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, 2024
OR

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

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.)

101 Lindenwood Drive, Suite 225
Malvern, PA 19355
(Address of principal executive offices including zip code)

(484) 875-3192
(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	New York Stock Exchange

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 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. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to Section 240.10D-1(b). ☐

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

As of June 30, 2024, 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 $51,312,050 based on the closing sale price as reported on the NYSE.

The number of shares of the issuer's common stock outstanding as of March 18, 2025, was 19,486,231.

Documents Incorporated by Reference

Certain portions, as expressly described in this report, of the registrant's proxy statement for the 2025 Annual Meeting of the Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

TABLE OF CONTENTS

Cautionary Note Regarding Forward-Looking Statements.

This Annual Report on Form 10-K contains express or implied 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 cash and cash equivalents balance, runway and needs, as well as financing plans;
- 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;
- our business strategies;
- risks relating to the timing and costs of clinical trials and the timing and costs of other organizational 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;
- 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.

- As a result of our history of operating losses and accumulated deficit, there is substantial doubt on our ability to continue as a going concern and therefore, an increased risk associated with an investment in our company.
- Our auditor's opinion on our audited financial statements for the year ended December 31, 2024 includes an explanatory paragraph relating to our ability to continue as a going concern.
- 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 substantial 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 our product candidates.
- We have limited operating history and no history of commercializing pharmaceutical products.
- Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.
- We are heavily dependent on the success of buntanetap, 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 will be materially harmed.
- We have concentrated our research and development efforts on the treatment of Alzheimer's disease ("AD") and Parkinson's disease ("PD"), diseases that have historically seen limited success in drug development. Further, buntanetap is based on a novel approach to treating AD and PD, which makes it difficult to predict the time and cost of development and subsequently, obtaining regulatory approval.
- If we are not successful in discovering, developing, and commercializing additional product candidates, our ability to expand our business and achieve our strategic objectives may be impaired.
- Clinical trials, including the enrollment and retention of patients, are expensive, time-consuming, difficult to design and implement, and involve an uncertain outcome(s).
- 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 buntanetap or any other product candidates, our business will be substantially harmed.
- Results of preclinical studies, early clinical trials or analyses may not be indicative of results obtained in later trials. 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 further subject to audit and verification procedures that could result in material changes in the final data. Furthermore, undue reliance on interim analyses may be detrimental to our long-term clinical development plans, which could harm our business, operating results, prospects or financial condition.

- 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.

- The market opportunities for buntanetap or any other product candidates, if approved, may be smaller than we anticipate, which could adversely affect our business, financial condition and results of operations.

- Even if we obtain regulatory approval for buntanetap or any of our product candidates, we will still face extensive and ongoing regulatory requirements and obligations.

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

- The successful commercialization of buntanetap and any other product candidates we develop will depend in part on market acceptance; the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels, and pricing policies; and our sales, marketing and distribution capabilities.

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

- We currently rely on third parties for the production of clinical supply of buntanetap and for the conduct, supervision and monitoring of our clinical trials. If those third parties do not successfully carry out their contractual duties, or if they perform in an unsatisfactory manner or do not comply with regulatory standards and requirements, it may harm our business.

- Changes in methods of product candidate manufacturing or formulation may result in additional costs or delays.

- Enacted and future healthcare and other legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates, if approved, and increase the liabilities to which we may become subject, as well as affect the prices we may set or the manner in which we conduct and plan to conduct our business.

- If we are unable to obtain, maintain and enforce patent or other intellectual property protection for buntanetap or any future product candidates or technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors or other third parties could develop and commercialize products similar or identical to ours, our ability to successfully commercialize buntanetap or any future product candidates may be adversely affected and we may not be able to compete effectively in our markets.

- We may be subject to claims challenging the inventorship of our patents and other intellectual property. We may additionally 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.

- The cash and cash equivalents that we use to meet our working capital and operating expense needs are held in deposit accounts at two financial institutions. If one or both financial institutions fail, our deposit accounts could be adversely affected due to the loss of or delay in obtaining access to all or a portion of our uninsured funds.

- The market price of our common stock has been volatile and fluctuated substantially in the past, and may continue to experience volatility and substantial fluctuations in the future, which could result in substantial losses for purchasers of our common stock.

- We have been subject to securities class action litigation in the past and could be subject to such litigation in the future.

PART I

Item 1. Business.

Our Company

We are a late-stage clinical drug platform company addressing neurodegeneration, such as Alzheimer's disease ("AD") and Parkinson's disease ("PD"). We are developing our lead product candidate, buntanetap, which is designed to address AD, PD, and potentially other chronic neurodegenerative diseases. Buntanetap is a synthetically produced small molecule, orally administered, brain penetrant compound. In several studies, buntanetap was observed to inhibit the synthesis of neurotoxic proteins — APP/Aβ ("APP"), tau/phospho- tau ("tau") and α-Synuclein ("αSYN") — that are some of the main causes of neurodegeneration. High levels of neurotoxic proteins lead to reduced axonal transport, which is responsible for the communication between and within nerve cells. When that communication is compromised, the immune system is activated and attacks the nerve cells, eventually killing them. We have observed in our clinical studies in early AD and early PD patients and pre-clinical studies in mice and rats that buntanetap lowered neurotoxic protein levels leading to improved axonal transport, reduced inflammation, lower nerve cell death and improved affected function.

In 2021, we completed two Phase 1/2 clinical studies: one in 14 early AD patients, and one in 54 early PD patients (together, the "AD/PD Trial"). In the AD/PD Trials, early AD patients were defined as those with a Mini Mental State Examination ("MMSE") score between 19 and 28 and early PD patients as those patients at Hoehn & Yahr stages 1, 2 or 3. MMSE is a brief screening instrument used to assess cognitive function, with total scores ranging from 0 to 30 and a lower score indicating greater disease severity, while the Hoehn & Yahr scale is a medical assessment used to measure staging of the functional disability associated with PD where a higher stage indicates greater disease severity. In collaboration with the Alzheimer's Disease Cooperative Study ("ADCS"), we also conducted a trial in 16 early AD patients (the "ADCS Trial"). In the ADCS Trial, early AD patients were defined as those patients with a MMSE score between 19 and 28. At the completion of the ADCS Trial, the data showed that buntanetap acts as a translational inhibitor in humans just like in animals, and we further observed that there was statistical improvement in cognition in early AD patients, just like in the AD/PD Trials.

All three clinical trials above were double-blind, placebo-controlled. We designed the studies by applying our understanding of the underlying neurodegenerative disease states and measured both target and pathway validation in the spinal fluid of patients to determine whether patients underlying disease condition improved following treatment. In addition to meeting their primary endpoints of safety and tolerability and secondary endpoint of pharmacokinetics ("PK") of buntanetap, our AD/PD Trials also met exploratory endpoints of measures of biomarkers and improvements in cognition in AD patients, as well as function in PD patients. We believe that the AD/PD Trial represents the first double-blind, placebo-controlled study that showed improvements in AD patients, as measured by Alzheimer's Disease Assessment Scale-Cognitive Subscale ("ADAS-Cog") and in PD patients, as measured by Unified Parkinson's Disease Rating Scale ("MDS-UPDRS" or "UPDRS"). ADAD-Cog is an assessment scale that measures cognitive functions and non-cognitive functions such as mood and behavior. More specifically, ADAS-Cog 11 is the cognitive assessment scale used to measure areas commonly seen to decline in AD patients. It consists of 11 specific tasks such as word recall, comprehension, object-naming, etc., in order to produce a scale measurement. UPDRS Part II and III are composed of a 42-item rating scale designed to assess Parkinson's disease-related disability and impairment and also evaluate the activities of daily living and motor function.

Following completion of the AD/PD Trial, we submitted our data to the U.S. Food and Drug Administration ("FDA") and requested direction to further pursue the development of buntanetap in early PD patients. With the FDA's guidance, we initiated a Phase 3 study in early PD patients in August 2022 (our "Phase 3 PD Study"). In the Phase 3 PD Study, early PD patients were defined as those at Hoehn & Yahr stages 1, 2 or 3 and OFF times of less than two hours per day. OFF time refers to periods when PD motor and/or non-motor symptoms occur between medication doses. We also submitted a proposed protocol for the treatment of moderate AD to the FDA, and after receiving permission to proceed, we initiated a Phase 2/3 study in mild to moderate AD patients in February 2023 (our "Phase 2/3 AD Study"). In the Phase 2/3 AD Study, mild to moderate AD patients were defined as those with a MMSE score between 14 and 24. Our Phase 3 PD Study and Phase 2/3 AD Study each had built in interim analyses.

Our Phase 3 PD Study incorporated an interim analysis at two months, the results of which were disclosed on March 31, 2023. The pre-planned interim analysis was conducted by our data analytics provider based on 132 patients from all cohorts collectively, for which baseline and two-month data was available. Based on the results of the interim analysis, we proceeded

with the Phase 3 PD Study as planned in accordance with the previously established protocol. The study was completed on December 4, 2023, and we released the topline PD Study efficacy data on July 2, 2024. The study data showed that in two subgroups, buntanetap improved UPDRS 2, 3, 2+3 and total. It also showed that in the entire intent to treat ("ITT") population, buntanetap stopped the loss of cognition and that in the 12% of patients that already had cognitive issues, buntanetap improved cognition in a dose-dependent, statistically significant way. We expect to discuss the Phase 3 PD data with the FDA in a Type C meeting during 2025. During that meeting, we plan to propose continued development of buntanetap with an additional, pivotal Phase 3 trial.

With respect to the Phase 2/3 AD Study, we disclosed the results of the interim analysis on October 23, 2023, and similar to our PD study, based on the outcome of the interim analysis, we proceeded with the study as planned. The Phase 2/3 AD study was completed on February 13, 2024, and on April 29, 2024, we announced topline efficacy data. The data showed that in early AD patients, buntanetap improved ADAS-Cog11 in a dose-dependent fashion and was statistically significant from placebo and from baseline.

On October 10, 2024, the Company met with the FDA in an end-of-phase 2 meeting to discuss its Phase 2/3 AD data and to agree on a regulatory path forward. Annovis and the FDA have aligned on a development path for buntanetap towards the filing of New Drug Applications (NDAs), one for short-term and one for long-term efficacy. The Phase 3 AD program will investigate buntanetap in patients with early AD and will consist of one study that first incorporates a 6-month period aimed at confirming buntanetap's symptomatic effects, while continuing blinded for an additional 12 months to show potential disease-modifying efficacy at 18 months. The completion of the first 6-month period, if well-designed and well-executed, may be sufficient to support an NDA filing, potentially within one year of the 6-month treatment period initiation.

During the end-of-phase 2 meeting for AD, the FDA raised no concerns with the Company's data on buntanetap's safety, including impact on liver enzymes, drug interactions, dose selection, pharmacokinetics and population pharmacokinetics. Further, the FDA confirmed that future development can proceed using the new crystal form of buntanetap.

We believe that we are the only company developing a drug for AD and PD that is designed to inhibit more than one neurotoxic protein and has a mechanism of action designed to restore nerve cell axonal and synaptic activity. By improving brain function, our goal is to treat memory loss and dementia associated with AD, as well as body and brain function issues associated with PD. Based on pre-clinical and clinical data collected to date, we believe that buntanetap has the potential to be the first drug to interfere with the underlying mechanism of neurodegeneration, potentially enabling buntanetap to be the only drug to improve cognition in AD and motor function in PD. The industry has historically encountered challenges in specifically targeting one neurotoxic protein, be it APP, tau or αSYN, indicating that doing so does not change the underlying course of neurodegeneration. Our ultimate goal is to develop a disease modifying drug ("DMD") for patients with neurodegeneration by leveraging our clinical and pre-clinical data, which shows inhibition of the most relevant neurotoxic proteins. Studies have found that AD and PD are the most common neurodegenerative diseases in the U.S., and accordingly these diseases present two unmet needs of the aging population and two potentially large U.S. markets, if a DMD is developed and approved.

Our leadership team has substantial experience and extensive industry knowledge and has been successful with respect to meeting clinical timelines, enrollment progression and data readouts.

Company Leadership

Maria L. Maccecchini, our Founder, President and CEO, founded Annovis in May 2008 to develop improved therapeutics for neurodegeneration. She was previously the Founder and CEO of Symphony Pharmaceuticals/Annovis, a biotech company that was sold to Transgenomic in 2001. She was previously the General Manager of Bachem Bioscience, the U.S. subsidiary of Bachem AG, Switzerland. Dr. Maccecchini completed one postdoc at Caltech and another at the Roche Institute of Immunology. Her PhD in biochemistry is from the Biocenter of Basel with a two-year visiting fellowship at The Rockefeller University.

Cheng Fang, Senior Vice President, Research and Development, has broad scientific knowledge and over a decade of experience working in the field of neurodegenerative diseases. She previously worked at Clarivate Analytics and the Cornell Institute for Medical Research. As a Research Assistant Professor at Boston University, she designed projects that addressed prion diseases and AD. Dr. Fang has a PhD in biology and neuroscience from Pennsylvania State University. She also holds a B.S. in biopharmaceutics from Nanjing University.

Eve Damiano, Senior Vice President, Regulatory, has spent over 35 years in the biotechnology sector, focusing on the definition and execution of regulatory strategies. Ms. Damiano has held various senior management positions throughout her career, with experience garnered at companies including Centocor, MedImmune, OraSure Technologies and Vicuron Pharmaceuticals. Ms. Damiano holds a track record in the definition and execution of regulatory strategies. She holds an M.S. from the Drexel University College of Medicine.

Melissa Gaines, Senior Vice President, Clinical Operations, is an accomplished clinical research professional with over 20 years of experience garnered from positions held in academia, contract research organizations and pharmaceutical companies. She was previously Senior Director, Clinical Operations, for Worldwide Clinical Trials, and has over a decade of experience at INC Research. She has demonstrated proven success in leading cross-functional teams as well as driving operational success. Ms. Gaines holds a B.A. in Psychology from Millersville University of Pennsylvania.

Mike Christie, our Vice President, Process Chemistry, has spent over 40 years working in the pharmaceutical industry, with a focus on process chemistry R&D, pilot plant production and good manufacturing practice ("cGMP") operations. He has held senior management positions in both large (SmithKline, Rhodia, Teva) and mid-size (Cephalon) companies, as well as being the founder of a company providing contract process R&D services (later acquired by ChiRex). Dr. Christie is co-author or co-inventor on several publications and patents. He earned his BS in chemistry from the University of Michigan and his doctorate from MIT.

Andrew Walsh, our Vice President, Finance, has over 13 years of diverse finance experience at both public and private companies. Prior to joining Annovis, Mr. Walsh served as Senior Director, Finance and Treasury at Ocugen, a Nasdaq-listed biotech developing gene and cell therapies. There he provided oversight over all areas of finance, including SEC Reporting, FP&A, as well as Treasury. He also previously served as Director, Treasury and Tax at Potters Industries, a private equity sponsored materials manufacturer. Mr. Walsh began his career at KPMG as a member of its tax practice. He holds a B.S. in Accounting from Drexel University, summa cum laude.

Mechanism of Action

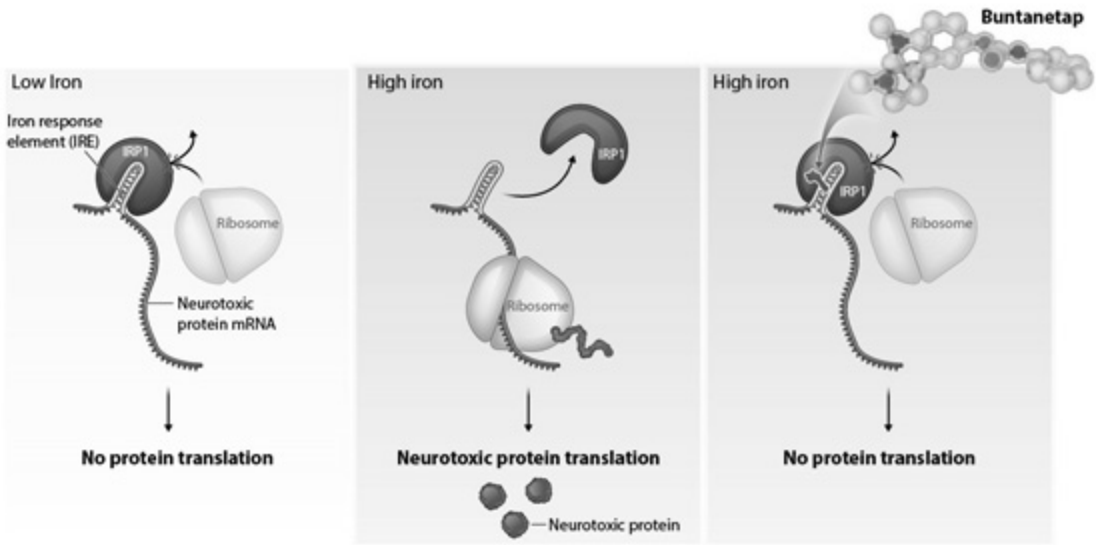
Our lead product candidate, buntanetap, is designed as an oral translational inhibitor of neurotoxic aggregating proteins such as APP, tau and αSYN. To understand how buntanetap can potentially inhibit translation, we undertook two complementary approaches: a macro approach to examine all proteins in the cell whose translation is affected by buntanetap, and a micro approach to study the mechanism of action using molecular biology, to understand and validate the binding and function.

First, the non-biased proteomics approach was applied to explore what proteins in the total protein universe were specifically downregulated by buntanetap. We have observed that, in addition to the proteins already known to be reduced by buntanetap, other neurotoxic aggregating proteins - huntingtin protein ("HTT") and TDP43 - were downregulated as well.

A detailed analysis of the reduction of these protein levels was conducted in five different laboratories using multiple methodologies. The results observed in the analysis revealed that the mRNAs of these proteins have a special region, an atypical stem loop, that is preserved and responsible for their translation. When this region is bound to an RNA binding protein, the mRNA is not translated. When this region is free, the mRNA is translated. In neurodegenerative conditions, the mRNA coding for these neurotoxic proteins is over-translated, produces high levels of these proteins and causes them to become toxic. Buntanetap was observed to specifically increase the affinity between this special region and the RNA binding protein, preventing the mRNA from being released and translated.

The process outlined above leads to lower translation, lower levels of neurotoxic proteins, and less toxicity in the brain. By preventing the overexpression of these neurotoxic proteins, buntanetap is designed to reverse the downstream toxic cascade that leads to neurodegeneration and reinstates homeostasis.

The following illustration visually depicts the mechanism of action of buntanetap:

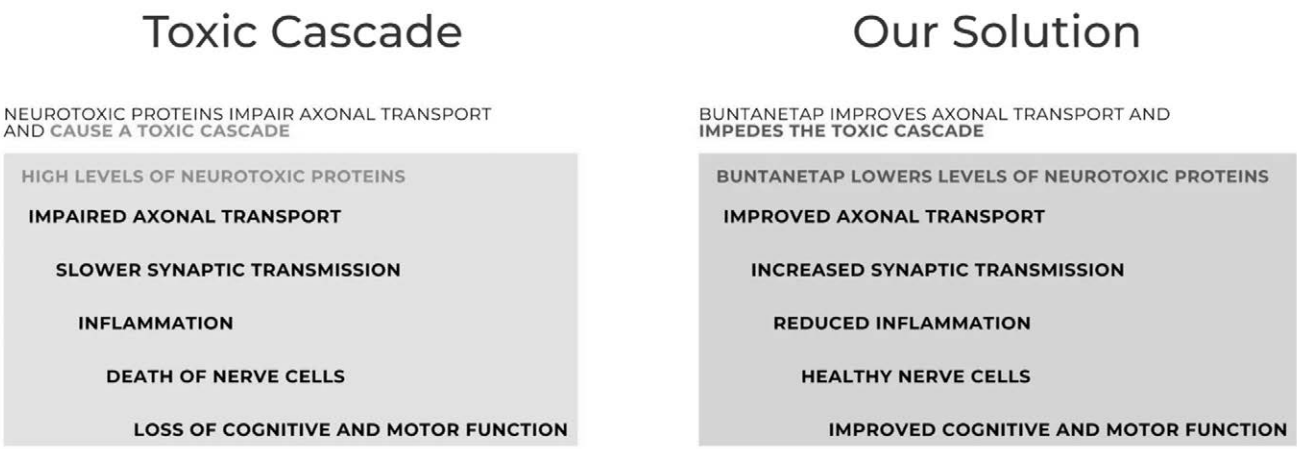


MOA; Chen XQ et al. Pharmaceutics 09-2021 Iron and Neurodegeneration; Wong f. et al. Frontiers Aging Neuroscience; 03-2022

The special region in the mRNA is a 5'UTR iron responsive element ("IRE") present in all mRNAs of neurotoxic aggregating proteins. The RNA binding protein is the Iron Regulatory Protein -1 ("IRP1") that specifically binds the IREs of neurotoxic aggregating proteins.

