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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, 2020

☐ **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 ☒

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

As of June 30, 2020, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's common stock held by non-affiliates of the registrant was $18,689,114 based on the closing sale price as reported on the NYSE American.

The number of shares of the issuer's common stock outstanding as of March 1, 2021, was 6,946,904.

Documents Incorporated by Reference

Certain portions, as expressly described in this report, of the registrant's proxy statement for the 2021 Annual Meeting of the Stockholders to be held June 1, 2021 are incorporated by reference into Part III of this Annual Report on Form 10-K.

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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.

Summary of Risk Factors.

The following is a summary of the principal risks described below in Part I, Item 1A "Risk Factors" in this Annual Report on Form 10-K. We believe that the risks described in the "Risk Factors" section are material to investors, but other factors not presently known to us or that we currently believe are immaterial may also adversely affect us. The following summary should not be considered an exhaustive summary of the material risks facing us, and it should be read in conjunction with the "Risk Factors" section and the other information contained in this Annual Report on Form 10-K .

- We have incurred significant net losses since inception and anticipate that we will continue to incur net losses for the foreseeable future and may never achieve or maintain profitability.
- We will require additional capital to fund our operations, and if we fail to obtain necessary funding, we may not be able to complete the development and commercialization of ANVS401.
- We are heavily dependent on the success of ANVS401, our lead product candidate, which is still under clinical development, and if it does not receive regulatory approval or is not successfully commercialized, our business may be harmed.
- We have concentrated our research and development efforts on the treatment of Alzheimer's disease and Parkinson's disease, both of which have seen limited success in drug development.
- Clinical trials are expensive, time-consuming, difficult to design and implement, and involve an uncertain outcome.
- Results of preclinical studies and early clinical trials may not be indicative of results obtained in later trials.
- If we are unable to obtain, maintain and defend patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our target markets.

PART I

Item 1. Business.

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 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.

We are presently conducting two Phase 2a clinical trials. In collaboration with the Alzheimer's Disease Cooperative Study ("ADCS") we are conducting a trial in 24 early AD patients (the "ADCS Trial"). We are also conducting a Phase 2a clinical trial in 14 AD and 54 PD patients (the "AD/PD Trial") which began treating patients in August 2020. Both clinical trials are double-blind, placebo-controlled studies. We have designed the two Phase 2a studies by applying our understanding of the underlying disease states in neurodegeneration and are measuring not just target, but also pathway validation in the spinal fluid of these patients. This means that we are measuring as many factors as possible associated with the toxic cascade which begins with high levels of neurotoxic proteins which lead to impaired axonal transport, inflammation, the death of nerve cells and loss of cognition and motor function. 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.

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 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 20 animal studies conducted in leading institutions such as the Karolinska Institute, Columbia University and Harvard University. 18 of the studies are published and two 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. 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 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. Since AD studies are very large, time consuming and capital intensive, we plan to initially conduct a Phase 3 trial in AD-DS, an orphan population that is substantially similar to AD, but in a very controlled and limited setting. In DS, the APP gene is triplicated, leading to early onset AD with similar pathology as sporadic AD. 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").

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. We are conducting two Phase 2a clinical trials for ANVS401.

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. The program has been funded by a grant from the U.S. Army which has been completed, 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

Safety

Three clinical studies have been completed 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; therefore, higher doses were not tested. ANVS401 is not an AChE inhibitor, but its N1 dimethyl metabolite 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. In the repeat dose studies, treatment with 60 mg four times a day was not associated with any side effects not also seen in placebo.

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)

Proof-of-Concept Study in Humans

In the human proof-of-concept ("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 a previous safety 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's 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 12-hour period tested. 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 *		

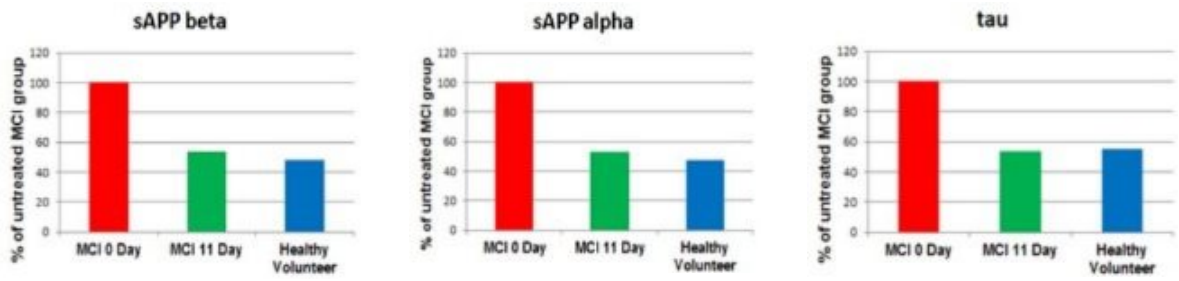
* Represents unpublished results.

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.

Comparison with Healthy Volunteers

We also 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.

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.

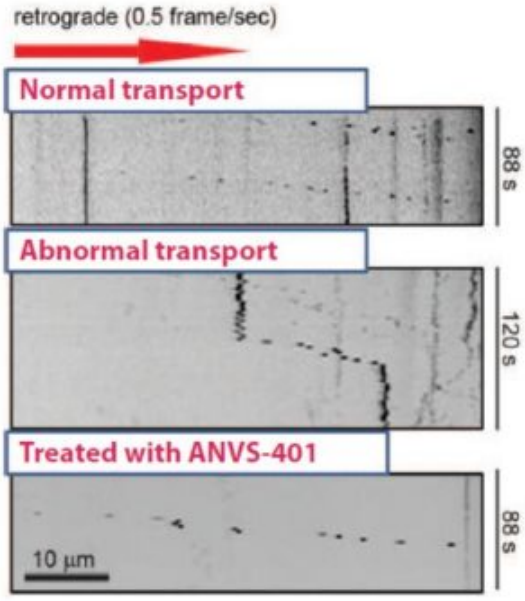


The percentages in the bar diagrams are derived from the CSF levels of sAPPα, sAPPβ and tau in four MCI patients and four healthy volunteers, with red representing average of MCI patients at Day 0 before ANVS401 treatment; green representing average of MCI patients at day 11 after 10 days of ANVS401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

Axonal Transport in Human Nerve Cells

When the information highway of a nerve cell slows down, the nerve cell is unable to properly communicate with other nerve cells, internal organs and the periphery and it gets sick and dies.

