, as amended. The Executive acknowledges and agrees that the Executive's separation from employment with the Company in compliance with the terms of the Employment Agreement shall not serve as the basis for any claim or action (including, without limitation, any claim under the Age Discrimination in Employment Act of 1967).

4. Time to Consider. Executive acknowledges that she has been advised that she has [twenty-one (21)]/[forty-five (45)][1] days from the date of receipt of this Release to consider all the provisions of this Release and, further, that if Executive signs this Release prior to the expiration of such [twenty-one (21)]/[forty-five (45)] day period, she does hereby knowingly and voluntarily waive said given [twenty-one (21)]/[forty-five (45)] day period. EXECUTIVE FURTHER ACKNOWLEDGES THAT SHE HAS READ THIS RELEASE CAREFULLY, HAS BEEN ADVISED BY THE COMPANY TO, AND HAS IN FACT, CONSULTED AN ATTORNEY, AND FULLY UNDERSTANDS THAT BY SIGNING BELOW SHE IS GIVING UP CERTAIN RIGHTS WHICH SHE MAY HAVE TO SUE OR ASSERT A CLAIM AGAINST ANY OF THE RELEASEES, AS DESCRIBED IN SECTION 1 OF THIS RELEASE AND THE OTHER PROVISIONS HEREOF. EXECUTIVE ACKNOWLEDGES THAT SHE HAS NOT BEEN FORCED OR PRESSURED IN ANY MANNER WHATSOEVER TO SIGN THIS RELEASE, AND EXECUTIVE AGREES TO ALL OF ITS TERMS VOLUNTARILY. [EXECUTIVE ALSO ACKNOWLEDGES THAT SHE HAS RECEIVED ALL INFORMATION REQUIRED TO BE DISCLOSED IN CONNECTION WITH AN EXIT INCENTIVE OR OTHER EMPLOYMENT TERMINATION PROGRAM.]

5. Revocation. Executive hereby acknowledges and understands that Executive shall have seven (7) days from the date of his execution of this Release to revoke this Release (including, without limitation, any and all claims arising under the ADEA) and that neither the Company nor any other person is obligated to provide any benefits to Executive pursuant to Section 4(d) or Section 4(e) of the Employment Agreement until eight (8) days have passed since Executive's signing of this Release without Executive having revoked this Release, in which event the Company immediately shall arrange and/or pay for any such benefits otherwise attributable to said eight-(8) day period, consistent with the terms of the Employment Agreement. If Executive revokes this Release, Executive will be deemed not to have accepted the terms of this Release, no action or forbearance of action will be required of the Company under any section of this Release, and Executive shall not be entitled to receive any portion of the severance compensation and benefits which are conditioned on the delivery of this Release.

6. No Admission. This Release does not constitute an admission of liability or wrongdoing of any kind by Executive or the Company.

[1] NTD: To be selected based on whether applicable termination was "in connection with an exit incentive or other employment termination program" (as such phrase is defined in the Age Discrimination in Employment Act of 1967).

7. Confidentiality. Executive agrees that Executive will not communicate or disclose the terms of this Release to any persons with the exception of members of Executive's immediate family and Executive's attorney and financial advisor, or as permitted by Section 3 above.

8. Return of Company Property. Executive represents that all equipment and other property of the Company, including any documents and files, whether electronically stored or maintained in hard copy, have been returned to the Company, and that Executive has not retained any copies of the same.

9. Non-Disparagement. Executive will not disparage any Releasee or otherwise take any action which could reasonably be expected to adversely affect the personal or professional reputation of any Releasee. The Company's directors, officers and senior executives shall not disparage or otherwise take any action which could reasonably be expected to adversely affect the personal or professional reputation of the Executive.

10. Post-Employment Obligations. Executive reaffirms that she will comply with all of his post-employment obligations as set forth in Section 5 of the Employment Agreement.

11. Entire Agreement. This Agreement constitutes the entire agreement between the parties and supersedes any and all prior representations, agreements, written or oral, expressed or implied, except for Section 5 of the Employment Agreement, which survives the termination of Executive's employment and is incorporated herein by reference, and except for any agreements with respect to Executive's options to acquire Common Stock of the Company. This Agreement may not be modified or amended other than by an agreement in writing signed by an officer of the Company.

12. Acknowledgement. Executive acknowledges and agrees that, subsequent to the termination of Executive's employment, Executive shall not be eligible for any payments from the Company or Company-paid benefits, except as expressly set forth in this Agreement. Executive also acknowledges and agrees that Executive has been paid for all time worked and has received all other compensation owed to her.

13. Assignment. This Agreement shall be binding upon and be for the benefit of the parties as well as Executive's heirs and the Company's successors and assigns.

14. General Provisions. A failure of any of the Releasees to insist on strict compliance with any provision of this Release shall not be deemed a waiver of such provision or any other provision hereof. If any provision of this Release is determined to be so broad as to be unenforceable, such provision shall be interpreted to be only so broad as is enforceable, and in the event that any provision is determined to be entirely unenforceable, such provision shall be deemed severable, such that all other provisions of this Release shall remain valid and binding upon Executive and the Releasees.

15. Governing Law. The validity, interpretations, construction and performance of this Release shall be governed by the laws of the Commonwealth of Pennsylvania without giving effect to conflict of laws principles.

IN WITNESS WHEREOF, Executive has hereunto set Executive's hand as of the day and year set forth opposite his signature below.

Date	Jeffrey B. McGroarty

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 of Annovis Bio, Inc. (Registration No. 333-236457) of our report dated March 25, 2020 relating to the balance sheets of Annovis Bio, Inc. as of December 31, 2019 and 2018, and the related statements of operations, redeemable convertible preferred stock and stockholders' equity (deficit) and cash flows for the years ended December 31, 2019 and 2018, which report is included in this Annual Report on Form 10-K filed on March 25, 2020.

/s/ WithumSmith+Brown, PC

East Brunswick, New Jersey
March 25, 2020

Exhibit 31.1

**CERTIFICATION PURSUANT TO EXCHANGE ACT RULES 13a-14(a) AND 15d-14(a),
AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Maria Maccecchini, certify that:

1. I have reviewed this Annual Report on Form 10-K of Annovis Bio, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 25, 2020

/s/ Maria Maccecchini

Maria Maccecchini
President and Chief Executive Officer

Exhibit 31.2

**CERTIFICATION PURSUANT TO EXCHANGE ACT RULES 13a-14(a) AND 15d-14(a),
AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Jeffrey McGroarty, certify that:

1. I have reviewed this Annual Report on Form 10-K of Annovis Bio, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 25, 2020

/s/ Jeffrey McGroarty
Jeffrey McGroarty
Chief Financial Officer

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Annovis Bio, Inc. (the "Company") on Form 10-K for the year ended December 31, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Maria Maccecchini, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

1. The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 25, 2020

/s/ Maria Maccecchini

Maria Maccecchini
President and Chief Executive Officer

Exhibit 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Annovis Bio, Inc. (the "Company") on Form 10-K for the year ended December 31, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Jeffrey McGroarty, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

1. The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 25, 2020

/s/ Jeffrey McGroarty
Jeffrey McGroarty
Chief Financial Officer