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

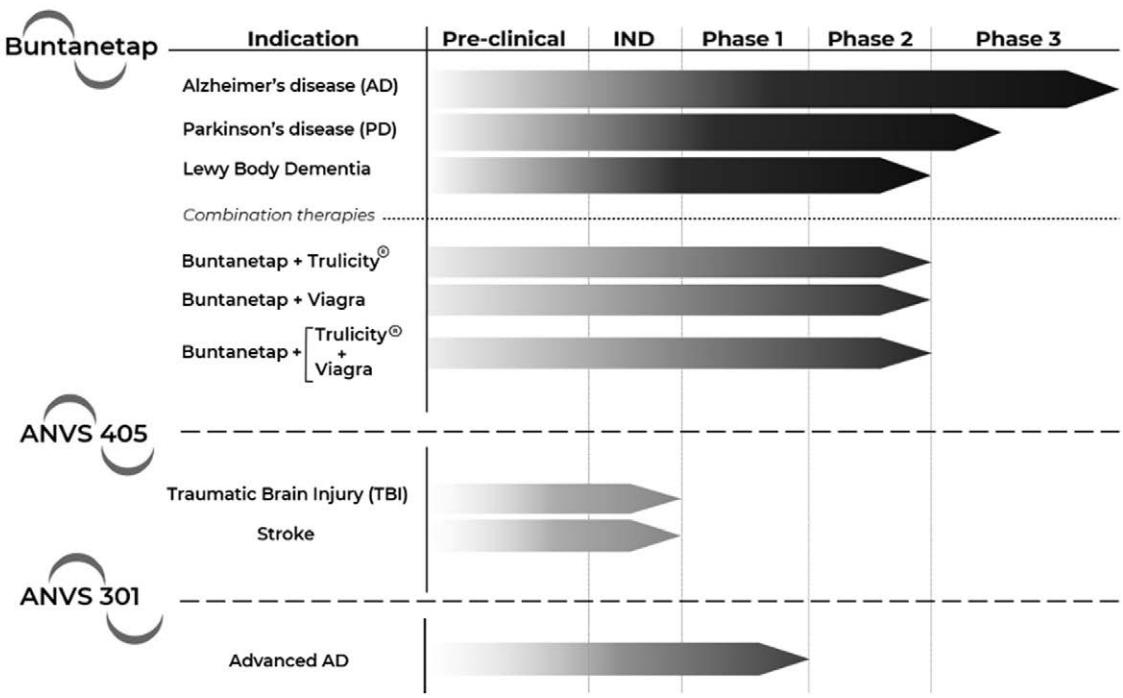
The toxic cascade in neurodegeneration begins with high levels of neurotoxic proteins which lead to impaired axonal transport, inflammation, death of nerve cells and loss of cognition and motor function. Buntanetap and ANVS405, our product candidates designed to treat acute neurodegeneration, including traumatic brain injury ("TBI"), have a mechanism of action we believe to be unique. The mechanism of action is designed to inhibit the over-translation of and ultimately reduce the levels of APP, tau and αSYN, which play a central role in the pathogenesis of both AD and PD. This leads us to believe that buntanetap has the potential to be 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 a technology platform that has the potential to target the mRNAs of multiple neurotoxic proteins, which are potentially impactful for multiple diseases.



In our AD/PD Trials in human AD and PD patients, we observed that buntanetap reduced levels of neurotoxic proteins, improved axonal transport and synaptic function, reduced inflammation, improved the health of nerve cells and improved cognition and function in mild to moderate AD and PD patients. Further, we have also observed that buntanetap reduced the levels of multiple neurotoxic proteins in animals, reversed the entire toxic cascade and recovered the affected function, be it in the brain, the body, or the eyes.

Pipeline

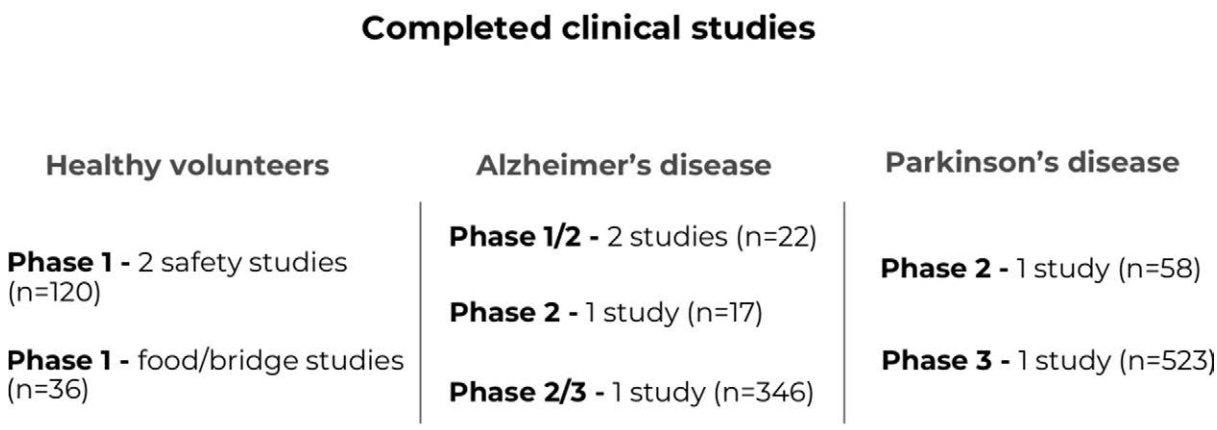
Our pipeline consists of: buntanetap for chronic neurodegeneration - including AD, PD and Lewy Body Dementia - as well as within certain combination therapies summarized below; ANVS405 for acute neurodegeneration; and ANVS301 for advanced AD.



Buntanetap

Our lead product candidate, buntanetap, is an orally administered drug being developed for chronic indications such as AD and PD. Buntanetap has been observed to improve axonal transport in these diseases in preclinical studies by inhibiting the overproduction of neurotoxic proteins that kill nerve cells. In Phase 2/3 early AD patients, we have seen a statistically significant improvement in ADAS-Cog. In Phase 3 PD patients, we have seen statistically significant improvement in cognition for an ITT population, as well as in UPDRS scores for a per protocol population. The drug has further demonstrated improvements of cognition, including memory and learning, in AD mice, as well as movement, including colonic motility and grip strength, in PD mice. Buntanetap 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 buntanetap for AD, PD, and potentially other chronic neurodegenerative diseases.

Below is a summary depiction of our previously completed clinical studies of buntanetap. To date, over 1,000 human patients have been treated in the clinic and the drug has consistently shown to be well tolerated with minimal side effects:



We believe that buntanetap has the potential to be the only drug to improve both cognition in AD patients, and motor function in PD patients.

ANVS405

ANVS405 is an intravenous drug being developed for acute indications and focused on protecting the brain after Traumatic Brain Injury ("TBI") and/or stroke. ANVS405 is the same compound as buntanetap, given in cases of acute head and brain trauma. In prior animal studies, ANVS405 was given to rats intravenously after TBI to determine whether ANVS405 would reach the brain in less than 15 minutes, as opposed to 1.5 hours if given orally. TBI rats that were treated with ANVS405 after the injury exhibited enhanced memory and learning and lower microglia activation, a measure of inflammation. The program has previously been funded by a grant from the U.S. Army and has since been completed. We therefore plan to seek additional grant funding to further the development of ANVS405 for acute indications of brain and nerve trauma. If and when we receive such sufficient funding, 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 a patient can effectively be treated. Our plan is to 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 later, continue with Phase 2 and Phase 3 efficacy studies.

ANVS301

ANVS301 is an orally administered drug being developed to increase cognitive capability in later stages of AD and dementia. ANVS301 was observed to improve memory and learning in rats of an advanced age by lowering the number of errors from six to three and shortening run times from approximately 75 to approximately 28 seconds. ANVS301 previously finished a single ascending dose Phase 1 clinical trial that was conducted and financed by the National Institutes of Health ("NIH").

Clinical Trials of Buntanetap

Future Development Plan for Alzheimer's Disease

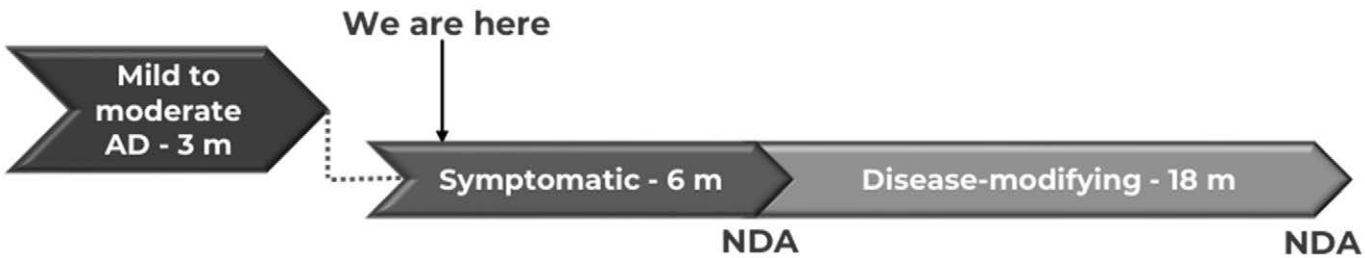
The future development of buntanetap for AD includes the recently initiated pivotal Phase 3 study for early AD patients. This study was designed to include both a 6-month treatment window to demonstrate symptomatic efficacy, combined with a 12-month extension that will allow the study to achieve an 18-month treatment window that demonstrates disease modifying effects. We also expect future development to include an open-label extension for AD.

In February of 2025, we initiated the Phase 3 AD study of buntanetap in 750 early AD patients, which will be separated into two cohorts of 375 patients (the "Phase 3 AD Trial"). The trial is expected to be conducted at up to 100 sites in the U.S. The Phase 3 AD Trial is a double-blind, placebo-controlled efficacy study which treats early AD patients. The inclusion criteria for early AD is an MMSE score of 21 to 28 and diagnosis according to NIA and NIA-AAA criteria. Patients participating in the trial are age 55-85, have a study partner, are of non-child-bearing age or agree to effective contraception, and have no evidence of suicidal ideation. Additionally, for Phase 3 AD we are incorporating a new biomarker-based inclusion criteria, for a positive reading of pTau217 levels in plasma. pTau217, a phosphorylated form of the tau protein, has been recognized by the FDA as an acceptable early detection biomarker for AD.

Patients participating in the trial can remain on any drugs they regularly take, whether for AD or for other conditions, as long as they are stable on such medication. Patients with uncontrolled diabetes, cardiovascular issues or seizures, patients with clinically significant abnormal laboratory values, patients with cancer within the last year and patients suffering from alcohol or substance abuse are excluded from participating.

Patients are to be randomly assigned to receive either 30 mg of buntanetap or placebo, once per day. Patients will visit the clinic for the first-time dosing in clinic, followed by an at home dosing period of 24/72 weeks. As described above, the study plan calls for opening the blind to a select group of individuals who will analyze the data after the 24-week treatment window, in order to evaluate 6-month efficacy of buntanetap. Study participants will remain blinded and will continue participation for an additional 48 weeks so that buntanetap's disease modifying efficacy can be evaluated over a total of 18 months.

Below is a visual depiction of the development path and study design for the active Phase 3 AD program:



We expect the 6-month symptomatic component of the combined AD trial to read-out in the second half of 2026. The 18-month disease modifying component is expected to read out in the second half of 2027.

Future Development Plan for Parkinson's Disease

As mentioned above, we also intend to propose a pivotal Phase 3 trial for Parkinson's patients to the FDA during 2025. Buntanetap has been shown to prevent worsening of cognition in the entirety of our previous Phase 3 ITT population. In the same study, the drug also showed statistically significant improvement in MDS-UPDRS Part II, III, IV, total and MMSE in a per protocol subgroup population. Our plan is to continuing refining a proposed pivotal Phase 3 program design during 2025 and when it is finalized, we will propose a meeting with the FDA to solidify the path forward for clinical development of buntanetap in PD.

Similar to the AD program, we also expect to ask the FDA for clearance to add an open-label extension to allow all patients that participate in our pivotal Phase 3 PD program to continue on the medication.

Initiation of the pivotal Phase 3 PD program and open-label extension is also currently contingent on additional fundraising.

Phase 3 PD Trial

In August 2022, we initiated a Phase 3 clinical trial of buntanetap in 450 early PD patients, which were separated into three cohorts of 150 patients (the "Phase 3 PD Trial"). The Phase 3 PD Trial was conducted at 53 sites in the U.S. and 49 sites in the EU. The Phase 3 PD Trial was a double-blind placebo-controlled efficacy study which treated early PD. The inclusion criteria for early PD was Hoehn & Yahr 1, 2 and 3 with less than 2 hours of OFF time, as well as a MMSE score of 22 to 30. Patients participating in the trial were age 40-85, were of non-child-bearing age or agree to effective contraception and had no evidence of suicidal ideation. Patients participating in the trial were permitted to remain on any drugs they regularly took, whether for PD or for other conditions, as long as were stable on such medication. Patients with uncontrolled diabetes, cardiovascular issues or seizures, patients with clinically significant abnormal laboratory values, patients with cancer within the last year and patients suffering from alcohol or substance abuse were excluded from the trial. Patients were randomly assigned to receive either 10 or 20 mg of buntanetap or placebo, once per day. Patients visit the clinic for the first-time dosing in clinic, followed by an at home dosing period of 6 months. The study plan incorporated an interim analysis at two months, the results of which were disclosed by the Company on March 31, 2023. Based on the results of the interim analysis, we proceeded with the Phase 3 PD Study as planned in accordance with the previously established protocol.

The Phase 3 PD Trial's primary endpoints were evaluated using the following measures: MDS-UPDRS Part II and III. Specifically, The FDA requested two co-primary endpoints to have an objective primary endpoint (MDS-UPDRS Part III, motor function) and a subjective primary endpoint (MDS-UPDRS Part II, activities of daily living). Together, these co-primary endpoints were intended to provide a more complete picture of the study and treatment results. The secondary endpoints were evaluated using the following measures: the MDS-UPDRS total score, which includes the Part II and III measures we well as mentation, behavior, and mood symptoms, and complications of dopaminergic therapy; the participant global impression of change ("PGIC"), a participant-reported outcome which asks how their condition has changed compared to their condition at the beginning of treatment; and the Change on Clinical Global Impression of Severity ("CGIS"), which measures the severity of movement impairment as assessed by a site rater.

The study was completed on December 4, 2023, and we released the topline PD Study efficacy data on July 2, 2024. The data showed that in two subgroups, buntanetap improved UPDRS 2, 3, 2+3 and total score. It also showed that in the entire ITT population, buntanetap stopped the loss of cognition and that in the 12% of patients that already had cognitive issues, buntanetap improved cognition in a dose-dependent, statistically significant way. We expect to discuss the PD data with the FDA at an end-of-study meeting during 2025. During that meeting, we plan to propose continued development of buntanetap with a pivotal Phase 3 trial.

Phase 2/3 AD Trial

In February 2023, we initiated a Phase 2/3 clinical trial of buntanetap in 320 mild to moderate AD patients, which were separated into four cohorts of 80 patients (the "Phase 2/3 AD Trial"). The Phase 2/3 AD Trial was conducted at 64 sites in the U.S. The Phase 2/3 AD Trial was a double-blind, placebo-controlled efficacy study which treated mild to moderate AD. The inclusion criteria for mild to moderate AD was a MMSE score of 14 to 24. Patients participating in the trial were age 55-85, had a study partner, were of non-child-bearing age or agreed to effective contraception, and had no evidence of suicidal ideation. Patients participating in the trial were permitted to remain on any drugs they regularly took, whether for AD or for other conditions, as long as they were stable on such medication. Patients with uncontrolled diabetes, cardiovascular issues or seizures, patients with clinically significant abnormal laboratory values, patients with cancer within the last year and patients suffering from alcohol or substance abuse were excluded from participating.

Patients were randomly assigned to receive either 7.5, 15 or 30 mg of buntanetap or placebo, once per day. Patients visited the clinic for the first-time dosing in clinic, followed by an at home dosing period of 12 weeks. The study plan incorporated an interim analysis at six-weeks, the results of which were disclosed on October 23,2023. Similar to above for the PD study, based on the outcome of the interim analysis, we proceeded with the remaining AD study as planned after the interim analysis.

The co-primary endpoints of the Phase 2/3 AD Trial were evaluated using the following measures: ADAS-Cog 11 and ADCS-Clinical Global Impression of Change ("ADCS-CGIC"), which focuses on clinicians' observations of change in the patient's cognitive, functional, and behavioral performance since the beginning of a trial. The FDA requested the inclusion of two co-primary endpoints to have an objective primary endpoint (ADAS-Cog, cognition) and a subjective primary endpoint (ADCS-CGIC, activities of daily living). Together, these co-primary endpoints were intended to provide a more complete picture of the study and treatment results. The secondary endpoints were evaluated using the following measures: the ADCS-Instrumental Activities of Daily Living Scale ("ADCS-ADL"), which measures 6 basic activities of daily living items, including basic self-care tasks such as feeding, mobility and bathing, and 17 instrumental activities of daily living items, which include a broad range of activities based on cultural norms and gender roles; MMSE; and the digital symbol substitution test ("DSST"), which asks individuals to record associations between different symbols and numbers within time limits to assess cognition.

The Phase 2/3 AD study was completed on February 13, 2024, and on April 29, 2024, we announced topline efficacy data. The data showed that in a subgroup of early AD patients, buntanetap improved ADAS-Cog11 in a dose-dependent fashion and was statistically significant from placebo and from baseline.

On October 10, 2024, the Company met with the FDA in an end-of-phase 2 meeting to discuss its Phase 2/3 AD data and to agree on a regulatory path forward. Annovis and the FDA have now aligned on a development path for buntanetap towards the filing of New Drug Applications (NDAs), one for short-term and one for long-term efficacy. The Phase 3 program will investigate buntanetap in patients with early AD and will consist of one study that first incorporates a 6-month study period aimed at confirming buntanetap's symptomatic effects and later moving into an 18-month study period designed to demonstrate potential disease-modifying effects. While the overall study will last for the entire 18 months, the completion of the first 6-month treatment period, if well-designed and well-executed, may be sufficient to support an NDA filing, potentially within one year of the study's initiation.

During the end-of-phase 2 meeting, the FDA raised no concerns with the Company's data on buntanetap's safety, including liver enzymes, drug interactions, dose selection, pharmacokinetics, population pharmacokinetics, and confirmed that development can proceed using the new crystal form of buntanetap.

.Phase 1/2 AD/PD Trials

In 2021, we completed a Phase 1/2 clinical trial of buntanetap in 14 early AD and 54 early PD patients (the "AD/PD Trials") which were conducted at 12 clinical sites in the U.S. The AD/PD Trials were double-blind, placebo-controlled studies which treated mild to moderate AD and early PD patients for 25 +/- 2 days. The inclusion criteria for the AD portion of the AD/PD Trials were MMSE 18-28 and age 45 and older. For the PD portion of the AD/PD Trials, inclusion criteria were MMSE 18-30, age 45 and older and Hoehn & Yahr 1, 2 or 3. Patients participating in the trial were of non-child-bearing age or agreed to effective contraception and had no evidence of suicidal ideation. Patients participating in the trial could remain on any drugs they regularly took, whether for PD, for AD or for other conditions, as long as they were stable on such medication. Patients with uncontrolled diabetes, cardiovascular issues or seizures, patients with clinically significant abnormal laboratory values, patients who had cancer within the prior year and patients who suffered from alcohol or substance abuse were excluded from the trial.