The transfer of information in a nerve cell is called axonal transport and when transport and synaptic transmission are impaired, the cell releases lower levels of neurotransmitters, leading to impaired nerve cell health. The sick cell is then attacked by the immune system, which is activated when it detects a sick cell, and it eventually kills the cell. Impairment in axonal transport, therefore, leads to inflammation and eventually to nerve cell death.



ANVS-401 improved anterograde and retrograde vesicle transport in fully differentiated Down syndrome nerve cells:

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

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

At the bottom: When the Down Syndrome nerve cells were treated with ANVS-401, their transport was improved and the vesicles carrying BDNF moved smoothly along the axon.

Inflammation

In the brain of all people suffering from a neurodegenerative disorder, there is severe inflammation. We used the same 18 samples collected from the CSF of the mildly cognitive impaired patients and measured four inflammatory factors and one control factor. In accordance with our hypothesis the levels of inflammatory markers were significantly reduced. We also measured Factor FH, a complement regulatory protein, 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.

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.

APP/PS1 Transgenic Mouse Model of AD

APP/PS1 AD transgenic ("tg") mice were treated for one month with ANVS401, before behavioral evaluation. ANVS401 improved spatial-working memory in a 2-day radial arm water maze test in this mouse AD model at a 25

mg/kg oral dose 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. ANVS401 treatment did not affect wild-type mice.

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.

SNCAA53T and SNCAA30P 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. Furthermore, even after we stopped treatment for nine weeks, the constipation was still reduced.

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.

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. 10 mg/kg ANVS405 improved memory and learning as measured by water maze performance. 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. Thus, ANVS405 protects the striatum following FPI in rats.

Because FPI can induce microglial activation, we next checked whether ANVS405 would reverse this pathology. In our study, we found that ANVS405 increased the number of resting microglia and reduced the number of activated microglia.

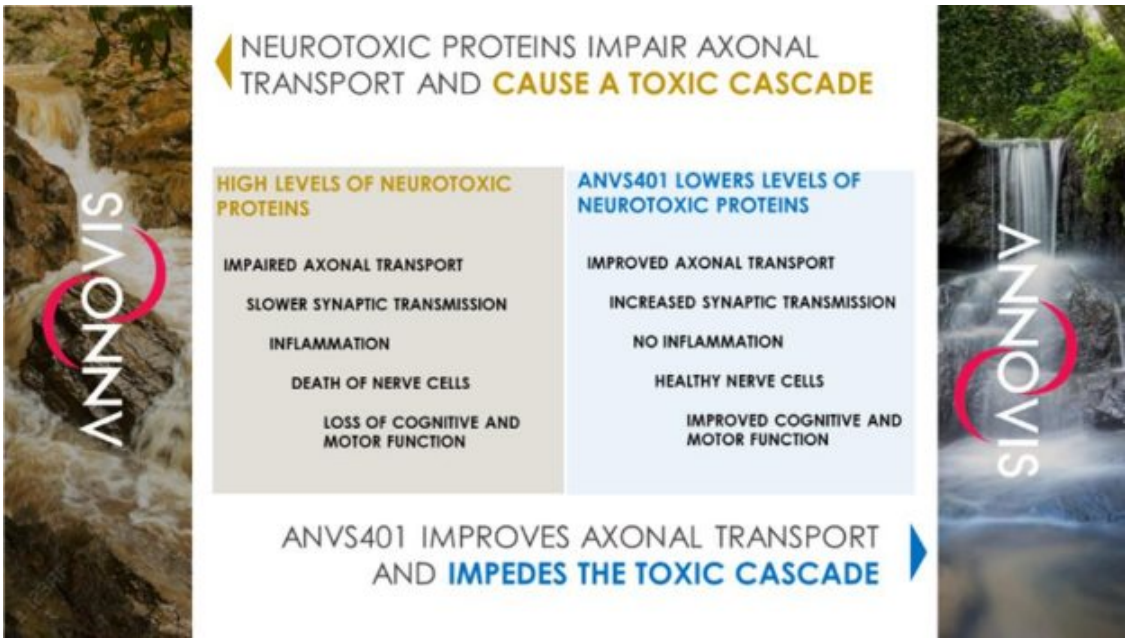
Stroke Mice

ANVS401 was tested in a stroke model, in which mice were challenged with MCAo-induced stroke (middle carotid artery occlusion induced stoke) and after four weeks, the number of surviving neurons was quantified. After four weeks the locomotor function, behavior, and cognition of these mice were also evaluated.

ANVS401 in combination with pifithrin-α (PFT-α) given to mice after the induced stroke improved mice locomotor activity and cognitive function. While both treatments yielded improvements in locomotor and cognitive function, the combined ANVS401/PFT-α treatment proved able to enhance stroke-induced endogenous neurogenesis and improve the functional recovery in stroke animals. The combined treatment also significantly improved cognitive function more than the single treatment with PFT-α

The Toxic Cascade Leading to Nerve Cell Death and Loss of Function

The toxic cascade in neurodegeneration begins with high levels of neurotoxic proteins which lead to impaired axonal transport, inflammation, death of nerve cells and loss of cognition and motor function. 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 leads us to believe that ANVS401 is a promising drug for the treatment of both AD and PD. Our approach is innovative in that we do not have a single therapeutic target for a single disease; instead, we are developing one drug that targets the mRNAs of multiple neurotoxic proteins, applicable to multiple diseases.



In animals we have seen that by reducing the levels of multiple neurotoxic proteins, ANVS401 reversed the toxic cascade. Now we want to prove that the drug also reverses the toxic cascade in humans, such as AD and PD patients in our two Phase 2a studies. We have been able to reverse the entire toxic cascade in animals and recover function, be it in the brain, the body, or the eyes. In humans, to date we have measured how ANVS401 reduces neurotoxic proteins, improves axonal transport and reduces inflammation. In our ongoing AD and PD phase 2a studies, we want to reproduce the measurements we already have and add measures of the reversal of nerve cell death and recovery of function.