The AD/PD Trials were designed to assess the safety, tolerability, and PK of buntanetap. The studies met their primary endpoints of safety and tolerability, as measured by the percentage of patients with treatment-emergent adverse events in the buntanetap treatment arms as compared to the placebo groups, and secondary endpoint of pharmacokinetics of buntanetap, as measured by the concentration of buntanetap in plasma. The studies also met exploratory endpoints of measures of biomarkers related to neurotoxic protein cascade, and improvements in cognition in AD patients and function in PD patients. We believe the AD/PD Trials were the first double-blind, placebo-controlled studies that showed improvements in AD patients as measured by ADAS-Cog, and in PD patients as measured by UPDRS.

The studies were conducted in two parts. The first part of the AD/PD Trials was in 14 early AD patients and 14 early PD patients. Patients were randomly assigned to receive either 80 mg of buntanetap or placebo, once per day. The second part of the AD/PD Trials was a dose response analysis performed in 40 early PD patients in which patients were randomly assigned to receive 5 mg, 10 mg, 20 mg, or 40 mg of buntanetap, once per day. In both parts of the AD/PD Trials, patients visited the clinic for the first-time dosing in clinic, followed by an at home dosing period of 25 +/- 2 days. We measured levels of neurotoxic proteins, neurotransmitters, neurotrophic factors, inflammation, and nerve cell death in all patients, as well as cognitive and functional improvements.

Safety results showed that buntanetap was well-tolerated in all dose groups. No serious adverse events were reported. The adverse events seen included problems related to CNS sampling: headaches, back and leg pain. PK parameters for buntanetap in plasma of AD and PD patients were similar to those seen in Phase 1 in our single ascending dose ("SAD") and multiple ascending dose ("MAD") studies in healthy volunteers, and in a proof-of-concept study in mild-cognitive impaired ("MCI") patients.

We observed that buntanetap administration for 25 days lowered secreted APP α and β as well as total-tau and phosphorylated-tau levels in AD patients, and alpha-synuclein levels in PD patients. APP and its downstream products and tau are the neurotoxic proteins involved in AD, while αSYN is the primary neurotoxic culprit of PD.

CSF was extracted before starting the study at baseline and at time 0 to 6 hours at the end of the study in both placebo and buntanetap treated patients. The values from time 0 to 6 hours were pooled to lower variability and the placebo values were deducted from the treated values. In all but one case, Ab42, we saw that the levels in buntanetap treated patients were lower than in placebo patients. With respect to Ab42, we observed that levels were slightly higher, which is consistent with our hypothesis that Ab42 levels are lower in advanced AD and higher in early AD. We believe that higher Ab42 levels we observed suggest that the course of AD was reversed and the patients improved. Again, CSF was extracted at baseline and for 6 hours after the study and the values of the placebo patients were subtracted from the buntanetap treated patients. We observed that inflammatory markers were generally reduced in both patient populations.

We observed that buntanetap reduced neurofilament light ("NFL") levels in both AD and PD patients, suggesting a potential improvement in axonal integrity. We also observed that buntanetap reduced neurogranin ("NG") levels in both AD and PD, potentially suggesting more intact synaptic functions. The same CSF as above was used to measure neurofilament light and neurogranin before and after treatment and to compare buntanetap patients to placebo. In both patient populations, neurofilament light and neurogranin are lower in treated than in placebo patients.

These results suggest that buntanetap has the potential to reduce neurotoxic proteins, rescue axonal transport, reduce inflammation, and protect synaptic functions.

We performed ADAS-Cogs and WAIS coding tests to evaluate buntanetap's effects on AD patients' cognition. ADAS-Cog11 was performed at the beginning of the study at baseline and at the end at 25 days in the buntanetap-treated and the placebo groups. Although the study was not powered for efficacy, ADAS-Cog11 improved by 4.4 points, a statistically significant improvement of 28.57%. An improvement in ADAS-Cog11, which is reflected by a lower ADAS-Cog11 result, indicates increased cognitive performance. At 25 days, the treated group's improvement from baseline was 3.3 points, or 20.71%, better than the placebo group's improvement from baseline.

The WAIS coding test measures speed in movement and thinking. Treated AD patients showed a 6.6 point, or 16.17%, statistically significant improvement from baseline. Furthermore, the treated group's improvement from baseline was 3.1 points, or 8.8%, better than the placebo group's improvement from baseline.

In Parkinson's disease, we pooled the original 14 PD patients with the additional 40 PD patients and looked at the MDS-UPDRS and WAIS coding tests to evaluate buntanetap's effects on PD patients' mobility and functionality. The 54 PD patients received doses of either 5mg, 10mg, 20mg, 40mg or 80mg buntanetap treatment or placebo, once per day. We observed a statistically significant improvement in UPDRS Part II, III and IV individually. Specifically, Part III of the MDS-UPDRS measures the motor functions and has long been used as a standard to assess drugs' effects on patients' mobility.

We combined the two best doses, 10 and 20 mgs, and all doses, and saw an improvement of 3.6 (16.4%) for 10 and 20 mg, and of 2.4 (13.3%) for all doses combined compared to baseline. In the WAIS coding test, PD patients showed a statistically significant improvement both from baseline (17.1% for 10+20mg; 13.3% for all doses combined) and from placebo (27.1% for 10+20mg; 23.3% for all doses combined).

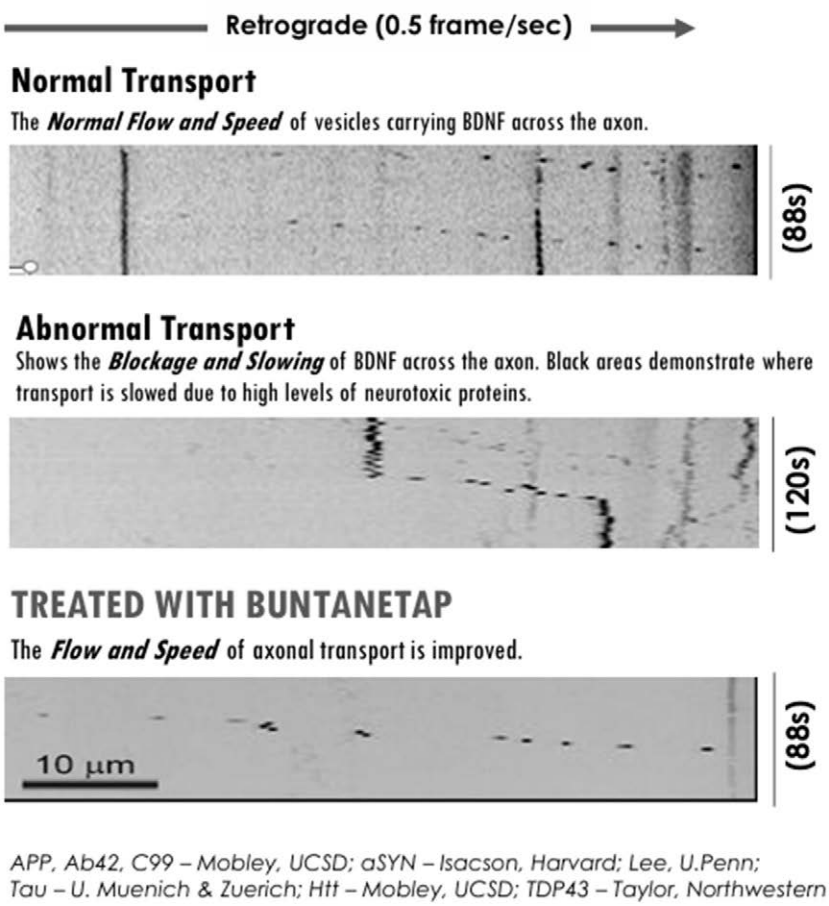
Axonal Transport in Human Nerve Cells

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. Axonal transport is responsible for:

- Neurotransmitters GABA (anxiety), ACh (cognition), dopamine (movement), serotonin (mood)
- Neurotrophic factors NGF, BDNF, and
- All communication within and between nerve cells

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



APP, Ab42, C99 – Mobley, UCSD; aSYN – Isacson, Harvard; Lee, U.Penn; Tau – U. Muenich & Zuerich; Htt – Mobley, UCSD; TDP43 – Taylor, Northwestern

TBI Study 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, 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 of the rats were first tested for their performance in a water

maze, and then they were sacrificed for brain staining of living cells and determination of microglia activation. 10 mg/kg ANVS405 was shown to improve 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 demonstrated the ability to protect 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.

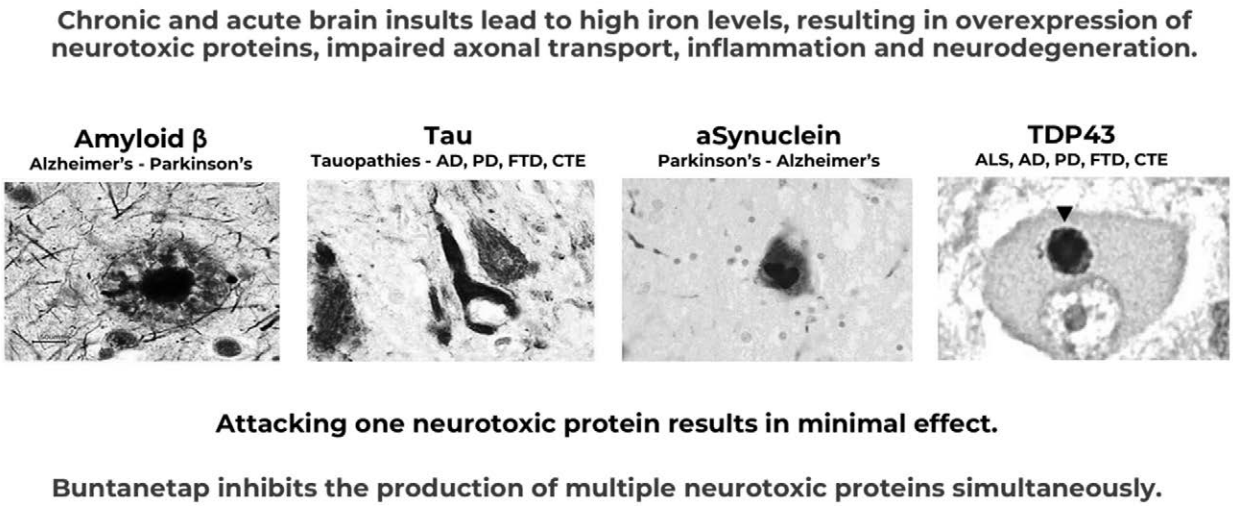
Stroke Mice Model

Buntanetap was also 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.

Buntanetap, 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 buntanetap/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.

Potential Markets for our Lead Drug Candidate

With there being a very large potential market for neurodegenerative diseases, most pharma companies have a program studying some aspect of nerve and brain degeneration. 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, we believe that generally, neither drugs attacking tau nor αSYN have shown positive results. Hence there is a substantial need for a new and 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. To prove that this approach is possible, we are studying the effects of buntanetap on the levels of several neurotoxic proteins and other surrogate markers, in parallel, in both AD and PD patients.

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 55 million victims of AD or some form of dementia exist in the world and by 2050, the number will grow to nearly 140 million people worldwide. In the United States, it is estimated that there are nearly seven million patients with AD currently and that by 2060, the number of people aged 65 and older with AD is projected to reach nearly 14 million people. Nearly eightfold as many people have preclinical AD as have symptomatic AD and are at risk for progressing to full manifestation of the 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.

The incidence rate of AD increases significantly with age. Individuals between ages 64 to 75 have an incidence rate of 0.4%, which increases to 3.2% for people between ages 75 and 84 and finally to 7.6% for people aged 85 and above. These incidence rates are cumulative as an individual ages, which means that an individual reaching 90 years of age will have a 38% chance of suffering from AD while an individual reaching the age of 95 will have a 76% chance of suffering from AD. 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 both 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 more than 10 million people worldwide, of which nearly one million are in the U.S. While a 2014 study estimated that the incidence in the U.S. will rise to 1.2 million by 2030, a later 2022 study found that there are nearly 90,000 new cases of PD diagnosed each year in the U.S., potentially supporting an even greater future incidence rate. By 2050, the number of worldwide PD patients is expected to grow to up to 30 million.

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. 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.

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 looked 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.

We believe that a therapy that only addresses Aβ, tau or αSYN is less likely to help people with mixed pathologies. Since buntanetap is designed to inhibit more than one neurotoxic protein, we believe that it may have the potential to slow or eventually stop AD, PD and mixed pathology diseases.

Therapeutic Approaches and Competition

Alzheimer's Disease Approaches

Drug development for AD has historically proven to be very difficult. Drugs which have been approved for the treatment of AD include cholinesterase inhibitors (tacrine, donepezil, rivastigmine, galantamine),an N-methyl-D-aspartate receptor antagonist (memantine) and more recently, monoclonal antibody treatments (donanemab, lecanemab). Many failures in AD drug development have occurred, with both small molecules and immunotherapies failing to show a dramatic drug/placebo difference or having unacceptable toxicity.

Most clinical trials conducted have addressed amyloid targets. Since Aβ accumulates for years before the symptoms of AD are visible, some pharmaceutical companies are testing their drugs earlier, including in cognitively normal people or those who have genetic profiles that place them at high(er) risk for developing AD.

An increasing number of agents are also 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. Several 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 few disease-modifying agents currently on the market and existing treatments show limited efficacy. Previous large efforts to develop a DMD for AD has targeted Aβ42, but many Aβ42 approaches to date have failed and again, have shown limited efficacy when treating AD. Further, most companies testing tau have shown negative results as well. As a result, many organizations have pulled out of AD research and are waiting to see if a new or alternative approach may have a better outcome. Since the AD brain contains several neurotoxic proteins—amyloid precursor protein and its toxic fragments Aβ42 and IC99, as well as tau and αSYN, we believe an Aβ42-only approach is not sufficient in order to develop a DMD drug. We believe that a DMD drug needs to target more than just one toxic protein to be efficacious and we are developing buntanetap with this approach in mind. A concerning observation derived from a review of the existing industry 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 ("COMT") inhibitors and the monoamine oxidase ("MAO") inhibitors allow patients to reduce L-DOPA dosing levels.

The current global market for PD drugs is estimated at $5 to $6 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, we believe that only buntanetap and Exenatide are in the later stages of clinical development for disease-modification and no products have yet shown efficacy in PD patients long term. 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 Overview

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.

Annovis has filed fourteen (14) families of patents and patent applications to prolong the patent life of buntanetap. The pending patent applications invented and filed by Annovis 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;
- a method of treating viral and bacterial infections of the brain, including COVID-19;
- a method of inhibiting cancer metastasis;
- combinations of buntanetap with some drugs and uses of these combinations to treat neurodegenerative diseases;
- a method of treating neuropsychiatric indications;
- a new composition of matter of Posiphen, Form B or ANVS402; and
- new methods for making buntanetap and Posiphen Form B.

Solid forms of chemical compounds can exist in different crystalline structures. One crystalline structure of Posiphen is buntanetap. Annovis, through its research efforts, invented a new crystalline form of Posiphen, known as Form B ("ANVS402"). Form B, or ANVS402, has demonstrated certain improvements over buntanetap and was filed as a new composition of matter patent application.

As of February 9, 2024, our patent portfolio comprised 39 total issued patents plus 18 pending patent applications in various jurisdictions.

The patents, granted and if granted based on the pending applications, have expiration dates between 2031 and 2045. The first patent application family we filed, which would be expected to expire in 2031, before any patent term adjustments or extensions, covers the use of buntanetap in the treatment of AD, PD and other neurodegenerative disorders such as Huntington's disease, prion diseases, amyotrophic lateral sclerosis, tauopathies, frontotemporal dementia, Lewy bodies disease, and chronic traumatic encephalopathy, 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 treatment of PD and Lewy body diseases. Subsequently, the USPTO also granted patents covering treatment frontotemporal dementia and Prion's disease, tauopathies, chronic traumatic encephalopathy, prion diseases, amyotrophic lateral sclerosis, Alzheimer's and Huntington's disease.

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 the whole patent and it has since been approved in most countries filed claiming a method of treating acute nerve and brain injuries by administering ANVS405 before and after the injury. The US patent office instead has asked us to separate the application into four divisional applications covering stroke, traumatic brain injury, nerve injury and spinal cord injury.

The third patent application family relates to the use of the mechanism of action of buntanetap and ANVS405 to prevent and treat neurodegenerative diseases and would be expected to expire in 2038, before any patent term adjustments or extensions. The first divisional of this application was approved in December 2022, it covers the prevention of neurodegenerative diseases.

The fourth patent application family relates to 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 buntanetap or related compounds. 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 buntanetap or related compounds, which would be expected to expire in 2041, before any patent term adjustments or extensions.

The fifth patent family application is directed to a method of maintaining heavy metal homeostasis avoiding the effect of toxic levels of a heavy metal in cells in a healthy human or restoring heavy metal homeostasis in a sick human patient. The USPTO granted the first patent in this family on March 7, 2023, which is expected to expire in 2039, before any patent term adjustments or extensions.

The sixth patent application family relates to treating brain metastasis via administration of buntanetap or related compounds. In September 2023, we filed a U.S. nonprovisional patent application directed to treatment of brain metastasis via administration of buntanetap or related compounds with the USPTO, which, if allowed, would be expected to expire in 2043, before any patent term adjustments or extensions.

The seventh patent application family relates to treatment of mental illness via administration of buntanetap or related compounds. In January 2024, we filed an International (PCT) application and a U.S. nonprovisional patent application directed to treatment of mental illness via administration of buntanetap or related compounds with the USPTO, which, if allowed, would be expected to expire in 2044, before any patent term adjustments or extensions.

The eighth patent application family relates to treatment of neurodegenerative diseases and other diseases via co-administration of buntanetap or related compounds and an antidiabetic agent. In September 2024, we filed an International (PCT) application and a U.S. nonprovisional patent application directed to treatment of neurodegenerative diseases and other diseases via administration of this combination.

The ninth patent application family relates to treatment of neurodegenerative diseases and other diseases via co-administration of buntanetap or related compounds and a phosphodiesterase inhibitor. In September 2024, we filed an International (PCT) application and a U.S. nonprovisional patent application directed to treatment of neurodegenerative diseases and other diseases via administration of this combination.

The tenth patent application family relates to treatment of neurodegenerative diseases and other diseases via co-administration of buntanetap or related compounds and an antihypertensive agent. In September 2024, we filed an International (PCT) application and a U.S. nonprovisional patent application directed to treatment of neurodegenerative diseases and other diseases via administration of this combination.

The eleventh patent application family relates to treatment of neurodegenerative diseases and other diseases via co-administration of buntanetap with two additional therapeutic agents. In August 2024, we filed a provisional U.S. Patent application directed to treatment of neurodegenerative diseases and other diseases via administration of this combination.

The twelfth patent application family relates to treatment of neurodegenerative diseases and other diseases via co-administration of buntanetap or related compounds and an additional therapeutic agent. In February 2025, we filed a provisional U.S. Patent application directed to treatment of neurodegenerative diseases and other diseases via administration of this combination.

The thirteenth patent application family relates to the new Form B of Posiphen (ANVS402); it demonstrates that it can be used instead of buntanetap, including in the foregoing uses of buntanetap of the Company's patent portfolio. Posiphen Form B may be the compound of choice in current uses of buntanetap, because it may have advantageous properties such as better stability and higher purity. In 2023, the Company filed with the USPTO two provisional patent applications as to Posiphen Form B. In 2024, the Company filed an International (PCT) as to Posiphen Form B and uses thereof. The "International Search Report and Written Opinion" issued by the USPTO in the prosecution of the PCT application was favorable, indicating that the searched claims directed to Posiphen Form

B are novel and inventive. The Company expects to further file patent applications in the U.S. and outside the U.S. as National and Regional Phase patent applications of the PCT application. As to this family of patent applications involving Posiphen Form B and uses thereof, patents would be expected to expire in 2044, before any patent term adjustments or extensions. The Company also expects to seek New Chemical Entity status for Posiphen Form B before the US Food and Drug Administration (FDA), and to seek additional regulatory exclusivity based thereon.