ADCS Trial

We are presently conducting a double-blind, placebo-controlled Phase 2a study in early AD patients in conjunction with the ADCS. We are treating patients for four weeks with ANVS401 and measuring target and pathway

engagement in the spinal fluid. This means that we are measuring levels of neurotoxic proteins, neurotransmitters, neurotrophic factors, inflammation and nerve cell death as well of cognitive improvement. Under an agreement with UC San Diego, where ADCS is located, we have contracted to provide study supplies at our cost but the remaining costs of the ADCS Trial are paid for by the NIH. This is a 24-patient study which is being conducted in six sites in the U.S., including the University of California San Diego, Johns Hopkins, Indiana University, Washington University, Cleveland Clinic, and Columbia University. 16 patients have now been enrolled and treated in this trial. Data from this trial is expected in early 2022.

AD/PD Trial

In our AD/PD Trial, we are conducting a double-blind placebo-controlled Phase 2a study in mild to moderate AD and PD patients in which we are measuring levels of neurotoxic proteins, neurotransmitters, neurotrophic factors, inflammation and nerve cell death as well of cognitive and functional improvement. This is a 68-patient study which is being conducted in up to 15 sites in the U.S. The first part of the trial is in 14 AD patients and 14 PD patients for which data is expected to be available starting at the end of March 2021. The second part of the trial is a dose response analysis in 40 PD patients for which data is expected to be available in mid-2021.

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 shown positive results. 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. 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 are studying the effects of ANVS401 on the levels of several neurotoxic proteins and other surrogate markers, in parallel, in AD and PD patients. Within three to nine months, we believe we will have data in two patient populations – AD and PD - from our AD/PD Trial.

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.

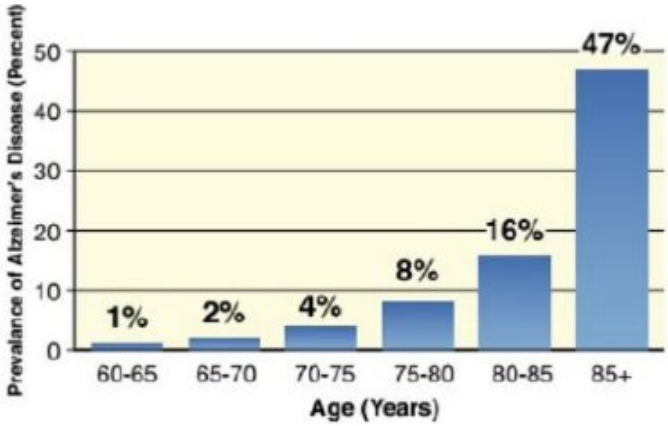
Just like in sporadic AD there is a prodromal or asymptomatic phase in DS when AD pathology progressively accumulates (30 - 40 years) but clinical signs of dementia may be delayed by up to a decade. This provides a therapeutic window or an opportunity for prevention that is unique to adults with Down 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 U.S., 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.

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. Disease modifying treatments ("DMTs") that will prevent or delay the onset or slow the progression of AD are urgently needed. 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 systems in developing countries improve. There is a significant 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 will not 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 but several studies in AD-DS or EOFAD are planned, ongoing or completed but results have either not been published or have been negative.

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 demonstrate that neurofibrillary tangle burden more closely correlates with cognitive decline than amyloid plaque load. The first two phase 3 studies conducted with tau approaches have failed. There are still several anti-tau approaches in the clinic.

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. The first companies testing tau have shown negative results. Many 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. 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.

The market for PD drugs is estimated at $2 to $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 contend with generic inroads. The size of the current market reflects the absence of innovative branded therapies more than it does the medical need.

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.

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 1, 2021, 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 Therapeutics PLC ("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 four families of patents and 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;

- 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; and
- a method of treating viral and bacterial infections of the brain, including COVID-19.

The patents have expiration dates between 2031 and 2041. In August 2019, the U.S. Patent and Trademark Office ("USPTO") granted the first of our Annovis patents covering PD and associated diseases. In March 2020, the European Patent Office ("EPO") granted our patent for a method of treating AD. In December 2020, the EPO approved our first patent for a method of treating acute nerve and brain injuries by administering ANVS405 after the injury.

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.

License Agreement

In November 2008 we entered into an exclusive world-wide agreement, as amended in November 2011 and May 2012, with a subsidiary of 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 annual fee is $46,000. Pursuant to the agreement we had deferred payment of the minimum annual fees prior to our initial public offering but during 2020 paid all accrued minimum annual fees through November 30, 2020. 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.

The agreement also provides us a buy-out option which we may exercise at any time, with an option price of $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 four-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 a US supplier for the manufacture of a new, large batch of good manufacturing practice ("cGMP") active pharmaceutical ingredient and with a local supplier for the storage stability, encapsulating, blister packing, blinding and distribution of the capsules or pills to the clinical sites. This material will allow us to enter large and long-term advanced clinical studies.

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. 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 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 ("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 ("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 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 ("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 www.clinicaltrials.gov.

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.

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 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.

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 a disease or condition, 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.

Marketing Approval and Post-Approval Requirements

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 ("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.

The FDA also may require submission of a 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. 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.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

The FDA may refer an application for a novel drug to an advisory committee. While the FDA is not bound by the recommendations of an advisory committee, it considers such recommendations carefully when making decisions.

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. 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.

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 the U.S. federal Health Insurance Portability and Accountability Act of 1996 ("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 European Economic Area ("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 ("MA"). There are two types of MAs:

- 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 ("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.

Human Capital Resources

As of March 1, 2021, we had two full-time employees. In addition to our employees, we contract with consultants and third parties for the conduct of certain clinical development, accounting and administrative activities. We expect to hire additional employees prior to beginning Phase 3 clinical trials.