The fourteenth patent application family relates to new, improved and commercially advantageous methods for preparing buntanetap and Posiphen Form B. The Company sees this patent application family as providing further protection as to methods that use buntanetap or Posiphen form B, and for Posiphen form B. More in particular, in 2024 the Company filed with the USPTO a provisional patent application directed to these new methods of for preparing buntanetap and Posiphen Form B. The Company expects in 2025 to further file at least an International (PCT) application, claiming priority from that provisional patent application, and directed to the new, improved and commercially advantageous methods for preparing buntanetap and Posiphen Form B, and thereafter patent applications in the U.S. and outside the U.S. as National and Regional Phase patent applications of the PCT application. As to this family of patent applications, patents would be expected to expire in 2045, before any patent term adjustments or extensions.

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 buntanetap or any other product candidate in the United States or in other foreign countries.

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.

Sales and Marketing

If buntanetap 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. We also may explore the use of a variety of types of collaboration, co-promotion, distribution and other marketing arrangements with one or more third parties to commercialize our product candidates.

Manufacturing

Buntanetap is a small molecule that is manufactured using a patented process. We do not own, operate, and currently have no plans to establish, any manufacturing facilities. We therefore rely, and expect to continue to rely, solely on third-party contractors for manufacturing clinical supplies for our current and future potential product candidates, and plan to do so for commercial supplies also if any of our product candidates received marketing approval. We also rely on these third parties for encapsulating, packaging and stabilizing clinical trial materials. Presently we are working with a U.S. supplier for the manufacture of cGMP active pharmaceutical ingredient (API) to meet our buntanetap clinical study supply demands. We have also engaged a backup API manufacturing contractor, with primary operations in China. We also have an agreement with a local U.S. supplier for the encapsulating, packaging, and stability of the clinical trial material. These arrangements will allow us to enter large and long-term advanced clinical studies. We have only limited supply agreements in place with respect to buntanetap and our product candidates, and these arrangements do not currently extend to commercial supply. We do not have long-term committed arrangements with respect to buntanetap, any of our other product candidates, or other materials.

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, manufacturing, 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, manufacturing, 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 Investigational New Drug application ("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 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. Annovis would like to petition the FDA to classify buntanetap as a breakthrough therapy in the future.

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, buntanetap, or any other candidate 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 buntanetap 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 of 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 27 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

As of February 28, 2025, we had eight full-time employees. We also utilize the services of seven key part-time employees or consultants. We contract with consultants and third parties for the conduct of certain clinical development, accounting and administrative activities. We anticipate hiring of additional employees as we continue to advance our clinical trial programs. None of our employees are represented by labor unions or covered by collective bargaining agreements.

Our human capital resource objectives include, as applicable, identifying, recruiting, retaining, training, incentivizing, and integrating our existing and new employees, advisors and consultants. We offer competitive compensation packages that are competitive within our industry. We incentivize high performance through an annual bonus program based on organizational performance, for which all employees are eligible. We also offer equity incentive plans, the purpose of which are to attract, retain and reward personnel through the granting of stock-based compensation awards. These awards are granted in order to align employee and consultant performance incentives with objectives that will increase stockholder value.

Corporate Information

We were incorporated in Delaware in 2008. Our principal executive offices are located at 101 Lindenwood Drive, Suite 225, Malvern, PA 19355 and our telephone number is (484) 875 3192.

Available Information

We file annual, quarterly, and current reports, proxy statements, and other documents with the SEC under the Securities Exchange Act of 1934, as amended (the "Exchange Act"). The SEC maintains an internet website, www.sec.gov, that contains reports, proxy, and information statements, and other information regarding issuers, including us, that file electronically with the SEC. Copies of each of our filings with the SEC on Form 10-K, Form 10-Q, and Form 8-K and amendments to those reports, can be viewed and downloaded free of charge at our website, www.annovisbio.com, as soon as reasonably practicable after the reports and amendments are electronically filed with or furnished to the SEC. Our website and the information contained on, or that can be accessed through, our website shall not be deemed to be incorporated by reference in, and is not considered part of this Annual Report on Form 10-K.

Item 1A. Risk Factors

Risks Related to Our Financial Position and Need for Additional Capital

Our recurring operating losses, negative cash flows from operations, and accumulated deficit raise substantial doubt about our ability to continue as a going concern, if we are unable to obtain additional financings.

Management has concluded that substantial doubt exists about the Company's ability to continue as a going concern for the next twelve months from the date of the financial statements included in this Annual Report on Form 10-K. As of December 31, 2024, we had cash and cash equivalents of $10.6 million and current liabilities of $3.9 million. We believe that we have sufficient resources

available to support our development activities and business operations and satisfy our obligations into the fourth quarter of 2025. We do not have sufficient cash and cash equivalents as of the date of this Annual Report on Form 10-K to support our operations for at least the 12 months following the date that the financial statements are issued.

We will require substantial additional financing to fund our ongoing clinical trials and future operations, and to continue to execute our corporate strategy. To alleviate the conditions that raise substantial doubt about our ability to continue as a going concern, we plan to explore various dilutive and non-dilutive opportunities, including equity and debt financings, strategic partnerships, business development and other transactions. The future success of the Company is dependent upon our ability to obtain additional funding. There can be no assurance, however, that we will be successful in obtaining sufficient amounts of funding, on terms acceptable to us, or at all. Failure to obtain sufficient capital on acceptable terms when needed would have a material adverse effect on our business, results of operations, and financial condition. Accordingly, we have concluded that substantial doubt exists with respect to our ability to continue as a going concern within one year after the date that these financial statements are issued.

The report of our independent registered accounting firm on our audited financial statements for the fiscal year ended December 31, 2024 contains an explanatory paragraph relating to our ability to continue as a going concern.

The auditor's opinion on our audited financial statements for the year ended December 31, 2024 includes an explanatory paragraph stating that we have incurred recurring losses from operations that raise substantial doubt about our ability to continue as a going concern for the next twelve months from the date of the financial statements included in this Annual Report on Form 10-K. While we believe that we will be able to raise the capital we need to continue our operations, there are no assurances that we will be successful in these efforts or will be able to resolve our liquidity issues or eliminate our operating losses. If we are unable to obtain sufficient funding, we would need to significantly reduce our operating plans and curtail some or all of our development efforts. Accordingly, our business, prospects, financial condition, and results of operations will be materially and adversely affected, and we may be unable to continue as a going concern. If we seek additional financing to fund our business activities in the future and there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide additional funding on commercially reasonable terms or at all.

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

Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We are a clinical stage biopharmaceutical company with a limited operating history and have incurred losses since our formation. We incurred net losses of $24.6 million and $56.2 million for the years ended December 31, 2024 and 2023, respectively. In addition, the Company's operating loss was $26.7 million and $45.0 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we had an accumulated deficit of $134.8 million. We have not commercialized any products and have never generated revenue from the commercialization of any product. To date, we have devoted most of our financial resources to research and development, including our preclinical and clinical work, and to intellectual property.

We expect to incur significant additional operating losses for the next several years, at least, as we advance buntanetap 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:

- continue to progress our development in AD and PD with additional pivotal Phase 3 studies, or conduct clinical trials for any other product candidates;

- scale-up cGMP drug supply manufacturing and complete necessary work to support an NDA for buntanetap in AD or in PD;

- are required by the FDA to complete additional toxicological/pharmacological studies to support an NDA for buntanetap in AD 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." This will require us to be successful in a range of challenging activities, including completing clinical trials of buntanetap and any other product candidates, acquiring additional product candidates, obtaining regulatory approval for buntanetap and any other product candidates, and manufacturing, marketing, and selling any products for which we may obtain regulatory approval. 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 company will be materially and adversely affected. Furthermore, this could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product candidates, achieve our strategic objectives or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We will require substantial 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 buntanetap.

The development of biopharmaceutical product candidates is capital-intensive. Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts to advance the clinical development of buntanetap. If we obtain receive regulatory approval for buntanetap or any other product candidates, we also expect to incur significant commercialization expenses related to product manufacturing, marketing, sales, and distribution. We will require additional capital for the further development and potential commercialization of buntanetap and may also need to raise additional funds sooner to pursue a more accelerated development of buntanetap. Because the outcome of any clinical trial or preclinical study is highly uncertain, we cannot reliably estimate the actual amount of financing necessary to successfully complete the development and commercialization of buntanetap or any other product candidates. 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.

Based on our current operating plan, we believe that our current cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2025. 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 operating plans and other demands on our cash resources may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned. Our current cash and cash equivalents will not be sufficient to complete development of buntanetap or any other product candidates, and we will require substantial capital in order to advance buntanetap or any other product candidates through clinical trials, regulatory approval and commercialization. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. Our ability to raise additional funds may be adversely impacted by

potential worsening global economic conditions and the disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from factors that include but are not limited to, inflation, progression of geopolitical events (including in the relation to the conflict between Russia and Ukraine and the conflict between Hamas and Israel), diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, and uncertainty about economic stability. If the equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. 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, or even cease operations. We expect to finance our cash needs through public or private equity or debt financings or other capital sources, including potential collaborations, licenses and other similar arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Attempting to secure additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop buntanetap or any other product candidates.

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 buntanetap or any other future product candidates;
- the clinical development plans we establish for buntanetap and any other future product candidates, including any modifications to clinical development plans based on feedback that we may receive from regulatory authorities;
- the number and characteristics of product candidates that we discover or in-license and develop;
- the outcome, timing and cost of regulatory meetings and reviews 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;
- the requirements of regulatory authorities in any additional jurisdictions in which we may seek approval for buntanetap and any future product candidates and our anticipated timing for seeking approval in such jurisdictions;
- the costs of filing, prosecuting, defending and enforcing any patent claims and maintaining and enforcing other intellectual property and proprietary rights;
- the effects of competing technological and market developments;
- the costs associated with hiring additional personnel and consultants as our business grows, including additional executive officers and clinical development, regulatory, CMC, quality and commercial personnel;
- the costs and timing of the implementation of commercial-scale manufacturing activities, if any product candidate is approved, including as a result of inflation, any supply chain issues or component shortages;
- the costs and timing of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval;
- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third-party payors and adequate market share and revenue for any approved products;
- the terms and timing of establishing and maintaining collaborations, licenses and other similar arrangements; and
- the costs associated with any products or technologies that we may in-license or acquire;

Conducting clinical trials and preclinical studies and potentially identifying future product candidates is a time consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to

obtain regulatory approval and commercialize buntanetap or any future product candidates. If approved, buntanetap and any future product candidates may not achieve commerciab success. Our commercial revenue, if any, will initially be derived from sales of buntanetap, which we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. 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, that 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, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. 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. Such restrictions could adversely impact our ability to conduct our operations and execute our business plan. 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 and/or that may reduce the value of our common stock. If we are unable to raise additional funds through equity or debt financings when needed, we would be required to delay, limit, reduce or terminate product candidate development or future commercialization efforts, or grant rights to develop and market product candidates that we might otherwise prefer to develop and market ourselves, or on less favorable terms than we would otherwise choose.

We have limited operating history and no history of commercializing pharmaceutical products.

We were established and began operations in 2008. Our operations to date have been primarily focused on conducting preclinical and clinical studies. We have not yet demonstrated the ability to successfully complete a large-scale, pivotal clinical trial, obtain marketing approval, manufacture a commercial scale product, arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing biopharmaceutical products. In addition, as a business with a limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors.

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, reliance should not be placed upon the results of any particular quarterly or annual period as indications of future operating performance.

Our ability to use our tax net operating losses is uncertain.

We have incurred significant net operating losses since our inception. As of December 31, 2024, we had U.S. federal net operating loss carryforwards of approximately $54.1 million. Our ability to utilize these net operating losses to offset future tax liabilities depends on the successful development of our product candidates and future financial performance.

Additionally, our net operating losses may be subject to Section 382 of the Internal Revenue Code of 1986, as amended (“Section 382”). Generally, if an ownership change occurs within three years of the closing date of an entity’s most recent change in control transaction, any existing net operating losses and certain built-in losses would be subject to an additional limitation, pursuant to Section 382. Change in control as defined by Section 382 occurs when there is an ownership change among stockholders owning directly or indirectly 5% or more of our common stock, as well as an aggregate ownership change with respect to such stockholders of

more than 50% of our common stock. We have not yet conducted a comprehensive study to assess whether a change of ownership as defined by Section 382 has occurred since our inception. If it is determined that we are unable to use our net operating losses to reduce future tax liabilities, our financial condition, results of operations, and cash flows may be adversely affected.

Inflation could adversely affect our business and results of operations.

While inflation in the United States has been relatively low in recent years, during 2023 and 2024, the economy in the United States encountered a material level of inflation. The residual impacts of COVID-19, geopolitical developments such as the Russia-Ukraine and Israel-Hamas conflict and global supply chain disruptions continue to increase uncertainty in the outlook of near-term and long-term economic activity, including whether inflation will continue and how long, and at what rate. Increases in inflation raise our costs for commodities, labor, materials and services and other costs required to grow and operate our business, and failure to secure these on reasonable terms may adversely impact our financial condition. Additionally, increases in inflation, geopolitical developments and global supply chain disruptions, have caused, and may in the future cause, global economic uncertainty and uncertainty about the interest rate environment, which may make it more difficult, costly or dilutive for us to secure additional financing. A failure to adequately respond to these risks could have a material adverse impact on our financial condition, results of operations or cash flows.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.

The global credit and financial markets have recently experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. The financial markets and the global economy may also be adversely affected by the current or anticipated impact of military conflict, including the conflict between Russia and Ukraine, Isreal and Hamas, terrorism or other geopolitical events. Sanctions imposed by the United States and other countries in response to such conflicts, including the one in Ukraine, may also adversely impact the financial markets and the global economy, and any economic countermeasures by the affected countries or others could exacerbate market and economic instability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market our product candidates even if we would otherwise prefer to develop and market such product candidates ourselves, or on less favorable terms than we would otherwise choose. In addition, if one or more of our current service providers, manufacturers and other partners may not survive an economic downturn, which could directly affect our ability to attain our clinical development goals on schedule and on budget.

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

We are heavily dependent on the success of buntanetap, 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 will be materially harmed.

We do not have any products that have gained regulatory approval. Currently, our lead clinical stage product candidate is buntanetap. As a result, our business is entirely dependent on our ability to successfully complete clinical development of, obtain regulatory approval for, and, if approved, successfully commercialize buntanetap in a timely manner. This may make an investment in our company riskier than similar companies that have multiple product candidates in active development and may be able to better sustain the delay or failure of a lead product candidate. We cannot commercialize buntanetap in the United States without first obtaining regulatory approval from the FDA; similarly, we cannot commercialize buntanetap outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of buntanetap 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 buntanetap is safe and effective for use for that target indication and that the manufacturing

facilities, processes and controls are adequate. If the FDA is not satisfied with the quantity and nature of the data we collect, we may be forced to undertake additional preclinical studies or clinical trials to obtain regulatory approval, which will lead to delays in our clinical development plans and cause us to incur additional costs, both of which may have a material adverse effect on our business. Even if buntanetap 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 buntanetap 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 buntanetap, 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 buntanetap, we may not be able to earn sufficient revenue to continue our business.

If we are not successful in discovering, developing and commercializing additional product candidates, our ability to expand our business and achieve our strategic objectives would be impaired.

Research programs to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following:

- competitors may develop alternatives that render any product candidates we develop obsolete;
- any product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- a product candidate may be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by physicians, patients, the medical community or third-party payors.

We have limited financial and personnel resources and, as a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater market potential. Our resource allocation decisions may cause it to fail to capitalize on viable commercial drugs or profitable market opportunities. If we do not accurately evaluate the commercial potential or target market for a particular product, we may relinquish valuable rights to that product through collaboration, licensing or other royalty arrangements in circumstances under which it would have been more advantageous for us to retain sole development and commercialization rights to such product. If we are unsuccessful in identifying and developing additional product candidates or are unable to do so, our business, results of operations, cash flows, financial condition and/or prospects may be materially and adversely affected.

Business disruptions could harm our ability to complete or could materially delay our clinical trials, as well as cause disruptions to the FDA and other governmental authorities.

Our operations and the operations of our suppliers, contract research organizations ("CROs"), hospitals, clinical trial sites, regulators, consultants and other third parties with whom we conduct business could be subject to earthquakes, power shortages, telecommunications or infrastructure failures, cybersecurity incidents, physical security breaches, water shortages, floods, hurricanes, typhoons, blizzards and other extreme weather conditions, fires, and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. We rely on third-party manufacturers or suppliers to produce buntanetap and its components and on CROs and clinical sites to conduct our clinical trials, and do not have a redundant source of supply for all components of our product candidate. Our ability to obtain clinical or, if approved, commercial, supplies of buntanetap or any future product candidates could be disrupted if the operations of these suppliers were affected by a man-made or natural disaster or other business interruption, and our ability to commence, conduct or complete our clinical trials in a timely manner could be similarly adversely affected by any of

the foregoing. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

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

Clinical development 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, buntanetap and our other product candidates may not have favorable results in later preclinical and clinical studies or receive regulatory approval. The historical failure rate for product candidates in our industry is high, particularly in the earlier stages of development. Furthermore, product candidates in later stages of clinical trials may fail to show the desired safety and efficacy characteristics despite having progressed through preclinical studies and initial clinical trials. 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 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;
- patients failing to 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 buntanetap 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 buntanetap 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. Approval from the FDA and comparable foreign authorities may be delayed or denied for a variety of reasons, including:

- 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 and PD, the FDA has stated that one single Phase 3 trial is adequate for approval if it demonstrates robust and unquestionable efficacy. However, the circumstances under which a single adequate and controlled study can be used as the sole basis of demonstrating efficacy of a drug are exceptional.

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

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;

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

Of the large number of drugs in development, only a small percentage successfully complete the regulatory approval processes and are commercialized. This lengthy approval process, as well as the unpredictability of future clinical trial results, may result in our failing to obtain regulatory approval to market buntanetap or another product candidate, which would significantly harm our business, results of operations and future commercial 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, buntanetap 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 few FDA-approved disease modifying therapeutic options available for patients with AD and PD. As a result, the design and conduct of clinical trials of buntanetap or any future product candidate may take longer, be more costly or be less effective as a result of the novelty of development in these diseases. We cannot be certain that our approach will lead to the development of approvable or marketable products. In some cases, we may use endpoints or methodologies that regulatory authorities may not consider to be clinically meaningful and that we may not continue to use in clinical trials or that we may determine after the initiation of the trial to no longer be an appropriate endpoint or methodology. Any such regulatory authority may require evaluation of additional or different clinical endpoints in our clinical trials or ultimately determine that these clinical endpoints do not support marketing approval. In addition, if we are required to use additional or different clinical endpoints by regulatory authorities, buntanetap may not achieve or meet such clinical endpoints in our clinical trials. Even if a regulatory authority finds our clinical trial success criteria to be sufficiently validated and clinically meaningful, we may not achieve the pre-specified endpoint to a degree of statistical significance in any pivotal or other clinical trials we may conduct for our product candidate. Further, even if we do achieve the prespecified criteria, our trials may produce results that are unpredictable or inconsistent with the results of other efficacy endpoints in the trial. Regulatory authorities also could give overriding weight to other efficacy endpoints over a primary endpoint even if we achieve statistically significant results on that primary endpoint if we do not do so on our secondary efficacy endpoints. Regulatory authorities also weigh the benefits of a product against its risks and may view the efficacy results in the context of safety as not being supportive of approval.

The majority of drugs approved by the FDA to treat AD and PD to date address only the diseases' symptoms. Only a small number of new treatments have been approved for AD since 2003. From 2004 to 2025, phase 2 and 3 clinical trials for unique compounds with various mechanisms of action intended to combat AD had a development success rate of just 8%. AD drug candidates have the highest failure rate of nearly 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 buntanetap. This could result in a longer than expected regulatory review process, increased expected development costs or the delay or prevention of commercialization of buntanetap for the treatment of AD and PD. We cannot be sure that buntanetap, or any other product candidate we develop, will ultimately prove to be safe and effective, scalable or profitable. Moreover, public perception of drug safety issues, including adoption of new therapeutics or novel approaches to treatment, may adversely influence the willingness of subjects to participate in clinical trials, or if approved, of physicians to prescribe novel treatments.

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates progress through clinical trials to marketing approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize safety, efficacy, yield and manufacturing batch size, minimize costs and achieve consistent quality and results. For example,

the manufacturing process being used to produce clinical material for our planned clinical trials is different than that used in prior trials of buntanetap. There can be no assurance that such changes will achieve these intended objectives. These changes and any future changes we may make to buntanetap or any future product candidates may also cause such candidates to perform differently and affect the results of future clinical trials conducted with the altered materials. Such changes or related unfavorable clinical trial results could delay initiation or completion of additional clinical trials, require the conduct of bridging studies or clinical trials or the repetition of one or more studies or clinical trials, increase development costs, delay or prevent potential marketing approval and jeopardize our ability to commercialize buntanetap or any future product candidates, if approved, and generate revenue.

We may develop buntanetap and future product candidates for use in combination with other therapies, which could expose us to additional regulatory risks.

We may develop buntanetap and future product candidates for use in combination with one or more other approved therapies for AD or PD. Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risk that the FDA or comparable foreign regulatory authorities could revoke approval of the therapy used in combination with our product candidate or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies. This could result in our own products being removed from the market or being less successful commercially.

Further, we will not be able to market and sell any product candidate we develop in combination with an unapproved AD or PD therapy for a combination indication if that unapproved therapy does not ultimately obtain marketing approval either alone or in combination with our product. In addition, unapproved AD and PD therapies face the same risks described with respect to our product candidates currently in development and clinical trials, including the potential for serious adverse effects, delay in their clinical trials and lack of FDA approval.

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 and exclusion criteria as defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the nature and design 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 and risks 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 obtain and maintain patient consents; and

- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

Potential patients for any planned clinical trials may not be adequately diagnosed or identified with the diseases which we are targeting, which could adversely impact the outcomes of our trials and could have safety concerns for the potential patients. Additionally, other pharmaceutical companies targeting these same diseases are recruiting clinical trial patients from these patient populations, which may make it more difficult to fully enroll our clinical trials. We may not be able to initiate or continue clinical trials if we are unable to locate a sufficient number of eligible patients to participate in the clinical trials required by the FDA or comparable foreign regulatory authorities. In addition, the process of finding and recruiting patients may prove costly. The timing of our clinical trials depends, in part, on the speed at which we can recruit patients to participate in our trials, as well as completion of required follow-up periods. If patients are unwilling or unable to participate in our trials for any reason, including the existence of concurrent clinical trials for similar target populations, the availability of approved or authorized therapies, or the fact that enrolling in our trials may prevent patients from taking a different product, or we otherwise have difficulty enrolling a sufficient number of patients, the timeline for recruiting patients, conducting trials and obtaining regulatory approval of our product candidates may be delayed. Our inability to enroll a specified number of patients for any of our future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether.

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. Furthermore, results of early clinical trials may differ from results of later clinical trials due to changes in patient population size. The clinical trials that we have completed to date included a limited patient population, and we may observe differences in the safety and efficacy of buntanetap and our other product candidates as the patient population increases in size. Accordingly, the data that we have observed to date may not be reflective of ongoing and future clinical trial data. 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 buntanetap are completed as planned, we cannot be certain that their results will support the safety and efficacy sufficient to obtain regulatory approval.

Further, others, including regulatory agencies may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular development program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed meaningful by others with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the interim, topline or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, product candidates may be harmed, which could significantly harm our business prospects.

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 further subject to audit and verification procedures that could result in material changes in the final data. Furthermore, undue reliance on interim analyses may be detrimental to our long-term clinical development plans, which could harm our business, operating results, prospects or financial condition.

From time to time, we may publish interim "top-line" or preliminary data from our clinical studies, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to evaluate all data fully and carefully. 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. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

In addition, others, including regulatory authorities, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. Moreover, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, product candidate or our business. If the interim "topline" or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, buntanetap and any future product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

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.

As is the case with biopharmaceuticals generally, it is likely that there may be adverse side effects associated with buntanetap or any future product candidates' use. Serious adverse events or undesirable side effects caused by buntanetap 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 buntanetap to date, at high doses have experienced adverse events that include nausea, vomiting and dizziness.

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 future commercial prospects significantly.

Moreover, if buntanetap or any future product candidates are associated with undesirable side effects in clinical trials or demonstrate characteristics that are unexpected, we may elect to abandon their development or limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, which may limit the commercial expectations for the product candidate if approved. We may also be required to modify our development and clinical trial plans based on findings in our ongoing clinical trials. Many product candidates that initially showed promise in early-stage testing have later been found to cause side effects that prevented further development of the product candidates.

It is possible that as we test buntanetap or any future product candidates in larger, longer and more extensive clinical trials, including with different dosing regimens, or as the use of these product candidates becomes more widespread following any regulatory approval, more illnesses, injuries, discomforts and other adverse events than were observed in earlier trials, as well as new conditions that did not occur or went undetected in previous trials, may be discovered. If such side effects become known later in development or upon approval, if any, such findings 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 future commercial prospects.

The market opportunities for buntanetap or any other product candidates, if approved, may be smaller than we anticipate, which could adversely affect our business, financial condition and results of operations.

We expect to initially seek approval for buntanetap for AD and PD in the U.S. The precise incidence and prevalence for the conditions we aim to address with buntanetap or any future product candidates are unknown. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on a number of internal and third-party estimates. These estimates have been derived from a variety of sources, including relevant scientific literature, patient foundations and market research, and may prove to be incorrect. Further, new trials may change the estimated incidence or prevalence of these indications. While we believe our assumptions and the data underlying our estimates are reasonable, we have not independently verified the accuracy of the third-party data on which we have based our assumptions and estimates, and these assumptions and estimates may not be correct and the conditions supporting our assumptions or estimates may change at any time, including as a result of factors outside our control, thereby reducing the predictive accuracy of these underlying factors. The total addressable market across all of the potential indications for buntanetap and any future product candidates will ultimately depend upon, among other things, the diagnosis criteria included in the final label for each such product candidate which receives marketing approval for these indications, the availability of alternative treatments and the safety, convenience, cost and efficacy of such product candidates relative to such alternative treatments, acceptance by the medical community and patient access, drug pricing and reimbursement. The number of patients in the United States and other major markets and elsewhere may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our product candidates or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our business, financial condition and results of operations. 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. Further, even if marketing approval is obtained, we have no experience as a company in commercializing products.

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.

Furthermore, we have no internal sales, marketing or distribution capabilities, nor have we commercialized a product. If buntanetap or any future product candidates ultimately receives marketing approval, we must build a marketing and sales organization with technical expertise and supporting distribution capabilities to commercialize each such product in major markets, which will be expensive and time consuming, or collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. We have no prior experience as a company with the marketing, sale or distribution of biopharmaceutical products and there are significant risks involved in the building and managing of a sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. We may not be able to enter into collaborations or hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms, or at all. In addition, our product revenue and our profitability, if any, may be lower if we rely on third parties for these functions than if we were to market, sell and distribute any products that we develop ourselves. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we are not successful in commercializing our products, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would incur significant additional losses.

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

Our future growth may depend, in part, on our ability to develop and commercialize buntanetap and any future product candidates in foreign markets. We are not permitted to market or promote any product candidate before we receive regulatory approval from applicable regulatory authorities in foreign markets, and we may never receive such regulatory approvals for buntanetap or any future product candidates. 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.

If we obtain regulatory approval of product candidates and ultimately commercialize our products in foreign markets, we would be subject to additional risks and uncertainties, including:

- different regulatory requirements for approval of drugs in foreign countries;
- reduced protection for intellectual property rights;
- the existence of additional third-party patent rights of potential relevance to our business;
- unexpected changes in tariffs, trade barriers and regulatory requirements;

- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with export control and import laws and regulations;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- foreign reimbursement, pricing and insurance regimes;
- workforce uncertainty in countries where labor unrest is common;
- differing regulatory requirements with respect to manufacturing of products;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

Even if we obtain regulatory approval for buntanetap 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.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, such as buntanetap or any future product candidates, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we receive marketing approval for buntanetap or any future product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The U.S. federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The government has also required companies to enter into consent decrees or imposed permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of buntanetap or any future product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

We may seek a Breakthrough Therapy designation for buntanetap from the FDA in PD and AD. 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 buntanetap 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, delay or cease commercialization of any products that we may develop.

The use of buntanetap 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. This risk will be even greater if we commercialize our product candidates, especially if our products are prescribed for off-label uses (even if we do not promote such uses). For example, we may be sued if our product candidates allegedly cause injury or are found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product candidate, negligence, strict liability and a breach of warranties. 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. Claims could also be asserted under state consumer protection acts. 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 or be required to limit, delay or cease the commercialization of our products. Even a successful defense would require significant financial and management resources. 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 and our resources from our primary business;
- substantial monetary awards to patients or other claimants;
- inability to commercialize buntanetap or any other product candidate;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- decreased market demand for any product;

- significant negative financial impact; and

- a decline in our stock price.

The product liability insurance coverage we carry or acquire in the future may not be sufficient to reimburse us for any expenses or losses we may suffer. In connection with all our clinical studies, we carry insurance for product liability claims in the United States and in Europe. Insurance coverage is increasingly expensive. Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of buntanetap or any future product candidates. Although we maintain such insurance, 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. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage.

Our insurance policies are expensive and only protect us from some business risks, which will leave us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, cyber security liability, employment benefits liability, workers' compensation, products liability, and directors' and officers' insurance. We do not know, however, if we will be able to maintain insurance with adequate levels of coverage. No assurance can be given that an insurance carrier will not seek to cancel or deny coverage after a claim has occurred. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our financial position and results of operations.

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 buntanetap 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 side 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 buntanetap. Our competitors may also obtain FDA or other regulatory approval for their product candidates more rapidly than we may obtain approval for buntanetap, which could result in our competitors establishing or strengthening their market position before we are able to enter the market. Competing products could present superior treatment alternatives, including by being more effective, safer, more convenient, less expensive or marketed and sold more effectively than any products we may develop. Competing products may render buntanetap or any future product candidates we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. If we are unable to compete effectively, our opportunity to generate revenue from the sale of our products we may develop, if approved, could be adversely affected.

The successful commercialization of buntanetap 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 buntanetap, 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. Accordingly, we will need to successfully implement a coverage and reimbursement strategy for any approved product candidate. 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.

For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization. We cannot be sure that coverage and reimbursement in the United States, the European Union or elsewhere will be available, or at an acceptable level, for 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 buntanetap 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, which would adversely affect our business.

Buntanetap and any future product candidates may not be commercially successful. If buntanetap or any other 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;
- the indications for which our product candidates are approved;
- the limitation of our targeted patient population and other limitations or warnings contained in any FDA-approved labeling;
- 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 willingness of patients to pay all, or a portion of, out-of-pocket costs associated with our products in the absence of sufficient third-party coverage and adequate reimbursement;
- the prevalence and severity of any side effects;
- any restrictions on the use of our product together with other medications;
- potential product liability claims;
- the timing of market introduction of our products as well as availability, safety and efficacy of competitive drugs; and
- unfavorable publicity relating to the product.

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. Our efforts to educate the medical community and third-party payors regarding the benefits of our products may require significant resources and may never be successful.

If we are unable to establish sales, marketing and distribution capabilities, we may not be successful in commercializing buntanetap, if approved.

We do not have any infrastructure for the sales, marketing or distribution of buntanetap, 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 buntanetap, if approved, for certain markets overseas; however, there can be no assurance 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 buntanetap, 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 buntanetap 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 buntanetap 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:

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

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

Risks Related to Our Dependence on Third Parties

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

Our employees and independent contractors, including principal investigators, consultants, vendors and any third parties we may engage in connection with development and commercialization of our product candidates, could engage in misconduct, including intentional, reckless or negligent conduct or unauthorized activities that violate: the laws and regulations of the FDA or other similar regulatory requirements of other authorities, including those laws that require the reporting of true, complete and accurate information to such authorities; manufacturing standards; data privacy, security, fraud and abuse and other healthcare laws and regulations; or laws that require the reporting of true, complete and accurate financial information and data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities

subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creation of fraudulent data in preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid, other U.S. federal healthcare programs or healthcare programs in other jurisdictions, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

We currently rely on third-party contract manufacturing organizations ("CMOs") for the production of clinical supply of buntanetap and intend to rely on CMOs for the production of commercial supply of buntanetap, 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 buntanetap 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 buntanetap drug substance to enable us to complete our clinical trials, and we have also engaged two CMOs 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 currently rely and in the future 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. Our reliance on CROs for clinical development activities limits our control over these activities, yet 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 ("GLP") 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. There can be no assurance 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. Additionally, working with collaborators presents risks, including but not limited to:

- 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.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there may be additional challenges and amendments to the ACA in the future. 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;

- Health Insurance Portability and Accountability Act of 1996 ("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 Federal Food, Drug and Cosmetic Act ("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 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 U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We could face criminal liability and other serious consequences for violations, which could harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls and anti-corruption and anti-money laundering laws and regulations, including the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, CROs, contractors and other collaborators and partners from authorizing, promising, offering, providing, soliciting or receiving, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties for clinical trials outside of the United States, to sell our products abroad if and when we enter a commercialization phase, and/or to obtain necessary permits, licenses, patent registrations and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, CROs, contractors and other collaborators and partners, even if we do not explicitly authorize or have actual knowledge of such activities, and any training or compliance programs or other initiatives we undertake to prevent such activities may not be effective. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

Furthermore, U.S. export control laws and economic sanctions prohibit the provision of certain products and services to countries, governments, and persons targeted by U.S. sanctions. U.S. sanctions that have been or may be imposed as a result of military conflicts in other countries may impact our ability to continue activities at future clinical trial sites within regions covered by such sanctions. If we fail to comply with export and import regulations and such economic sanctions, penalties could be imposed, including fines and/or denial of certain export privileges. These export and import controls and economic sanctions could also adversely affect our supply chain.

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.

We and any contract manufacturers and suppliers we engage 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. While the materials we use require operations involving the use of hazardous and flammable materials, including chemicals and biological materials, we do not produce any materials ourselves and contract with third parties for the manufacture and the disposal of these materials and wastes.

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 remains 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.

Risks Related to Our Intellectual Property

If we are unable to obtain, maintain and enforce patent or other intellectual property protection for buntanetap, Posiphen Form B or any future product candidates or technology or if the scope of the patent protection obtained is not sufficiently broad, our competitors or other third parties could develop and commercialize products similar or identical to ours, our ability to successfully commercialize buntanetap, Posiphen Form B, or any future product candidates may be adversely affected and 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. These legal measures afford only limited protection, and competitors or others may gain access to or use our intellectual property and proprietary information. 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 buntanetap, Posiphen Form B, and any future product candidates. Because we have not conducted a formal freedom to operate analysis for patents related to buntanetap since 2008, we may not be aware of patents issued since then that a third-party might assert are infringed by buntanetap, Posiphen Form B, or any future product candidates, which could materially impair our ability to commercialize buntanetap, Posiphen Form B, or any future product candidates. We generally seek to protect our proprietary position, in part, by filing patent applications in the United States and abroad relating to buntanetap, Posiphen Form B, and any future product candidates, manufacturing processes, and methods of use. If we are unable to obtain, maintain or enforce patent protection, our business, financial condition, results of operations and prospects could be materially harmed.

Changes in either the patent laws or their interpretation in the United States and other jurisdictions may diminish our ability to protect our intellectual property, obtain, maintain and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our protection. We cannot predict whether the patent applications we currently or may in the future pursue will issue as patents in any particular jurisdiction, will provide sufficient protection against competitors or other third parties, or if these patents are challenged by our competitors, will be found to be invalid, unenforceable, or not infringed. Our pending and future patent applications may not result in patents being issued which protect our technology or product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and product candidates. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection before public disclosures are made. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, third-party collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. Consequently, we may not be able to prevent any third party from using any of our technology that is in the public domain to compete with buntanetap, Posiphen Form B, and any future product candidates or technologies. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable in light of the prior art. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we or our licensors were the first to invent or file on the inventions claimed in any of our licensed patents or pending patent applications, or that we or our licensors were the first to make the inventions claimed in those owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions. If a third party can establish that we or our licensors were not the first to make or the first to file for patent protection of such inventions, our owned or licensed patents and patent applications may not issue as patents and even if issued, may be challenged and invalidated or rendered unenforceable. Furthermore, even if a patent is granted, our competitors or other third parties may be able to circumvent the patent by developing similar or alternative technologies or products in a non-infringing manner which could materially adversely affect our business, financial condition, results of operations and prospects.

If we are unable to obtain additional patent protection to prolong the patent life of our product candidates, we may not be able to continue development of our product candidates.

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 buntanetap, Posiphen Form B, 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 fourteen families of patent applications to prolong the patent life of buntanetap, Posiphen Form B. Unless these applications are approved by the U.S. and international patent offices, the patent life of using buntanetap, and Posiphen Form B is limited. The first patent application family we filed, which would be expected to expire in 2031, before any patent term adjustments or extensions, covers the use of buntanetap in the treatment of AD, PD and other neurodegenerative disorders such as Huntington's disease, prion diseases, amyotrophic lateral sclerosis, tauopathies, frontotemporal dementia, Lewy bodies disease, and chronic traumatic encephalopathy, 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 treatment of PD and Lewy body diseases. Subsequently, the USPTO also granted patents covering treatment frontotemporal dementia and Prion's disease, tauopathies, chronic traumatic encephalopathy, prion diseases, amyotrophic lateral sclerosis, Alzheimer's and Huntington's disease. 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 the whole patent and it has since been approved in most countries filed claiming a method of treating acute nerve and brain injuries by administering ANVS405 before and after the injury. The US patent office instead has asked us to separate the application into four divisional applications covering stroke, traumatic brain injury, nerve injury and spinal cord injury. The third patent application family relates to the use of the mechanism of action of buntanetap and ANVS405 to prevent and treat neurodegenerative diseases and would be expected to expire in 2038, before any patent term adjustments or extensions. The first divisional of this application was approved in December 2022, it covers the prevention of neurodegenerative diseases. The fourth patent application family relates to 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 buntanetap or related

compounds. 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 buntanetap or related compounds, which would be expected to expire in 2041, before any patent term adjustments or extensions. The fifth patent family application is directed to a method of maintaining heavy metal homeostasis avoiding the effect of toxic levels of a heavy metal in cells in a healthy human or restoring heavy metal homeostasis in a sick human patient. The USPTO granted the first patent in this family on March 7, 2023, which is expected to expire in 2039, before any patent term adjustments or extensions. The sixth patent application family relates to treating brain metastasis via administration of buntanetap or related compounds. In September 2023, we filed a U.S. nonprovisional patent application directed to treatment of brain metastasis via administration of buntanetap or related compounds with the USPTO, which, if allowed, would be expected to expire in 2043, before any patent term adjustments or extensions. The seventh patent application family relates to treatment of mental illness via administration of buntanetap or related compounds. In January 2024, we filed an International (PCT) application and a U.S. nonprovisional patent application directed to treatment of mental illness via administration of buntanetap or related compounds with the USPTO, which, if allowed, would be expected to expire in 2044, before any patent term adjustments or extensions. The eighth patent application family relates to treatment of neurodegenerative diseases and other diseases via co-administration of buntanetap or related compounds and an antidiabetic agent. In September 2024, we filed an International (PCT) application and a U.S. nonprovisional patent application directed to treatment of neurodegenerative diseases and other diseases via administration of this combination. The ninth patent application family relates to treatment of neurodegenerative diseases and other diseases via co-administration of buntanetap or related compounds and a phosphodiesterase inhibitor. In September 2024, we filed an International (PCT) application and a U.S. nonprovisional patent application directed to treatment of neurodegenerative diseases and other diseases via administration of this combination. The tenth patent application family relates to treatment of neurodegenerative diseases and other diseases via co-administration of buntanetap or related compounds and an antihypertensive agent. In September 2024, we filed an International (PCT) application and a U.S. nonprovisional patent application directed to treatment of neurodegenerative diseases and other diseases via administration of this combination. The eleventh patent application family relates to treatment of neurodegenerative diseases and other diseases via co-administration of buntanetap with two additional therapeutic agents. In August 2024, we filed a provisional U.S. Patent application directed to treatment of neurodegenerative diseases and other diseases via administration of this combination. The twelfth patent application family relates to treatment of neurodegenerative diseases and other diseases via co-administration of buntanetap or related compounds and an additional therapeutic agent. In February 2025, we filed a provisional U.S. Patent application directed to treatment of neurodegenerative diseases and other diseases via administration of this combination. The thirteenth patent application family relates to the new Form B of Posiphen (ANVS402); it demonstrates that it can be used instead of buntanetap, including in the foregoing uses of buntanetap of the Company's patent portfolio. Posiphen Form B may be the compound of choice in current uses of buntanetap, because it may have advantageous properties such as better stability and higher purity. In 2023, the Company filed with the USPTO two provisional patent applications as to Posiphen Form B. In 2024, the Company filed an International (PCT) as to Posiphen Form B and uses thereof. The International Search Report and 'Written Opinion" issued by the USPTO in the prosecution of the PCT application was favorable, indicating that the search claims directed to Posiphen Form B are novel and inventive. The Company expects to further file patent applications in the U.S. and outside the U.S. as National and Regional Phase patent applications of the PCT application. As to this family of patent applications involving Posiphen Form B and uses thereof, patents would be expected to expire in 2044, before any patent term adjustments or extensions. The Company also expects to seek New Chemical Entity status for Posiphen Form B before the US Food and Drug Administration (FDA), and to seek additional regulatory exclusivity based thereon. The fourteenth patent application family relates to new, improved and commercially advantageous methods for preparing buntanetap and Posiphen Form B. The Company sees this patent application family as providing further protection as to methods that use buntanetap or Posiphen Form B, and for Posiphen form B. More in particular, in 2024 the Company filed with the USPTO a provisional patent application directed to new methods of preparing buntanetap and Posiphen Form B. The Company expects in 2025 to further file at least an International (PCT) application, claiming priority from that provisional patent application, and directed to the new, improved and commercially advantageous methods for preparing buntanetap and Posiphen Form B, and thereafter patent applications in the U.S. and outside the U.S. as National and Regional Phase patent applications of the PCT application. As to this family of patent applications, patents would be expected to expire in 2045, before any patent term adjustments or extensions. 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 buntanetap, Posiphen Form B, or any other product candidate in the United States or in other foreign countries.