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 $5,462,047 and $990,980 for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $14,239,075. 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 candidates through clinical development, complete clinical trials, seek regulatory approval and commercialize the drug or any other product candidates, 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 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 future commercialization efforts, as well as to support our requirements as 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 our current cash and cash equivalents and funding from existing grants will enable us to fund our operating expenses and capital expenditure requirements until at least March 31, 2022. 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.

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.

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. In addition, as a business with a limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors.

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, 2020, we had net operating loss carryforwards ("NOLs"), of $7,821,413 for federal income tax purposes, which may be available to offset our future taxable income, if any. NOLs generated in 2017 and prior of $2,764,240 will expire beginning in 2032. In general, under Section 382 of the U.S. Internal Revenue Code of 1986, as amended (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 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. In March 2020, the clinical trial sites participating in our Phase 2a trial in AD patients in collaboration with the ADCS temporarily suspended enrollment of new patients because of the ongoing COVID-19 pandemic. The trial sites have reopened and patient recruitment and treatment have resumed. In addition, due to restrictions related to COVID-19 during 2020, we experienced delays in opening clinical trial sites for our AD/PD Trial. 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.

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 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 ("IRB") approval at each site, or Independent Ethics Committee ("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 diseases' 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 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 candidates in the United States, we may never obtain approval for or commercialize ANVS401 or any other product candidates 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 candidates, 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 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 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 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 2a clinical studies, we carry 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 candidates 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, 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 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, 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 a third-party contract manufacturing organization ("CMO"), 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. 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 2a 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 (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 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 (“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;

- 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 ("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 EEA may subject us to the General Data Protection Regulation.

If we conduct clinical trial programs or enter into research collaborations in the EEA, we may be subject to the General Data Protection regulation ("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 ("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.

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act ("CARES Act") was enacted in response to the COVID-19 pandemic. The CARES Act, among other things, permits NOL carryovers and carrybacks to offset 100% of taxable income for taxable years beginning before 2021. Previously, NOLs generated after December 31, 2017 were limited to 80% of taxable income in future years. In addition, the CARES Act allows NOLs incurred in 2018, 2019 and 2020 to be carried back to each of the five preceding taxable years to generate a refund of previously paid income taxes. The NOL carryback provision of the CARES Act had no impact on us due to our tax losses generated during all prior years.

U.S. tax legislation enacted in 2017 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. The legislation could be subject to potential amendments and technical corrections, as well as interpretations and implementing regulations by the U.S. Treasury and Internal Revenue Service, 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.

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.

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 2022 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 four 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 ("USPTO") granted the first of our Annovis patents from this family covering PD and Lewy body diseases and in March 2020, the European Patent Office ("EPO") approved another patent in this family covering AD. 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. In December 2020, the EPO approved our first patent from this family for a method of treating acute nerve and brain injuries by administering ANVS405 after the injury. 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. In May 2020, we filed a patent application with the USPTO concerning a method of inhibiting, preventing, or treating neurological injuries due to viral, bacterial, fungal, protozoan, or parasitic infections in humans and in animals via administration of ANVS401 or related compounds which would be expected to expire in 2041, before any patent term adjustments or extensions.

While the issuance of our new patents 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. 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 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 ("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 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 candidates;
- inability to obtain additional funding;
- regulatory or legal developments in the United States and other countries applicable to ANVS401 or any other product candidates;
- adverse regulatory decisions;
- changes in the structure of healthcare payment systems;
- inability to obtain adequate product supply for ANVS401 or any other product candidates, 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, including but not limited to the impact of the COVID-19 pandemic; 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 37.0% 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.

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 ("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, we are 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 comply with Section 404, we are required to engage 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, 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 ("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 initial public offering ("IPO") on January 31, 2020, (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.

Holders of Record

As of March 1, 2021, there were approximately 34 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

We did not issue any equity securities during the year ended December 31, 2020 that were not registered under the Securities Act and that have not otherwise been described in a Quarterly Report on Form 10-Q or a Periodic Report on Form 8-K.

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 mildly cognitive impaired 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 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 two Phase 2a clinical trials. In collaboration with the Alzheimer's Disease Cooperative Study ("ADCS") we are conducting a trial in 24 early AD patients (the "ADCS Trial"). We are also conducting a Phase 2a clinical trial in 14 AD and 54 PD patients (the "AD/PD Trial") which began treating patients in August 2020. Both clinical trials are double-blind, placebo controlled studies. Under an agreement with UC San Diego, where ADCS is located, we have contracted to provide study supplies at our cost but the remaining costs of the ADCS Trial are paid for by the National Institutes of Health ("NIH"). We have designed the two Phase 2a studies 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 have never been profitable and have incurred net losses since inception. Our net losses were $5,462,047 and $990,980 for the years ended December 31, 2020 and 2019, respectively, and our accumulated deficit at December 31, 2020 was $14,239,075. 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 ("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 2020 primarily related to the AD/PD Trial which began treating patients in August 2020 and 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 2021 and for the next several years will be higher than in 2020 as a result of the continuation of our AD/PD Trial and costs associated with the initiation of our planned Phase 3 trial in AD-DS. 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 2021 and for the next several years will be higher than in 2020 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, as modified in September 2020, we received a Notice of Award for a $1.9 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. The costs of the studies and the grant income were substantially completed as of December 31, 2020.

Income Taxes

As of December 31, 2020, the Company had U.S. federal net operating loss ("NOL") carryforwards of $7,821,413, which may be available to offset future income tax liabilities. Federal NOL carryforwards generated in 2017 and prior of $2,764,240 will expire beginning 2032. The remaining federal NOL carryforwards generated in 2018 through 2020, do not expire, and following the enactment of the Coronavirus Aid, Relief, and Economic Security Act in March 2020, are permitted to offset 100% of taxable income in future years.