Our patents may be challenged in courts, in patent offices or before other administrative bodies which could result in the invalidation, narrowing or unenforceability of our patents and our patent portfolio, along with the unpredictable nature of patent prosecution, may not provide us with sufficient rights to similarly challenge other parties or exclude others from commercializing products similar or identical to ours.

Even if patents do successfully issue and even if such patents further cover buntanetap, Posiphen Form B, 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. Our patent rights may be subject to such priority, validity, inventorship, scope and enforceability disputes. Legal proceedings relating to intellectual property claims, with or without merit, are unpredictable and generally expensive and time-consuming and likely to divert significant resources from our core business, including distracting our management and scientific personnel from their normal responsibilities and generally harm our business. 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. 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 U.S. 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." 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.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We or our licensors may be subject to claims that former employees, consultants, collaborators or other third parties have an interest in our patent rights, any potential trade secrets, or other intellectual property as an inventor, co-inventor or owner of any potential trade secrets. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates and other proprietary technologies we may develop. Litigation may be necessary to defend against these and other claims challenging inventorship or our patent rights, any potential trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates and other proprietary technologies we may develop. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to our management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

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. 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 possibly different 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. Changes in patent law and regulations in other countries or jurisdictions or changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we have licensed or that we may obtain in the future. 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. Furthermore, the requirements for patentability differ in certain jurisdictions and countries. 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. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many 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. Prosecution of patent applications in other jurisdictions is often a longer process and patents may grant at a later date, and with a shorter term, than in the United States.

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. We may not be able to prevent third parties from practicing our or our licensors' inventions in all countries outside the United States, or from selling or importing products made using our intellectual property in and into the United States or other jurisdictions. 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.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and under similar legislation in foreign countries, 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. If we do not have sufficient patent life to protect our products, our business, financial condition, results of operations, and prospects will be adversely affected.

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 buntanetap, Posiphen Form B, 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 or file on the inventions covered by the patents or patent applications that we own, license or will own or 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.

In addition to seeking patent protection for our product candidates and proprietary technologies, we may also rely on trade secret protection and confidentiality agreements to protect our unpatented know-how, technology, and other proprietary information and to maintain our competitive position. 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 buntanetap, Posiphen Form B, and any future product candidates, and we expect to collaborate with third parties on the development of buntanetap, Posiphen Form B, 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. Furthermore, we cannot guarantee that we have entered into applicable agreements with each party that may have or have had access to any potential trade secrets or proprietary technology and processes. 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. If any of our potential trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

We have not yet registered our trademarks in the United States or other jurisdictions. Failure to secure such registrations could adversely affect our business.

We have not yet registered our trademarks in the United States or other jurisdictions. If we do not successfully register our trademarks, we may encounter difficulty in enforcing, or be unable to enforce, our trademark rights against third parties, which could adversely affect our business and our ability to effectively compete in the marketplace. We have also not yet registered trademarks for any of our product candidates in any jurisdiction. When we file registration applications for trademarks relating to our product candidates, those applications may be rejected, and registered trademarks may not be obtained, maintained or enforced. During trademark registration proceedings in the United States and foreign jurisdictions, we may receive rejections. We are given an opportunity to respond to those rejections, but we may not be able to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties may oppose pending trademark registration applications or seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademark registrations may not survive such proceedings.

In addition, any proprietary name we may propose to use with buntanetap, Posiphen Form B, or any future product candidate in the United States must be approved by the FDA, regardless of whether we have registered, or applied to register, the proposed proprietary name as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA or an equivalent administrative body in a foreign jurisdiction objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe, misappropriate or otherwise violate the existing rights of third parties and be acceptable to the FDA.

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, misappropriating or violating 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. During trademark registration proceedings, we may receive rejections of our applications by the USPTO or in other foreign jurisdictions. Although we are given an opportunity to respond to such rejections, we may be unable to overcome them. 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, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. 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. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark. 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 names, domain names 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.

In response to an inability to enforce our patent rights, or in the event of successful litigation against us by third parties, or in the normal course of future business 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.

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. Furthermore, if we or our licensors are unsuccessful in any proceedings sought to enforce our patent rights, such patents and patent applications may be narrowed, invalidated or held unenforceable, we may be required to obtain licenses from third parties. Although at this time, we are unaware of any intellectual property that interferes with ours or is complementary and needed to commercialize buntanetap, or Posiphen Form B, a third party may also hold intellectual property, including patent rights that are important or necessary to the future development or commercialization of buntanetap, Posiphen Form B, or our future product candidates. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize buntanetap, Posiphen Form B, or our product candidates, in which case we would be required to obtain a license from these third parties. If any of these situations were to occur, such a license may not be available on commercially reasonable terms, or at all, which could materially harm our business. 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.

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 or claims asserting ownership of what we regard as our own intellectual property.

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, contractors, collaborators and other third parties with whom we do business include provisions requiring such parties to assign rights in inventions to us and not use the proprietary information or know-how of others in their work for 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. In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. 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 any of the foregoing 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. Certain federal, state and foreign government requirements include obligations of companies to notify individuals of security breaches involving particular categories of personally identifiable information, which could result from breaches experienced by us or by our vendors, contractors, or organizations with which we have formed strategic relationships. 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, delays in our regulatory approval efforts, damage to our reputation, costs to recover or reproduce the data 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.

If any security breach or other incident, whether actual or perceived, were to occur, it could impact our reputation and/or operations, cause us to incur significant costs and liabilities, including legal expenses, harm customer confidence, hurt our expansion into new markets, cause us to incur remediation costs, or cause us to lose existing customers. For example, the loss of clinical trial data from clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. We also rely on third parties to manufacture buntanetap, or Posiphen Form B, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any actual or perceived disruption or security breach affects our systems (or those of our third-party collaborators, service providers, contractors or consultants) or were to result in a loss of or accidental, unlawful or unauthorized access to, use of, release of, or other processing of personally identifiable information, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, the further development and commercialization of buntanetap, Posiphen Form B, or any future product candidates could be delayed, and we could be subject to significant fines, penalties or liabilities. In addition, a security failure could result in violations of applicable privacy and other laws. If this information is inappropriately accessed and used by a third party or a team member for illegal purposes, such as identity theft, we may be responsible to the affected individuals for any losses they may have incurred as a result of misappropriation. In such an instance, we may also be subject to regulatory action, investigation or liable to a governmental authority for fines or penalties associated with a lapse in the integrity and security of our team members' or patients' information. We may be required to expend significant capital and other resources to protect against and remedy any potential or existing security breaches and their consequences. In addition, our remediation efforts may not be successful, and we may not have adequate insurance to cover these losses.

Security breaches could also significantly damage our brand and our reputation with existing and prospective clients and third parties with whom we do business. Any publicized security problems affecting our businesses and/or those of such third parties may negatively impact the market perception of our products and discourage third parties from doing business with us.

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.

Other pharmaceutical companies with which we compete for qualified personnel have greater financial and other resources, different risk profiles, and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are not able to attract, integrate, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

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. 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. Furthermore, we may experience losses related to investments in other companies, including as a result of failure to realize expected benefits or the materialization of unexpected liabilities or risks, which could have a material negative effect on our results of operations and financial condition. Accordingly, although there can be no assurance that we will undertake or successfully complete any additional transactions of the nature described above, any additional transactions that we do complete could have a material adverse effect on our business, results of operations, financial condition and prospects.

We may seek to enter into collaborations, license agreements and other similar arrangements in the future, and may not be successful in doing so.

We may seek to enter into collaborations, joint ventures, licensing arrangements or other similar arrangements with third parties for the development or commercialization of buntanetap and any future product candidates, due to capital costs required to develop or commercialize the product candidate or manufacturing constraints. These relationships or those like them may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our stockholders or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish or maintain a strategic partnership or other alternative arrangements for any future product candidates and programs because our research and development pipeline may be insufficient, our product candidates and programs may be deemed to be at too early a stage of development for collaborative effort and third parties may not view our product candidates and programs as having the requisite potential to demonstrate safety and efficacy. Even if we are successful in our efforts to establish such collaborations, the terms that we agree upon may not be favorable to us. For example, we may need to relinquish valuable rights to our future revenue streams, research programs, intellectual property or product candidates, or grant licenses on terms that may not be favorable to us, as part of any such arrangement, and such arrangements may restrict us from entering into additional agreements with other potential collaborators. If we license products or businesses, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate

them with our existing operations and company culture. In addition, if we enter into such collaborations, we will have limited control over the amount and timing of resources that our collaborators will dedicate to the development or commercialization of our product candidates. Our ability to generate revenue from these arrangements will depend on any future collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot be certain that, following a strategic transaction or license, we will achieve the revenues or specific net income that justifies such transaction. Furthermore, we may not be able to maintain such collaborations if, for example, the development or approval of a product candidate is delayed, the safety of a product candidate is questioned or the sales of an approved product candidate are unsatisfactory. Any delays in entering into new strategic partnership agreements related to our drug candidates could also delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market.

Collaborations involving buntanetap or any future product candidates would pose significant risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected or at all;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or drugs, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to any product candidate that achieves regulatory approval may not commit sufficient resources to the marketing and distribution of such products;
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws, resulting in civil or criminal proceedings;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays in or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly enforce, maintain or defend our or their intellectual property rights or may use our or their proprietary information in such a way as to invite litigation that could jeopardize or invalidate such intellectual property or proprietary information or expose us to potential litigation;

- collaborators may infringe, misappropriate or otherwise violate the intellectual property rights of third parties, which may expose us to litigation and potential liability;

- collaborators may not provide us with timely and accurate information regarding development, regulatory or commercialization status or results, which could adversely impact our ability to manage our own development efforts, accurately forecast financial results or provide timely information to our stockholders regarding our out-licensed product candidates;

- we may be required to invest resources and attention into such collaboration, which could distract from other business objectives;

- disputes may arise between the collaborators and us regarding ownership of or other rights in the intellectual property generated in the course of the collaborations;

- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all;

- if a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated; and

- collaborations may be terminated, including for the convenience of the collaborator, prior to or upon the expiration of the agreed upon terms and, if terminated, we may find it more difficult to enter into future collaborations or be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Any termination of collaborations we enter into in the future, or any delay in entering into collaborations related to buntanetap or any future product candidates, could delay the development and commercialization of our product candidates and reduce their competitiveness if they reach the market, which could have a material adverse effect on our business, financial condition, results of operations and future commercial prospects.

Our business and operations would suffer in the event of failures involving our information technology systems, or those of any of our service providers.

We are increasingly dependent upon information technology systems, infrastructure and data to operate our business. 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), team member misconduct, human error, 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 buntanetap or any other product candidate could be delayed. It is not possible to prevent all threats or to our information technology systems and information and those of our third-party service providers, over which we exert less control, and any controls we implement to do so may prove to be ineffective.

Disruption, failure or cybersecurity breaches affecting or targeting computers and infrastructure used by us or our business partners may adversely impact our business and operations.

We use computers and telecommunication systems to analyze and store financial and operating data and to communicate within our company, with outside business partners, and across international borders. These systems can be subject to technical system flaws; power loss; cyber attacks, including viruses, malware, phishing, ransomware, terrorism, and surveillance, unauthorized access, malicious software, intentional or inadvertent data privacy breaches by employees or others with authorized access, hacktivism, ransomware, physical or electronic break-ins, fires or natural disasters, supply chain attacks, and other cybersecurity issues. We have no assurance that our systems are appropriately redundant to withstand these events. Accordingly, such events could cause adverse

effects and material disruptions to our operations or systems or those of our business partners; compromise the security, integrity, availability, and confidentiality of customer information, employee information, strategic projects, product formulas and other trade secrets, other business or personal sensitive data, including third party confidential information in our possession. Release of third party confidential information could materially harm our reputation, affect our relationships with such parties and expose us to liability. Although we have introduced many security measures, including firewalls and information technology security policies and training, these measures may not offer the appropriate level of security. A security breach or other compromise of our information security safeguards could expose our confidential information, including third party confidential information in our possession (such as customer information) to theft and misuse, which could in turn adversely affect our relationships with such third parties and have an adverse effect on our business, financial condition, results of operations and cash runway.

The cash and cash equivalents that we use to meet our working capital and operating expense needs are held in deposit accounts at two financial institutions. If one or both financial institutions fail, our deposit accounts could be adversely affected due to the loss of or delay in obtaining access to all or a portion of our uninsured funds.

The cash and cash equivalents that we use to meet our working capital and operating expense needs are held in deposit accounts at two financial institutions. The balance held in these accounts regularly exceeds the Federal Deposit Insurance Corporation ("FDIC"), standard deposit insurance limit or similar government guarantee schemes. If one or both of the financial institutions in which we hold such funds fails or is subject to significant adverse conditions in the financial or credit markets, we could be subject to a risk of loss of all or a portion of such uninsured funds or be subject to a delay in accessing all or a portion of such uninsured funds. Any such loss or lack of access to these funds could adversely impact our short-term liquidity and ability to meet our operating expense obligations.

For example, on March 10, 2023, Silicon Valley Bank ("SVB") and Signature Bank, were closed by state regulators and the FDIC was appointed as the receiver for each bank. The FDIC created successor bridge banks and all deposits of SVB and Signature Bank were transferred to the bridge banks under a systemic risk exception approved by the U.S. Department of the Treasury, the Federal Reserve and the FDIC. If one or both of the financial institutions in which we hold our funds for working capital and operating expense needs were to fail, we cannot provide any assurances that such governmental agencies would take action to protect our uninsured deposits in a similar manner.

Risks Related to Our Common Stock

The market price of our common stock has been volatile and fluctuated substantially in the past and may continue to experience volatility and substantial fluctuations in the future, which could result in substantial losses for purchasers of our common stock.

The market price of our common stock is highly volatile. For example, from July 1, 2024 to February 28, 2025, the closing price of our common stock on the New York Stock Exchange ranged from as low as $1.74 to as high as $15.46 and daily trading volume ranged from 67,300 shares to 40,734,200 shares. The market price of our common stock may be subject to wide fluctuations in response to a variety of factors, including the following:

- results of our clinical trials, and the results of trials of our competitors or those of other companies in our market sector;
- our ability to enroll subjects in our future clinical trials;
- delays or unanticipated developments in the completion of our planned clinical trials;
- any delay in submitting an NDA and any adverse development or perceived adverse development with respect to the FDA's review of that NDA;
- our ability to obtain and maintain regulatory approval of buntanetap or any future product candidates or additional indications thereof, or limitations to specific label indications or patient populations for its use, or changes or delays in the regulatory review process;
- failure to successfully develop and commercialize buntanetap or any future product candidates;

- the degree and rate of physician and market adoption of any of our current and future product candidates;
- inability to obtain additional funding or obtaining funding on unattractive terms;
- regulatory or legal developments in the United States and other countries applicable to buntanetap or any other product candidates;
- adverse regulatory decisions;
- changes in the structure of healthcare payment systems;
- manufacturing, supply or distribution delays or shortages, including our inability to obtain adequate product supply for buntanetap or any other product candidates, or the inability to do so at acceptable prices;
- the success or failure of our efforts to identify, develop, acquire or license additional product candidates;
- 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;
- any changes to our relationship with any manufacturers, suppliers, collaborators or other strategic partners;
- 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 stockholders in the future;
- changes in our capital structure, such as future issuances of securities and the incurrence of additional debt;
- changes in accounting standards, policies, guidelines, interpretations or principles;
- trading volume of our common stock;
- actual or anticipated fluctuations in our financial condition and results of operations;
- publication of news releases by other companies in our industry, and especially direct competitors, including about adverse developments related to safety, effectiveness, accuracy and usability of their products, reputational concerns, reimbursement coverage, regulatory compliance, and product recalls;

- announcement or progression of geopolitical events (including in relation to the conflict between Russia and Ukraine or Isreal and Hamas); 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 our stockholders may lose some or all of their investment.

Our failure to meet the New York Stock Exchange's continued listing requirements could result in a delisting of our common stock.

If we fail to satisfy the continued listing requirements of the New York Stock Exchange, such as the corporate governance requirements, market capitalization or the minimum closing bid price requirement, the New York Stock Exchange may take steps to delist our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair our stockholders' ability to sell or purchase our common stock when they wish to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, or prevent future non-compliance with the listing requirements of the New York Stock Exchange.

We have been subject to securities class action litigation in the past and could be subject to such litigation in the future.

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. During the year ended December 31, 2021, two securities class action complaints were filed against us and our executive officers following disclosure of interim results from the AD/PD Trials. Both complaints were voluntarily dismissed without prejudice by the plaintiffs. If we again face such litigation in the future, it could result in substantial costs, a diversion of management's attention and resources, and damage to our reputation, which could have a material adverse effect on our business, financial condition and results of operations and prospects.

Our directors, executive officers and certain stockholders 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 stockholder approval.

Our directors, executive officers, and stockholders affiliated with our directors and executive officers own 14.3% of the current voting power of our outstanding common stock. Therefore, acting together, they have the ability to substantially influence all matters submitted to our board of directors or stockholders for approval. For example, these holders may be able to control the appointment of our management, elections and removal 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 stockholders, and they may act in a manner with which our stockholders may not agree or that may not be in the best interests of our other stockholders. This concentration of ownership may have the effect of delaying, deferring or preventing a change in control, impeding a merger, consolidation, takeover or other business combination involving us, or discouraging a potential acquiror from making a tender offer or otherwise attempting to obtain control of our business, even if such a transaction would benefit other stockholders. 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, our business, our market or our competitors. 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 the sole source of gain for our stockholders.

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. In addition, any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock would be our stockholders' sole source of gain on an investment in our common stock for the foreseeable future. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which stockholders have purchased their shares. See "Dividend Policy" for additional information.

We incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to 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. The Sarbanes-Oxley Act of 2002 ("SOX"), the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the New York Stock Exchange, 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 devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly. For example, 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 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 maintain 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. We have had a material weakness in our internal control over financial reporting in the past, and cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting once that firm begins its Section 404 reviews, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by the NYSE, SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

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 $1.235 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 settlements, and we believe the risk of a court declining to enforce this provision is remote, as the General Assembly of Delaware has specifically amended the Delaware General Corporation Law to authorize the adoption of such provisions.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

Risk Management and Strategy

The Company has adopted processes designed to identify, assess and manage material risks from cybersecurity threats, which are integrated into the Company's overall risk management systems and processes. Those processes include response to and an assessment of internal and external threats to the security, confidentiality, integrity and availability of our data and information systems, along with other material risks to our operations. The Company references the National Institute of Standards and Technology Cybersecurity Framework to help identify, assess, and manage cybersecurity risks and has adopted and tested a formal cybersecurity incident response plan. As part of our risk management process, the Company engages a third-party provider to conduct periodic maturity assessments. The Company stores data in cloud environments, with security appropriate to the data involved and has adopted controls around, among other things, access and acceptable use, backup and recovery and vendor risk assessment.

Our cybersecurity program is managed by the Annovis Incident Management Committee (the "AIMC"). The AIMC serves as the core team responsible for managing the enterprise-wide cybersecurity policy, maintenance and compliance across all platforms. The AIMC is responsible for the detection and initial assessment of potential cybersecurity threats and incidents. The AIMC classifies detected cyber incidents to allow prioritization, response and escalation. Incidents (if any) are documented for internal reporting processes and regularly shared with senior management.

Our third-party IT service provider is a key part of our cybersecurity program. We partner with a cybersecurity company and leverage their technology and expertise to better protect the Company. From time to time, we engage this vendor to monitor our environment, which includes an outsourced security operations center. We may also from time to time engage partners for periodic penetration testing and vulnerability assessments. We intend to continue to work to formalize our cybersecurity program, including developing processes for third-party service provider cyber-risk oversight and management.

In the event of a potential cybersecurity incident, the AIMC will conduct an assessment to determine the nature and scope of the incident and manages the incident in accordance with our incident response plan until the incident is contained and resolved. The AIMC will document findings and make them available to the Disclosure Committee, which includes cross functional senior management representation from, legal, finance, investor relations and business segments. The Disclosure Committee, in conjunction with third-party experts, including outside legal counsel, is responsible for assessing the materiality of any cybersecurity incident and coordinating external communications and disclosures, including with the Securities and Exchange Commission.

As of December 31, 2024, we are not aware of any cybersecurity threats that have materially affected or are reasonably likely to materially affect the Company's business strategy, results of operations, or financial condition, although we may be materially affected in the future by such risks or future material incidents. See "Risk Factors—Risks Related to Our Business Operations—Disruption, failure or cyber security breaches affecting or targeting computers and infrastructure used by us or our business partners may adversely impact our business and operations" for additional information regarding cybersecurity risks.

Governance

Roles and Responsibilities

Cybersecurity is an important part of our risk management processes and an area of focus for the Annovis management and Board of Directors. We continue to invest in cybersecurity and enhance our internal controls and processes, which are designed to help protect our systems and the information they contain.

Our Board is actively involved in the assessment, oversight and management of the material risks that could affect the Company. The Board has delegated to the Audit Committee the responsibility to oversee the integrity of the Company's information technology and cybersecurity risks and to assess the risks and incidents relating to cybersecurity threats. While our Board and Audit Committee oversee cybersecurity risk, management, through the AIMC, is responsible for the implementation and management of cybersecurity risk management systems and processes and for the communication of incidents to senior management and the Audit Committee.

The AIMC meets with the Audit Committee on a quarterly basis and meets with the BOD at least annually. Additionally, the Audit Committee regularly meets with members of the Company's internal audit function to discuss risk management activities, compliance, best practices, and other related matters.

Item 2. Properties.

Our offices are in Malvern, Pennsylvania, where we have leased and have access to approximately 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 New York Stock Exchange under the symbol "ANVS". Our common stock began trading on the New York Stock Exchange on November 18, 2021. From January 29, 2020, the date of our initial public offering, to November 17, 2021, our common stock traded on the NYSE American. Prior to January 29, 2020, there was no public market for our stock.

Holders of Record

As of March 18, 2025, there were approximately 23 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

None.

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 late-stage clinical drug platform company addressing neurodegeneration, such as Alzheimer's disease ("AD") and Parkinson's disease ("PD"). We are developing our lead product candidate, buntanetap, which is designed to address AD, PD, and potentially other chronic neurodegenerative diseases. Buntanetap is a synthetically produced small molecule, orally administered, brain penetrant compound. In several studies, buntanetap was observed to inhibit the synthesis of neurotoxic proteins — APP/Aβ ("APP"), tau/phospho- tau ("tau") and α-Synuclein ("αSYN") — that are some of the main causes of neurodegeneration. High levels of neurotoxic proteins lead to reduced axonal transport, which is responsible for the communication between and within nerve cells. When that communication is compromised, the immune system is activated and attacks the nerve cells, eventually killing them. We have observed in our clinical studies in early AD and early PD patients and pre-clinical studies in mice and rats that buntanetap lowered neurotoxic protein levels leading to improved axonal transport, reduced inflammation, lower nerve cell death and improved affected function.

We designed the studies by applying our understanding of the underlying neurodegenerative disease states, and measured both target and pathway validation in the spinal fluid of patients to determine whether patients underlying disease condition improved following treatment. In addition to meeting their primary endpoints of safety and tolerability and secondary endpoint of pharmacokinetics ("PK") of buntanetap, our AD/PD Trials also met exploratory endpoints of measures of biomarkers and improvements in cognition in AD patients, as well as function in PD patients. We believe that the AD/PD Trials represent the first double-blind, placebo-controlled study that showed improvements in AD patients, as measured by ADAS-Cog, and in PD patients, as measured by UPDRS. Following completion of the AD/PD Trials, we submitted our data to the U.S. Food and Drug Administration ("FDA") and requested direction to further pursue the development of buntanetap in early PD patients. With the FDA's guidance, we initiated a Phase 3 study in early PD patients in August 2022 (our "Phase 3 PD Study"). In the Phase 3 PD Study, early PD patients were defined as those at Hoehn & Yahr stages 1, 2 or 3 and OFF times of less than two hours per day. OFF time refers to periods when PD motor and/or non-motor symptoms occur between medication doses. We also submitted a proposed protocol for the treatment of moderate AD to the FDA, and after receiving permission to proceed, we initiated a Phase 2/3 study in mild to moderate AD patients in February 2023 (our "Phase 2/3 AD Study"). In the Phase 2/3 AD Study, mild to moderate AD patients were defined as those with a MMSE score between 14 and 24. Our Phase 3 PD Study and Phase 2/3 AD Study each had built in interim analyses.

Our Phase 3 PD Study incorporated an interim analysis at two months, the results of which were disclosed on March 31, 2023. The pre-planned interim analysis was conducted by our data analytics provider based on 132 patients from all cohorts collectively, for which baseline and two-month data was available. Based on the results of the interim analysis, we proceeded with the Phase 3 PD Study as planned in accordance with the previously established protocol. The study was completed on December 4, 2023, and we released the topline PD Study efficacy data on July 2, 2024. The study data showed that in two subgroups, buntanetap improved UPDRS 2, 3, 2+3 and total. It also showed that in the entire intent to treat ("ITT") population, buntanetap stopped the loss of cognition and that in the 12% of patients that already had cognitive issues, buntanetap improved cognition in a dose-dependent, statistically significant way. We expect to discuss the Phase 3 PD data with the FDA at an end-of-study meeting during 2025. During that meeting, we plan to propose continued development of buntanetap with an additional, pivotal Phase 3 trial.

With respect to the Phase 2/3 AD Study, we disclosed the results of the interim analysis on October 23, 2023, and similar to our PD study, based on the outcome of the interim analysis, we proceeded with the study as planned. The Phase 2/3 AD study was completed on February 13, 2024, and on April 29, 2024, we announced topline efficacy data. The data showed that in early AD patients, buntanetap improved ADAS-Cog11 in a dose-dependent fashion and was statistically significant from placebo and from baseline.

On October 10, 2024, the Company met with the FDA in an end-of-phase 2 meeting to discuss its Phase 2/3 AD data and to agree on a regulatory path forward. Annovis and the FDA have aligned on a development path for buntanetap towards the filing of New Drug Applications ("NDAs"), one for short-term and one for long-term efficacy. The Phase 3 AD program will investigate buntanetap in patients with early AD and will consist of one study that first incorporates a 6-month study period aimed at confirming buntanetap's symptomatic effects, then later transitioning into an 18-month study period, designed to demonstrate potential disease-modifying effects. While the overall study will span the combined 18-month treatment period, the completion of the first 6-month period, if well-designed and well-executed, may be sufficient to support an NDA filing, potentially within one year of the 6-month treatment period initiation.

During the end-of-phase 2 meeting for AD, the FDA raised no concerns with the Company's data on buntanetap's safety, including impact on liver enzymes, drug interactions, dose selection, pharmacokinetics and population pharmacokinetics. Further, the FDA confirmed that future development can proceed using the new crystal form of buntanetap.

We believe that we are the only company developing a drug for AD and PD that is designed to inhibit more than one neurotoxic protein and has a mechanism of action designed to restore nerve cell axonal and synaptic activity. By improving brain function, our goal is to treat memory loss and dementia associated with AD, as well as body and brain function issues associated with PD. Based on pre-clinical and clinical data collected to date, we believe that buntanetap has the potential to be the first drug to interfere with the underlying mechanism of neurodegeneration, potentially enabling buntanetap to be the only drug to improve cognition in AD and motor function in PD. The industry has historically encountered challenges in specifically targeting one neurotoxic protein, be it APP, tau or αSYN, indicating that doing so does not change the underlying course of neurodegeneration. Our ultimate goal is to develop a disease modifying drug ("DMD") for patients with neurodegeneration by leveraging our clinical and pre-clinical data, which shows inhibition of the most relevant neurotoxic proteins. Studies have found that AD and PD are the most common neurodegenerative diseases in the U.S., and accordingly these diseases present two unmet needs of the aging population and two potentially large U.S. markets, if a DMD is developed and approved.

We believe that we are the only company developing a drug for AD and PD that is designed to inhibit more than one neurotoxic protein and has a mechanism of action designed to restore nerve cell axonal and synaptic activity. By improving brain function, our goal is to treat memory loss and dementia associated with AD, as well as body and brain function issues associated with PD. Based on pre-clinical and clinical data collected to date, we believe that buntanetap has the potential to be the first drug to interfere with the underlying mechanism of neurodegeneration, potentially enabling buntanetap to be the only drug to improve cognition in AD and motor function in PD. The industry has historically encountered challenges in specifically targeting one neurotoxic protein, be it APP, tau or αSYN, indicating that doing so does not change the underlying course of neurodegeneration. Our ultimate goal is to develop a disease modifying drug ("DMD") for patients with neurodegeneration by leveraging our clinical and pre-clinical data, which shows inhibition of the most relevant neurotoxic proteins. Studies have found that AD and PD are the most common neurodegenerative diseases in the U.S., and accordingly, these diseases present two unmet needs of the aging population and two potentially large U.S. markets, if a DMD is developed and approved.

We have never been profitable and have incurred net losses since inception. Our accumulated deficit at December 31, 2024 was $134.8 million. 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 we will be able to achieve or maintain profitability, if at all.

Financial Operations Overview

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

Segment Information

As of December 31, 2024, we viewed our operations and managed our business as one operating segment consistent with how our chief operating decision-maker, our Chief Executive Officer, makes decisions regarding resource allocation and assessing performance. As of December 31, 2024, substantially all of our assets were located in the United States. Our headquarters are located in Malvern, Pennsylvania.

Research and Development Expenses

Our research and development ("R&D") 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; and

- payments to third-party contract research organizations ("CROs"), contract manufacturing organizations ("CMOs"), contractor laboratories and other independent contractors.

Research and development costs are either expensed as incurred or recorded separately as a prepaid asset, whereby expense is recognized when the service is performed. 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 (e.g., patient population) 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. We often use third-party CROs, contractor laboratories and independent contractors to help us complete 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 (or study activity) completed at the end of each reporting period.

Our research and development expenses in 2024 were primarily related to the wind-down and analysis of our Phase 3 study in early PD patients and our Phase 2/3 study in AD patients, as well as preparatory work for our pivotal Phase 3 AD study program in early AD patients. Our research and development expenses in 2023 were primarily related to the execution of our Phase 3 study in early PD patients and our Phase 2/3 study in AD patients. We expect that our research and development expenses in 2025 and for the next several years will continue to remain elevated as a result of costs associated with completing our Phase 3 trial for AD, our planned Phase 3 trial for PD and other subsequent planned activities leading up to a potential NDA filing(s) with the FDA. These expenditures are subject to numerous uncertainties regarding timing and cost to achieve 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.

Due to the ongoing and uncertain nature of our research and development, we are unable to accurately determine the duration or completion costs of our development of buntanetap. As a result of the difficulties of forecasting research and development costs of buntanetap 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 ("G&A") expenses consist primarily of salaries, benefits and other related costs, including public company costs as well as stock-based compensation, for personnel serving in our executive, finance, accounting, and administrative functions. Our general and administrative expenses also include professional fees for legal services, including patent-related expenses, consulting, tax and accounting services, insurance, rent and general corporate expenses. We expect that our general and administrative expenses will increase as a result of the continued clinical development and potential commercialization of our product candidates.

Income Taxes

As of December 31, 2024, the Company had U.S. federal net operating loss ("NOL") carryforwards of $54.1 million, which may be available to offset future income tax liabilities. Federal NOL carryforwards generated in 2017 and prior of $2.8 million will expire beginning 2032. The remaining federal NOL carryforwards generated beginning in 2018, do not expire. NOL carryforwards generated beginning in 2018 are permitted to offset 80% of taxable income in future years. As of December 31, 2024, the Company also had U.S. state NOL carryforwards of $56.6 million, which may be available to offset future income tax liabilities and will expire beginning in 2028.

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. We have not yet conducted a comprehensive study to assess whether a change of ownership as defined by Section 382 has occurred since our inception.

Results of Operations

Years ended December 31, 2024 and 2023

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

	Year Ended December 31,		
	2024	2023	Change
		(in thousands)	
Operating expenses:			
Research and development	$ 19,995	$ 38,791	$ (18,796)
General and administrative	6,699	6,244	455
Total operating expenses	26,694	45,035	(18,341)
Other income (expense):			
Interest income	332	668	(336)
Other financing costs	(1,853)	—	(1,853)
Change in fair value of warrants	3,626	(11,837)	15,463
Other income (expense), net	2,105	(11,169)	13,274
Net loss	$ 24,589	$ 56,204	$ (31,615)

Research and Development Expenses

Research and development expenses decreased by $18.8 million for the year ended December 31, 2024 compared to the year ended December 31, 2023. The decrease was primarily the result of our Phase 3 PD and Phase 2/3 AD studies being active during the majority of 2023, whereas 2024 study activity was minimal because the aforementioned trials had been completed. This decrease related to timing of study costs was primarily offset by increases in statistics, bioanalytical and CMC costs during the year ended December 31, 2024. Year-over-year increases for these items took place as we analyzed data from our completed Phase 3 PD and Phase 2/3 AD studies and performed preparatory work for our pivotal Phase 3 AD study.

General and Administrative Expenses

General and administrative expenses increased by $0.5 million for the year ended December 31, 2024, compared to the year ended December 31, 2023. The increase was primarily a result of warrant exercise commissions expensed during the current year.

Interest Income

Interest income decreased by $0.3 million for the year ended December 31, 2024 compared to the year ended December 31, 2023. The decrease was primarily the result of lower cash and cash equivalent balances on hand year-over-year.

Other Financing Costs

Financing costs were $1.9 million for the year ended December 31, 2024. We did not incur any financing costs for the year ended December 31, 2023. The change was attributable to issuance costs as well as changes in derivative fair value associated with our ELOC financing with an ELOC Purchaser, described further below.

Change in Fair Value of Warrants

Change in fair value of warrants was a gain of $3.6 million for the year ended December 31, 2024 compared to a loss of $11.8 million the year ended December 31, 2023. This change was attributable to the fair value remeasurement with respect to our liability-classified Canaccord Warrants during 2024. The current year loss recorded in the statements of operations was primarily

driven by warrant exercises made at higher stock prices during the third quarter of 2024, triggering remeasurement. The remaining change in fair value was primarily driven by the change in our stock price during 2024. For the year ended December 31, 2023, the change in fair value was primarily attributable to issuance of the liability-classified Canaccord Warrants and the increase in our stock price during the fourth quarter.

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 and warrants. 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, 2024, our principal source of liquidity was our cash and cash equivalents, which totaled $10.6 million.

Equity Financings

March 2024 Registered Direct Offerings

On March 15, 2024 and March 21, 2024, we entered into two separate securities purchase agreements with the same institutional investor. When aggregating the results of both purchase agreements, we issued 0.4 million shares for net proceeds of $3.9 million registered direct offerings.

April 2024 ELOC Purchase Agreement

On April 25, 2024, we entered into an ELOC Purchase Agreement with an ELOC Purchaser, whereby we could offer and sell, from time to time at our sole discretion, and whereby the ELOC Purchaser committed to purchase, up to 2.0 million shares of shares of our common stock. The term of the agreement was until the expiration of our active S-3 Registration Statement, unless earlier terminated or exhausted.

Upon execution of the ELOC Purchase Agreement, we agreed to issue 33,937 shares of common stock as commitment shares to the ELOC Purchaser. In addition to the commitment shares referenced above, as of the year ended December 31, 2024 we have sold 2.0 million shares of our common stock under the purchase agreement and received net proceeds of $14.6 million. There are no shares remaining to sell under this agreement after December 31, 2024.

January and July 2024 Warrant Exercises

During July of 2024, 0.8 million of our Canaccord warrants were exercised at $9.00 per share in a series of transactions. The exercises resulted in gross proceeds of $7.5 million. There were also 0.1 million warrants exercised in January of 2024, for gross proceeds of $0.5 million. Total warrant commissions payable to Canaccord for these exercises totaled $0.5 million, which was expensed in the Statements of Operations for the year ended December 31, 2024.

December 2024 ATM

On December 11, 2024, we entered into an Equity Distribution Agreement ("Distribution Agreement") with Oppenheimer & Co. Inc. ("OpCo"), relating to the sale of shares of our common stock. In accordance with the terms of the Distribution Agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to $50.0 million from time to time through or to OpCo, acting as our agent or principal.

During the year ended December 31, 2024, we have sold 26,788 shares of common stock pursuant to the Distribution Agreement for gross proceeds of $0.2 million before commissions.

February 2025 ThinkEquity Offering

On February 3, 2025, we entered into an Underwriting Agreement with ThinkEquity LLC, acting as representative of the underwriters with respect to an underwritten public offering of 5.3 million units of the Company. Each unit sold consisted of one share

of common stock and one warrant to purchase one share of common stock (the "ThinkEquity Warrants"), at a per unit price of $4.00 (the "Offering"). Aggregate gross proceeds from the Offering were $21.0 million before deducting underwriting discounts and other estimated offering expenses. The Warrants have an exercise price of $5.00 per share, are immediately exercisable and expire five years from the date of issuance. The shares of Common Stock and Warrants were issued separately. We have agreed to suspend sales of our Common Stock under the OpCo ATM Facility for a period of six months after the closing of the Offering.

Future Capital Requirements

We do not have sufficient capital on hand to fund our operations for the next 12 months and will need to raise additional capital to meet our obligations as they become due. We believe that our current cash and cash equivalents will be sufficient to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2025. We will need to raise substantial additional capital to complete the development and commercialization of our product candidates through public or private equity offerings, debt financings, collaboration and licensing arrangements or other financing alternatives. However, there can be no assurance that we will be successful in raising additional capital or that such capital, if available, will be on terms that are acceptable to us. If we are unable to raise sufficient additional capital or defer sufficient operating expenses, we may be compelled to reduce the scope of our operations. Accordingly, we have concluded that substantial doubt exists with respect to our ability to continue as a going concern within one year after the date that these financial statements are issued.

We expect to incur significant operating losses for the foreseeable future. We also expect these losses to further increase, as we ramp up our clinical development programs and begin activities for commercial launch readiness. We may also encounter unforeseen expenses, difficulties, complications, delays and other currently unknown factors that could adversely affect our business.