NOL 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 no longer have to estimate the fair value of the common stock, rather we 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,	
	2020	2019
	(in thousands)	
Operating expenses:		
Research and development	$ 3,054.0	$ 776.3
General and administrative	3,586.2	829.4
Other income (expense):		
Change in fair value of derivative liability	(26.5)	(79.5)
Interest income (expense), net	47.2	(40.9)
Grant income	1,157.4	735.1

Years Ended December 31, 2020 and 2019

Research and Development Expenses

Research and development expenses increased by $2,277.7 thousand for the year ended December 31, 2020 compared to the year ended December 31, 2019. The increase was primarily the result of an increase of $1,878.7 thousand in costs related to our AD/PD Trial which began treating patients in August 2020, an increase of $61.7 thousand in costs associated with our long-term toxicology studies in rats and dogs which began in November of 2019, an increase in share-based compensation expense of $138.7 thousand and an increase of $130.1 thousand in personnel expenses.

General and Administrative Expenses

General and administrative expenses increased by $2,756.8 thousand for the year ended December 31, 2020 compared to the year ended December 31, 2019. The increase was primarily the result of increases of $1,717.7 thousand in share-based compensation expense, $650.9 thousand in other personnel expenses, $307.5 thousand in insurance expense and $134.1 thousand in stock listing fees and other financial filing and printing fees.

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. The fair value of the derivative liability was adjusted to $132.5 thousand immediately prior to the closing of our IPO on January 31, 2020. Effective upon the closing of the IPO, the derivative liability was eliminated, and the amount was reclassified to additional paid-in capital on the balance sheet.

Interest Income (Expense), Net

Interest income (expense), net increased $88.1 thousand for the year ended December 31, 2020 compared to the year ended December 31, 2019. The increase was primarily the result of interest income generated on cash and cash equivalents from the proceeds of our IPO which closed on January 31, 2020 and the conversion of our convertible promissory notes to common stock in conjunction with the IPO.

Grant Income

Grant income increased $422.3 thousand for the year ended December 31, 2020 compared to the year ended December 31, 2019. 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 and were substantially completed as of December 31, 2020.

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, 2020, our principal source of liquidity was our cash, which totaled $8,074.7 thousand.

Equity Financings

We closed our IPO on January 31, 2020, raising gross proceeds of $13,800.0 thousand and net proceeds of $12,034.4 thousand, after deducting underwriting discounts and commissions and offering expenses.

Debt Financings

At December 31, 2020 and 2019, we had outstanding $0.0 and $530.0 thousand principal amount of convertible promissory notes, which were issued in March 2019. 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 current cash and cash equivalents will be sufficient to fund our operations and capital requirements for at least the next 12 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,	
	2020	2019
	(in thousands)	
Statement of Cash Flows Data:		
Total net cash provided by (used in):		
Operating activities	$ (3,970.8)	$ (476.5)
Financing activities	12,043.6	443.1
Increase (decrease) in cash and cash equivalents	$ 8,072.8	$ (33.4)

Years ended December 31, 2020 and 2019

Operating Activities

For the year ended December 31, 2020, cash used in operations was $3,970.8 thousand compared to $476.5 thousand for the year ended December 31, 2019. The increase in cash used in operations was primarily the result of the costs associated with our AD/PD Trial, higher personnel expenses and insurance expense, and the payment of accounts payable, accrued license fees and other accrued expenses as of the end of the prior year.

We expect cash used in operating activities to increase in 2021 as compared to 2020 due to an expected increase in our operating losses associated with ongoing development of our product candidates, including our AD/PD Trial.

Financing Activities

Cash provided by financing activities was $12,043.6 thousand during the year ended December 31, 2020, attributable to net proceeds from our IPO of $12,034.4 thousand, after deducting underwriting discounts and commissions and offering expenses, and $9.2 thousand proceeds from the exercise of stock options.

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.

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 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 Tax Act did not have a significant impact on our financial statements.

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. The adoption of ASU 2018-13 in the first quarter of 2020 did 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

Management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Because of its

inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Management utilized the criteria established in the Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) to conduct an assessment of the effectiveness of our internal control over financial reporting as of December 31, 2020. Based on the assessment, management has concluded that, as of December 31, 2020, our internal control over financial reporting was effective.

As an emerging growth company, management's assessment of internal control over financial reporting was not subject to attestation by our independent registered public accounting firm.

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(d) of the Exchange Act that occurred during the quarter ended December 31, 2020 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

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 2021 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 2021 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 2021 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 2021 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 2021 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. (Incorporated by reference to Exhibit 4.2 to Form 10-K filed March 25, 2020.)
4.3	Description of Registrant's Securities. (Incorporated by reference to Exhibit 4.3 to Form 10-K filed March 25, 2020.)
10.1+	Second Amended and Restated Employment Agreement dated as of March 24, 2020 between the Registrant and Maria Maccecchini. (Incorporated by reference to Exhibit 10.1 to Form 10-K filed March 25, 2020.)
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.)

Exhibit Number	Description of Exhibit
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. (Incorporated by reference to Exhibit 10.9 to Form 10-K filed March 25, 2020.)
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.
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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders of Annovis Bio, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Annovis Bio, Inc. (the "Company"), as of December 31, 2020 and 2019, 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, 2020 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, 2020 and 2019, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2020, 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 audits 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 3, 2021

ANNOVIS BIO, INC.

Balance Sheets

	As of December 31,	
	2020	2019
Assets		
Current assets:		
Cash and cash equivalents	$ 8,074,658	$ 1,858
Grant receivable	—	735,075
Prepaid expenses and other current assets	44,676	10,579
Total current assets	8,119,334	747,512
Long-term assets:		
Deferred offering costs	—	369,595
Total long-term assets	—	369,595
Total assets	$ 8,119,334	$ 1,117,107
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 341,856	$ 1,233,877
Accrued expenses	236,524	776,871
Total current liabilities	578,380	2,010,748
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 at December 31, 2019	—	499,807
Total long-term liabilities	—	605,807
Total liabilities	578,380	2,616,555
Commitments and contingencies (Note 8)		
Redeemable convertible preferred stock—$0.0001 par value:		
Series A - 0 and 5,133,159 shares authorized, issued and outstanding at December 31, 2020 and 2019, respectively	—	6,509,303
Series A-1 - 0 and 1,111,111 shares authorized at December 31, 2020 and 2019, respectively, and 0 and 630,722 shares issued and outstanding at December 31, 2020 and 2019, respectively	—	567,649
Stockholders' equity (deficit):		
Preferred stock - $0.0001 par value, 2,000,000 and 0 shares authorized at December 31, 2020 and 2019, respectively	—	—
Common stock - $0.0001 par value, 35,000,000 and 10,150,000 shares authorized at December 31, 2020 and 2019, respectively, and 6,891,608 and 282,614 shares issued and outstanding at December 31, 2020 and 2019, respectively	689	28
Additional paid-in capital	21,779,340	200,600
Accumulated deficit	(14,239,075)	(8,777,028)
Total stockholders' equity (deficit)	7,540,954	(8,576,400)
Total liabilities and stockholders' equity (deficit)	$ 8,119,334	$ 1,117,107

See accompanying notes to financial statements.

ANNOVIS BIO, INC.

Statements of Operations

	Year Ended December 31,	
	2020	**2019**
Operating expenses:		
Research and development	$ 3,054,025	$ 776,256
General and administrative	3,586,196	829,366
Total operating expenses	6,640,221	1,605,622
Operating loss	(6,640,221)	(1,605,622)
Other income (expense):		
Change in fair value of derivative liability	(26,500)	(79,500)
Interest income (expense), net	47,225	(40,933)
Grant income	1,157,449	735,075
Total other income (expense)	1,178,174	614,642
Loss before income taxes	(5,462,047)	(990,980)
Income tax expense (benefit)	—	—
Net loss	$ (5,462,047)	$ (990,980)
Basic and diluted loss per common share	$ (0.87)	$ (3.51)
Weighted average number of common shares outstanding, basic and diluted	6,308,961	282,614

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, 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)
Conversion of redeemable convertible preferred stock to common stock upon completion of initial public offering	(5,133,159)	(6,509,303)	(630,722)	(567,649)	4,117,089	412	7,076,540	—	7,076,952
Conversion of convertible promissory notes, including embedded derivative, to common stock upon completion of initial public offering	—	—	—	—	118,470	12	672,512	—	672,524
Issuance of common stock in initial public offering, net of offering costs	—	—	—	—	2,300,000	230	11,955,565	—	11,955,795
Exercise of stock options	—	—	—	—	48,435	5	9,212	—	9,217
Issuance of common stock to consultants and advisors	—	—	—	—	25,000	2	122,748	—	122,750
Share-based compensation expense	—	—	—	—	—	—	1,742,163	—	1,742,163
Net loss	—	—	—	—	—	—	—	(5,462,047)	(5,462,047)
Balance, December 31, 2020	—	$ —	—	$ —	6,891,608	$ 689	$ 21,779,340	$ (14,239,075)	$ 7,540,954

See accompanying notes to financial statements.

ANNOVIS BIO, INC.

Statements of Cash Flows

	Year Ended December 31,	
	2020	2019
Cash flows from operating activities:		
Net loss	$ (5,462,047)	$ (990,980)
Adjustments to reconcile net loss to net cash used in operating activities:		
Amortization of deferred financing fees	129	1,191
Amortization of debt discount	396	3,738
Share-based compensation expense, including stock issued to consultants and advisors	1,864,913	8,483
Change in fair value of derivative liability	26,500	79,500
Changes in assets and liabilities:		
Grant receivable	735,075	(735,075)
Prepaid expenses and other current assets	(34,097)	5,101
Accounts payable	(695,660)	969,091
Accrued expenses	(406,032)	182,409
Net cash used in operating activities	(3,970,823)	(476,542)
Cash flows from financing activities:		
Proceeds from initial public offering of common stock, net of offering costs	12,034,406	—
Proceeds from issuance of convertible promissory notes	—	530,000
Proceeds from exercise of stock options	9,217	—
Payment of deferred offering costs	—	(78,611)
Payment of deferred financing fees	—	(8,301)
Net cash provided by financing activities	12,043,623	443,088
Net increase (decrease) in cash	8,072,800	(33,454)
Cash and cash equivalents, beginning of year	1,858	35,312
Cash and cash equivalents, end of year	$ 8,074,658	$ 1,858
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
Conversion of redeemable convertible preferred stock to common stock	$ 7,076,952	$ —
Conversion of convertible promissory notes, including embedded derivative, to common stock	$ 672,524	$ —

See accompanying notes to financial statements.

Annovis Bio, Inc.
Notes to Financial Statements

December 31, 2020 and 2019

(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 net losses of $5,462,047 and $990,980 for the years ended December 31, 2020 and 2019, respectively, and had an accumulated deficit of $14,239,075 as of December 31, 2020. 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 28, 2020, the Company announced the pricing of its initial public offering (the "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 were approximately $13.8 million. The net proceeds of the IPO were approximately $12.0 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 redeemable convertible preferred stock and convertible promissory notes converted into shares of Company common stock totaling 4,117,089 and 118,470, respectively.

As of the date these financial statements are issued, management believes that 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 $8,074,658 and $1,858 as of December 31, 2020 and 2019, respectively.

(e) Deferred Offering Costs

Included in long-term assets as of December 31, 2019, were deferred offering costs of $369,595 incurred in connection with the Company's IPO which primarily consisted of direct incremental legal, printing, listing and accounting fees. Offering costs of $601,635 were offset against proceeds received in the IPO and charged to additional paid-in capital in the year ended December 31, 2020. Of these offering costs, $78,611 was paid during the year ended December 31, 2019.

(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 personnel-related expenses and 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, in the case of stock 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, 2020 and 2019, the Company had a full valuation allowance against its 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, 2020 or December 31, 2019.

(k) Recent Accounting Pronouncements

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 Tax Act did not have a significant impact on the Company's financial statements.

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. The adoption of ASU 2018-13 in the year ended December 31, 2020 did not have a significant impact on the Company's 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 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, 2020 and December 31, 2019:

		Fair Value Measurement at December 31, 2020		
	Carrying Value	Level 1	Level 2	Level 3
Cash and cash equivalents	$ 8,074,658	$ 8,074,658	$ —	$ —

		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

The derivative liability was 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 immediately prior to the closing of the IPO was $132,500 and at December 31, 2019 was $106,000. The change in the fair value of the derivative liability is reflected in the statements of operations.

(4) Grant Receivable

In September 2019, as modified in September 2020, the Company received a Notice of Award for a $1.9 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. The Company recognized grant income of $1,157,449 and $735,075 for the years ended December 31, 2020 and 2019, respectively, in connection with the NIH grant. The Company received payments under the grant of $1,892,524 and $0 during the years ended December 31, 2020 and 2019, respectively and recorded a grant receivable of $0 and $735,075 as of December 31, 2020 and 2019, respectively, to reflect unreimbursed, eligible costs incurred under the grant. As of December 31, 2020, remaining funds available under the grant were $36,754.

(5) Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following:

	As of December 31,	
	2020	2019
Prepaid insurance	$ 26,542	$ —
Prepaid expenses	11,690	4,135
Security deposit	6,444	6,444
	$ 44,676	$ 10,579

(6) Accrued Expenses

Accrued expenses consisted of the following:

	As of December 31,	
	2020	2019
Payroll and related benefits	$ 16,493	$ 131,530
Accrued interest expense	—	36,041
Accrued professional and clinical fees	216,198	103,300
Accrued license payments	3,833	506,000
	$ 236,524	$ 776,871

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 accrued at 8% compounded annually on all Notes. The maturity date was 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 was 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.

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 were deducted from the face amount of the Notes on the balance sheets. The Company amortized the deferred financing fees and debt discount over the term of the Notes as additional interest expense using the effective interest method. The effective interest rate on the Notes was 9.8%. The Company made no cash payments for interest during the years ended December 31, 2020 or 2019.

On January 31, 2020, the Company closed its IPO. In accordance with the terms of the Notes, the outstanding Notes plus accrued interest converted into 118,470 shares of Company common stock at a 20% discount to the initial offering price of shares issued in the IPO.

(8) Commitments and Contingencies

(a) Leases

The Company leases its office facilities under a month-to-month operating lease. Total rental expense was $41,603 and $34,351 for the years ended December 31, 2020 and 2019, respectively.

(b) License Agreement

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 fee 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 fee 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. The Company had deferred payment of the minimum annual fees prior to the IPO. During the year ended December 31, 2020, the Company paid an aggregate of $494,000 to the Licensor in satisfaction of deferred minimum annual fees through November 2020.

At December 31, 2020 and December 31, 2019, the Company had accrued $3,833 and $506,000, respectively, in license payments under the terms of this license, included in accrued liabilities. 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 the United States	$ 5,750,000

No milestones have been achieved as of December 31, 2020.

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 $720,000 at December 31, 2020.

(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, 2020 and December 31, 2019, the Company did not have any pending legal actions.

(e) Risks and Uncertainties

In March 2020, the clinical trial sites participating in the Company's Phase 2a trial in AD patients in collaboration with the Alzheimer's Disease Cooperative Study temporarily suspended enrollment of new patients because of the ongoing COVID-19 pandemic. Prior to suspension of enrollment, 14 patients had been enrolled and completed treatment, out of a total trial size of 24 patients. The trial sites have reopened and patient recruitment and treatment have resumed. In addition, due to restrictions related to COVID-19 during 2020, the Company experienced delays in opening clinical trial sites for its Phase 2a clinical trial in AD and PD (the "AD/PD Trial"). In early 2021, all of the remaining sites which are participating in the AD/PD Trial opened for recruitment and treatment of patients. Although the Company currently believes its clinical trials will be completed on time, the extent to which the COVID-19 pandemic could have a material impact on the clinical trials is dependent on the spread of the disease and government and healthcare system responses to such spread, which are presently highly uncertain. Management continues to evaluate the potential impact. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

(9) Redeemable Convertible Preferred Stock and Stockholders' Equity

(a) Overview

The Company closed its IPO on January 31, 2020, issuing 2,300,000 shares of common stock. In connection with the closing of the Company's IPO, the then-outstanding 5,133,159 shares of Series A and 630,722 shares of Series A-1 redeemable convertible preferred stock converted into an aggregate of 4,117,089 shares of Company common stock. Each share of redeemable convertible preferred stock was converted 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 was $1.26, and the Series A conversion price was $0.70, as adjusted for the reverse stock split discussed in Note 2.

The Company's Amended and Restated Certificate of Incorporation was adopted on January 31, 2020 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 37,000,000, each with a par value of $0.0001 per share. Of these shares, 35,000,000 shall be common stock and 2,000,000 shall be preferred stock.

(b) Common Stock

1. Dividends

Subject to the rights of holders of all classes of Company stock outstanding having rights that are senior to or equivalent to holders of common stock, the holders of the common stock are entitled to receive dividends when and as declared by the Board.

2. Liquidation

Subject to the rights of holders of all classes of stock outstanding having rights that are senior to or equivalent to holders of common stock as to liquidation, upon the liquidation, dissolution or winding up of the Company, the assets of the Company will be distributed to the holders of common stock.

3. Voting

The holders of common stock are entitled to one vote for each share of common stock held. There is no cumulative voting.

(c) Preferred Stock

Preferred stock may be issued from time to time by the Board in one or more series.

(d) Warrants

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 the initial public offering price. The warrants have a five-year term and are not exercisable prior to January 29, 2021. All of the warrants were outstanding at December 31, 2020, and the Company accounts for the warrants as a component of stockholders' equity.

(10) Share-Based Compensation

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 Company's previous equity incentive plan. The previous plan had 352,282 options outstanding as of the effective date of the 2019 Plan. Under the 2019 Plan, 1,000,000 shares are authorized to be issued and no new options may be issued under the previous plan, although shares subject to grants which are cancelled or forfeited will again be available under the 2019 Plan. As of December 31, 2020, 168,664 shares were available for future grants.

The 2019 Plan provides for grants to employees, members of the Board, consultants and advisors to the Company, in the form of stock options, stock awards and other equity-based awards. The amount and terms of grants are determined by the Board. Stock options have a maximum term of 10 years after date of grant and are exercisable in cash or as otherwise determined by the Board.

As of December 31, 2020, and 2019, options to purchase common shares of the Company outstanding were as follows:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)
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	
Granted	810,000	3.46	
Exercised	(48,435)	0.19	
Forfeited	(2,381)	0.14	
Outstanding at December 31, 2020	1,111,466	2.57	8.4
Exercisable at December 31, 2020	1,061,466	2.54	8.3

As of December 31, 2020, the aggregate intrinsic value of options outstanding was $5,523,826 and options exercisable was $5,303,326.

810,000 options were issued during the year ended December 31, 2020. Under the grant agreements, 50,000 of the options vest after one year and the remainder of the options were vested and exercisable upon grant. These options have a 10-year term. No options were issued during the year ended December 31, 2019. The weighted average grant date fair value of options issued during the year ended December 31, 2020 was $2.19. The fair value was estimated using the Black Sholes option pricing model using the following weighted average assumptions:

	Year Ended December 31, 2020
Risk-free interest rate	0.38 %
Expected life	5.00
Expected volatility	80 %
Expected dividend yield	—

During the year ended December 31, 2020, the Company granted stock awards totaling 25,000 shares to consultants and advisors for services rendered which were vested upon grant. Based on the closing price of the Company's common stock on the NYSE American on the date of grant, these awards had an aggregate fair value of $122,750, which was recognized in share-based compensation expense upon grant. No stock awards were issued during the year ended December 31, 2019. As of December 31, 2020, there was no unrecognized compensation expense related to stock awards.

Share-based compensation expense in the statements of operations, including the fair value of stock awards to consultants and advisors for services rendered, for the years ended December 31, 2020 and 2019 was $1,864,913 and $8,483, respectively, of which $138,704 and $0, respectively, was included in research and development and the remainder in general and administrative expense. As of December 31, 2020 there was $31,970 unrecognized compensation expense related to unvested options. That cost is expected to be recognized over a weighted-average period of 0.3 years.

(11) Net Loss Per Share

The Company has reported a net loss for the years ended December 31, 2020 and 2019, 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,	
	2020	2019
Numerator		
Net loss	$ (5,462,047)	$ (990,980)
Denominator		
Weighted-average common shares outstanding, basic and diluted	6,308,961	282,614
Net loss per share, basic and diluted	$ (0.87)	$ (3.51)

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:

	December 31,	
	2020	2019
Redeemable convertible preferred stock, as converted	—	4,117,089
Stock options	1,111,466	352,282
Warrants	100,000	—

(12) Income Taxes

The federal and state provision (benefit) for income taxes was $0 for the years ended December 31, 2020 and 2019.

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, 2020 and 2019 is as follows:

	Year Ended December 31,	
	2020	2019
Federal income tax benefit at statutory rate	21.0 %	21.0 %
State and local tax, net of federal benefit	7.6 %	8.0 %
Permanent differences	(0.8)%	0.4 %
Research and development credit	1.9 %	— %
Change in valuation allowance	(29.7)%	(29.4)%
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,	
	2020	2019
Net operating loss carryforwards	$ 2,460,773	$ 1,430,716
Stock compensation	547,628	37,708
Convertible debt	—	24,049
Research and development tax credit carryforwards	241,414	137,826
Total deferred tax assets	3,249,815	1,630,299
Less valuation allowance	(3,249,815)	(1,630,299)
Net deferred taxes	$ —	$ —

As of December 31, 2020, the Company had U.S. federal net operating loss ("NOL") carryforwards of $7,821,413, which may be available to offset future income tax liabilities. Federal NOL carryforwards generated in 2017 and prior of $2,764,240 will expire beginning in 2032. The remaining federal NOL carryforwards generated in 2018 and later do not expire. As of December 31, 2020, the Company also had U.S. state NOL carryforwards of $10,368,296 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, 2020 and 2019 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 $1,619,516 and $291,575 in the years ended December 31, 2020 and 2019, respectively.

As of December 31, 2020, the Company had federal research and development tax credit carryforwards of $241,414 available to reduce future tax liabilities which expire beginning in 2028.

Under the provisions of the Internal Revenue Code, the NOL and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. NOL 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, including its IPO which closed on

January 31, 2020, which may have resulted in a change in control as defined by Sections 382 and 383 of the Internal Revenue Code, or could result in a change in control in the future.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. The Company's tax years from 2017 to the present remain open for review. All open years may be examined to the extent that tax credits or NOL 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, 2020, 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.

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act ("CARES Act") was enacted in response to the COVID-19 pandemic. The CARES Act, among other things, permits NOL carryovers and carrybacks to offset 100% of taxable income for taxable years beginning before 2021. Previously, NOLs generated after December 31, 2017 were limited to 80% of taxable income in future years. In addition, the CARES Act allows NOLs incurred in 2018, 2019 and 2020 to be carried back to each of the five preceding taxable years to generate a refund of previously paid income taxes. The NOL carryback provision of the CARES Act had no impact on the Company due to its tax losses generated during all prior years.

(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.

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 3, 2021
/s/ JEFFREY MCGROARTY Jeffrey McGroarty	Chief Financial Officer (principal financial and accounting officer)	March 3, 2021
/s/ MICHAEL HOFFMAN Michael Hoffman	Chairman of the Board and Director	March 3, 2021
/s/ CLAUDINE BRUCK Claudine Bruck	Director	March 3, 2021
/s/ ROBERT WHELAN Robert Whelan	Director	March 3, 2021
/s/ MARK WHITE Mark White	Director	March 3, 2021

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (Registration No. 333-252625) and Form S-8 (Registration No. 333-236457) of Annovis Bio, Inc. of our report dated March 3, 2021, relating to the financial statements, which appear in this Form 10-K.

/s/ WithumSmith+Brown, PC

East Brunswick, New Jersey
March 3, 2021

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)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) 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 is made known to us by others within the entity, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) 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

   (d) 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 3, 2021

/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)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) 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 is made known to us by others within the entity, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) 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

   (d) 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 3, 2021

/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, 2020 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 3, 2021

/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, 2020 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 3, 2021

/s/ Jeffrey McGroarty
Jeffrey McGroarty
Chief Financial Officer