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 buntanetap or any other future product candidates;
- the clinical development plans we establish for buntanetap and any other future product candidates, including any modifications to clinical development plans based on feedback that we may receive from regulatory authorities;
- the number and characteristics of product candidates that we discover or in-license and develop;
- the outcome, timing and cost of regulatory meetings and reviews 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;
- the requirements of regulatory authorities in any additional jurisdictions in which we may seek approval for buntanetap and any future product candidates and our anticipated timing for seeking approval in such jurisdictions;
- the costs of filing, prosecuting, defending and enforcing any patent claims and maintaining and enforcing other intellectual property and proprietary rights;
- the effects of competing technological and market developments;
- the costs associated with hiring additional personnel and consultants as our business grows, including additional executive officers and clinical development, regulatory, CMC, quality and commercial personnel;
- the costs and timing of the implementation of commercial-scale manufacturing activities, if any product candidate is approved, including as a result of inflation, any supply chain issues or component shortages;
- the costs and timing of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval;

- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third-party payors and adequate market share and revenue for any approved products;

- the terms and timing of establishing and maintaining collaborations, licenses and other similar arrangements; and

- the costs associated with any products or technologies that we may in-license or acquire.

A change in the outcome of any of these or other variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of that product candidate. Furthermore, our operating plans may change in the future, and we will continue to require additional capital to meet operational needs and capital requirements associated with such operating plans. If we raise additional funds by issuing equity securities, our stockholders may experience dilution. Any future debt financing into which we enter may impose upon us additional covenants that restrict our operations, including limitations on our ability to incur liens or additional debt, pay dividends, repurchase our common stock, make certain investments or engage in certain merger, consolidation or asset sale transactions. Any debt financing or additional equity that we raise may contain terms that are not favorable to us or our stockholders.

Adequate funding may not be available to us on acceptable terms or at all. Our potential inability to raise capital when needed could have a negative impact on our financial condition and our ability to pursue our business strategies. If we are unable to raise additional funds as required, we may need to delay, reduce, or terminate some or all development programs and clinical trials. We may also be required to sell or license our rights to product candidates in certain territories or indications that we would otherwise prefer to develop and commercialize ourselves. If we are required to enter into collaborations and other arrangements to address our liquidity needs, we may have to give up certain rights that limit our ability to develop and commercialize our product candidates or may have other terms that are not favorable to us or our stockholders, which could materially and adversely affect our business and financial prospects. See the section of this Annual Report on Form 10-K titled “Risk Factors” for additional risks associated with our substantial capital requirements.

Cash Flows

The following table summarizes our cash flows from operating, investing and financing activities the years ended December 31, 2024 and 2023.

	Year Ended December 31,	
	2024	2023
	(in thousands)	
Total net cash (used in) provided by:		
Operating activities	$ (21,895)	$ (39,967)
Financing activities	26,692	17,344
Net increase (decrease) in cash and cash equivalents	$ 4,797	$ (22,623)

Operating Activities

For the year ended December 31, 2024, cash used in operations was $21.9 million compared to $40.0 million for the year ended December 31, 2023. The decrease in cash used in operations was primarily the result of our Phase 3 PD and Phase 2/3 AD studies being active during the majority of 2023, whereas 2024 study activity was minimal because the aforementioned trials had been substantially completed in 2023. The reduction in clinical activity during 2024 significantly reduced our operating cash burn year-over-year.

We expect cash used in operating activities to once again increase in 2025 as compared to 2024, due to an expected increase in our operating losses associated with continued development of our product candidates (i.e., pivotal Phase 3 AD Program) as well as planned increases in our personnel count.

Financing Activities

Cash provided by financing activities was $26.7 million during the year ended December 31, 2024, which was primarily attributable to proceeds from issuance of common stock and warrants for capital raises, including our ELOC and ATM facilities, as well as proceeds from exercises of our Canaccord Warrants.

Cash provided by financing activities was $17.3 million during the year ended December 31, 2023, which was primarily attributable to proceeds from issuance of common stock and warrants for capital raises, including proceeds from our equity financing with Canaccord as well as proceeds from exercises of our Canaccord Warrants.

Off-Balance Sheet Arrangements

We did not have any off-balance sheet arrangements during the periods presented, and we do not currently have any off-balance sheet arrangements as defined in the rules and regulations of the SEC.

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 of America. 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, fair value of warrants and stock-based compensation. The clinical development cost to advance any of our product candidates to marketing approval is substantial and involves numerous risks and uncertainties associated with pharmaceutical product development. As a result, we are unable to accurately predict the timing or amount of increased expenses and, as a result, clinical development expense could be materially different as the costs are incurred. In determining warrant fair value, we maximize 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. We measure and record stock compensation expense using the applicable accounting guidance for share-based payments using the Black-Scholes option pricing model to value option awards which requires the use of subjective assumptions, including the expected life of the option and expected share price volatility. These assumptions used in calculating the fair value of stock-based awards represent our best estimates and involve inherent uncertainties and the application of judgment. As a result, if factors change and we used different assumptions, stock-based compensation expense could be materially different for stock-based awards.

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 and Clinical Trial Accruals

As part of the process of preparing the financial statements included elsewhere in this Annual Report on Form 10-K, we are required to estimate and record expenses, for which a large portion are research and development expenses. Research and development expenses include, among other categories - development, clinical trials, and regulatory compliance costs incurred with research organizations, contract manufacturers, and other third-party vendors. We rely on third-parties to conduct our clinical studies and to provide many of these services, including data and project management, statistical analysis and electronic compilation. At the end of each reporting period, the estimation process involves identifying services that have been performed on our behalf by third-parties, estimating and accruing expenses in our financial statements based on the evaluation of the progress to completion of specific tasks and the facts and circumstances known to us at the time of the estimate, and assessing the accuracy of these estimates going forward to determine if adjustments are required. We periodically collaborate with our third-party vendors to assist in determining our estimates. Payments for these activities performed by our third-party vendors are based on the terms of the individual arrangements with our third-party vendors, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development expense, as applicable. We believe our estimates and assumptions are reasonable under the current conditions; however, actual results may differ from these estimates. Any changes to estimates will be recorded in the

period in which a circumstance causing a change in estimate becomes known and the impact of any change in estimate could be material.

Stock-Based Compensation

We account for our stock-based compensation awards in accordance with the Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Topic 718, *Compensation—Stock Compensation* ("ASC 718"). We have issued stock-based compensation awards that are stock options, in accordance with ASC 718. ASC 718 requires all stock-based payments, including grants of stock options, to be recognized in the statements of operations based on their grant date fair values. We use the Black-Scholes option-pricing model to determine the fair value of options granted. We recognize forfeitures as they occur. Expense related to stock-based compensation awards are recorded to research and development expense or general and administrative expense based on the underlying function of the individual that was granted the stock-based compensation award. Estimating the fair value of stock options requires the input of subjective assumptions, including the expected term of the stock option, stock price volatility, the risk-free interest rate, and expected dividends. The assumptions used in our Black-Scholes option-pricing model represent our best estimates and involve a number of variables, uncertainties, assumptions, and the application of our judgment, as they are inherently subjective.

The assumptions used in our Black-Scholes option-pricing model for stock options are as follows:

Expected Term. As we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate expected term, the expected term of employee options is determined using the "simplified" method, as prescribed in SEC's Staff Accounting Bulletin No. 107, whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the option.

Expected Volatility. The expected volatility is based on our historical volatilities and that of similar entities within our industry for periods commensurate with the assumed expected term.

Risk-Free Interest Rate. The risk-free interest rate is based on the interest rate payable on U.S. Treasury securities in effect at the time of grant for a period that is commensurate with the assumed expected term.

Expected Dividends. The expected dividend yield is 0% because we have not historically paid, and do not expect for the foreseeable future to pay, a dividend on our common stock.

Stock-based compensation expense was $3.8 million and $4.6 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we had $2.4 million of unrecognized stock-based compensation expense, related to service-based options, which will be recognized over a remaining weighted-average period of 1.0 years.

Valuation of Common Stock Warrant Liabilities

The fair value of Common Stock Warrant Liabilities is determined using a Black-Scholes option-pricing model. Determining the appropriate fair value model and calculating the fair value of Common Stock Warrants requires considerable judgment. Any change in the estimates used may cause the value to be higher or lower than that reported. The Common Stock Warrants are not traded in an active market and the fair value is determined using valuation techniques. The estimates may be significantly different from those recorded in the financial statements because of the use of judgment and the inherent uncertainty in estimating the fair value of these instruments that are not quoted in an active market. All changes in the fair value are recorded in the statements of operations each reporting period.

Recently Adopted Accounting Pronouncements

Effective January 1, 2024, the Company retrospectively adopted Accounting Standards Update ("ASU") 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures* ("ASU 2023-07") on an annual basis, which requires public entities to disclose information about their reportable segments' significant expenses and other segment items. ASU 2023-07 also requires public entities with a single reportable segment to apply the disclosure requirements in ASU 2023-07, as well as all existing segment disclosures and reconciliation requirements in FASB ASC Topic 280, *Segment Reporting*. This guidance is effective for

fiscal years beginning after December 15, 2023 and interim periods within fiscal years beginning after December 15, 2024. See Note 11 for additional disclosures made as a result of adopting ASU 2023-07.

Recent Accounting Pronouncements

In December 2023, the FASB issued ASU No. 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures* ("ASU 2023-09"), which improves income tax disclosures by requiring: (1) consistent categories and greater disaggregation of information in the rate reconciliation, and (2) income taxes paid disaggregated by jurisdiction. It also includes certain other amendments to improve the effectiveness of income tax disclosures. ASU 2023-09 is effective for annual periods beginning after December 15, 2024. Early adoption is permitted. The ASU indicates that all entities will apply the guidance prospectively with an option for retroactive application to each period presented in the financial statements. The Company has not determined the impact ASU 2023-09 may have on the Company's financial statement disclosures but is not expecting material impacts.

In November 2024, the FASB issued ASU 2024-03, *Income Statement — Reporting Comprehensive Income — Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses ("*ASU 2024-03*")*, which requires public entities, at annual and interim reporting periods, to disclose in a tabular format additional information about specific expense categories in the notes to the financial statements. ASU 2024-03 is effective for annual reporting periods beginning after December 15, 2026, and interim reporting periods beginning after December 15, 2027, with early adoption permitted. The Company is still evaluating the impacts of this ASU on its future financial statements and disclosures.

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, has evaluated the effectiveness of our disclosure controls and procedures (as such term is defined in Rules 13a-15I 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 has 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 we file or submit 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, as our interim 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 assess the effectiveness of our internal control over financial reporting as of December 31, 2024. Based on the assessment, management has concluded that, as of December 31, 2024, 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 have been no changes in our internal control over financial reporting during our most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

During the three months ended December 31, 2024, the following directors or officers (as defined in Rule 16a-1(f) of the Exchange Act) adopted or terminated a "Rule 10b5-1 trading arrangement" or "non-Rule 10b5-1 trading arrangement," as each term is defined in Item 408(c) of Regulation S-K:

Name and Title	Action	Date	Plan	Aggregate Number of securities to be sold	Plan Expiration Date
Maria Maccecchini, CEO & Director	Adoption	17-Dec-24	Rule 10b5-1	270,000	16-Sep-26
Claudine Bruck, Director	Adoption	17-Dec-24	Rule 10b5-1	21,426	31-Dec-25
Mark White, Director	Adoption	17-Dec-24	Rule 10b5-1	51,426	30-Sep-26

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not Applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

We incorporate the information required by this Item 10 by reference to the definitive proxy statement for our 2025 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 2025 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 2025 annual meeting of shareholders, to be filed with the SEC.

Equity Compensation Plan Information

Plan category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted-average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c)
Equity compensation plans approved by security holders	2,336,020	$ 11.39	354,299
Equity compensation plans not approved by security holders	310,733	$ 8.99	—
Total	2,646,753	$ 11.11	354,299

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 2025 annual meeting of shareholders, to be filed with the SEC.

Item 14. Principal Accountant Fees and Services.

We incorporate the information required by this Item 14 by reference to the definitive proxy statement for our 2025 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 the Current Report on Form 8-K filed February 6, 2020.)
3.2	Amended and Restated Bylaws of the Registrant. (Incorporated by reference to Exhibit 3.2 to the Current Report on Form 8-K filed February 6, 2020.)
3.3	Certificate of Amendment to the Amended and Restated Certificate of Incorporation of the Registrant. (Incorporated by reference to Exhibit 3.1 to the Current Report on Form 8-K filed June 16, 2023.)
4.1	Specimen Certificate evidencing shares of the Registrant's common stock. (Incorporated by reference to Exhibit 4.1 to Amendment No. 3 to the Registration Statement on Form S-1 filed September 20, 2019.)
4.2	Form of Warrant Agreement (Incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed on November 1, 2023.)
4.3	Form of Warrant (Incorporated by reference to Exhibit 4.1 to the Current Report on Form 8-K filed on February 5, 2025)
4.4	Warrant Agency Agreement (Incorporated by reference to Exhibit 4.2 to the Current Report on Form 8-K filed on February 5, 2025)
4.5	Description of Registrant's Securities.
10.1+	Second Amended and Restated Employment Agreement dated as of March 24, 2020 between the Registrant and Maria Maccecchini. (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 4.3 to the Registration Statement on Form S-8 filed February 14, 2020.)
10.3+	Amendment to Annovis Bio, Inc. 2019 Equity Incentive Plan (Incorporated by reference to form DEF 14A filed April 29, 2024.)
10.4	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.)

Exhibit Number	Description of Exhibit
10.5+	Form of Non-Qualified Stock Option Award Agreement for the Annovis Bio, Inc. 2019 Equity Incentive Plan. (Incorporated by reference to Exhibit 10.6 to the Annual Report on Form 10-K filed on March 31, 2023).
10.6	Distribution Agreement, dated December 11, 2024, by and between Annovis Bio, Inc. and Oppenheimer & Co. Inc. (Incorporated by reference to Exhibit 1.1 to the Current Report on Form 8-K filed on December 12, 2024)
10.7	Underwriting Agreement, dated February 3, 2025, by and between Annovis Bio., Inc. and ThinkEquity LLC (Incorporated by reference to Exhibit 1.1 to the Current Report on Form 8-K filed on February 5, 2025)
19.1	Insider Trading Policy
23.1	Consent of Ernst & Young LLP
31.1	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.
97.1	Clawback Policy (Incorporated by reference to Exhibit 97.1 to the Annual Report on Form 10-K filed March 29, 2024)
101.INS	XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File – the cover page interactive data file does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.

+ Indicates management contract or compensatory plan.

(c) Financial Statement Schedules:

None.

Item 16. Form 10-K Summary.

Not Applicable.

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
Date: March 21, 2025

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.

Signature	Title	Date
/s/ MARIA MACCECCHINI Maria Maccecchini	President and Chief Executive Officer (principal executive officer; interim principal financial and accounting officer)	March 21, 2025
/s/ MICHAEL HOFFMAN Michael Hoffman	Chairman of the Board and Director	March 21, 2025
/s/ CLAUDINE BRUCK Claudine Bruck	Director	March 21, 2025
/s/ REID MCCARTHY Reid McCarthy	Director	March 21, 2025
/s/ MARK WHITE Mark White	Director	March 21, 2025

ANNOVIS BIO, INC.
Table of Contents

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors 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, 2024 and 2023, the related statements of operations, changes in stockholders' equity (deficit) and cash flows for each of the two years in the period ended December 31, 2024, 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 at December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2023.

Philadelphia, Pennsylvania

March 21, 2025

ANNOVIS BIO, INC.

Balance Sheets

	As of December 31,	
	2024	**2023**
Assets		
Current assets:		
Cash and cash equivalents	$ 10,551,916	$ 5,754,720
Prepaid expenses and other current assets	3,373,717	4,453,544
Total assets	$ 13,925,633	$ 10,208,264
Liabilities and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 2,305,974	$ 1,292,837
Accrued expenses	1,575,013	2,986,273
Total current liabilities	3,880,987	4,279,110
Non-current liabilities:		
Warrant liability	737,000	13,680,000
Total liabilities	4,617,987	17,959,110
Commitments and contingencies (Note 6)		
Stockholders' equity (deficit) :		
Preferred stock - $0.0001 par value, 2,000,000 shares authorized and 0 shares issued and outstanding	—	—
Common stock - $0.0001 par value, 70,000,000 shares authorized and 14,141,521 and 10,519,933 shares issued and outstanding at December 31, 2024 and December 31, 2023, respectively	1,414	1,052
Additional paid-in capital	144,155,694	102,507,189
Accumulated deficit	(134,849,462)	(110,259,087)
Total stockholders' equity (deficit)	9,307,646	(7,750,846)
Total liabilities and stockholders' equity (deficit)	$ 13,925,633	$ 10,208,264

See accompanying notes to financial statements.

ANNOVIS BIO, INC.

Statements of Operations

	Year Ended December 31,	
	2024	**2023**
Operating expenses:		
Research and development	$ 19,995,447	$ 38,790,603
General and administrative	6,699,481	6,244,408
Total operating expenses	26,694,928	45,035,011
Operating loss	(26,694,928)	(45,035,011)
Other income (expense):		
Interest income	331,849	667,898
Other financing costs (Note 7)	(1,853,189)	—
Change in fair value of warrants (Note 7)	3,625,893	(11,837,200)
Total other income (expense), net	2,104,553	(11,169,302)
Net loss	$ (24,590,375)	$ (56,204,313)
Net loss per share (Note 9)		
Basic	$ (2.02)	$ (6.23)
Diluted	$ (2.31)	$ (6.23)
Weighted-average number of common shares used in computing net loss per share		
Basic	12,182,475	9,023,138
Diluted	12,235,444	9,023,138

See accompanying notes to financial statements.

ANNOVIS BIO, INC.

Statements of Changes in Stockholders' Equity (Deficit)

	Stockholders' Equity (Deficit)				
	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount			
Balance, December 31, 2022	8,163,923	$ 816	$ 82,377,488	$ (54,054,774)	$ 28,323,530
Exercise of stock options	59,897	6	8,379	—	8,385
Stock-based compensation expense	—	—	4,628,406	—	4,628,406
Exercise of common stock warrants, inclusive of warrant reduction	50,000	5	1,056,196	—	1,056,201
Issuance of common stock, net of issuance costs and warrant liability	2,246,113	225	14,436,720		14,436,945
Net loss	—	—	—	(56,204,313)	(56,204,313)
Balance, December 31, 2023	10,519,933	$ 1,052	$ 102,507,189	$ (110,259,087)	$ (7,750,846)
Cashless exercise of stock options	220,339	22	(22)	—	—
Stock-based compensation expense	—	—	3,836,770	—	3,836,770
Exercise of common stock warrants, inclusive of warrant reduction	891,667	89	17,342,022	—	17,342,111
Issuance of common stock pursuant to Equity Distribution Agreement, net of issuance costs	26,788	3	156,766	—	156,769
Issuance of common stock pursuant to ELOC, net of issuance costs	2,051,428	205	16,438,012	—	16,438,217
Issuance of common stock pursuant to registered direct offering, net of issuance costs	431,366	43	3,874,957	—	3,875,000
Net loss	—	—	—	(24,590,375)	(24,590,375)
Balance, December 31, 2024	14,141,521	$ 1,414	$ 144,155,694	$ (134,849,462)	$ 9,307,646

See accompanying notes to financial statements.

ANNOVIS BIO, INC.

Statements of Cash Flows

	Year Ended December 31,	
	2024	**2023**
Cash flows from operating activities:		
Net loss	$ (24,590,375)	$ (56,204,313)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	3,836,770	4,628,406
Change in fair value of warrants	(3,625,893)	11,837,200
Non-cash other financing costs, including change in fair value of derivative	1,803,189	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	1,079,827	3,190,832
Accounts payable	1,013,138	(2,668,417)
Accrued expenses	(1,411,260)	(751,012)
Net cash used in operating activities	(21,894,604)	(39,967,304)
Cash flows from financing activities:		
Proceeds from issuance of common stock, net	18,666,797	16,885,946
Proceeds from exercise of warrants	8,025,003	450,000
Proceeds from exercise of stock options	—	8,385
Net cash provided by financing activities	26,691,800	17,344,331
Net increase (decrease) in cash and cash equivalents	4,797,196	(22,622,973)
Cash and cash equivalents, beginning of year	5,754,720	28,377,693
Cash and cash equivalents, end of year	$ 10,551,916	$ 5,754,720
Supplemental disclosure of cash flow information:		
Other adjustment to value of warrants related to exercises	$ 9,317,108	$ 606,201
Cash paid for financing costs	$ 50,000	$ —

See accompanying notes to financial statements.

(1) Nature of Business and Management's Plans

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") and Parkinson's disease ("PD"). 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. The Company's lead product candidate, buntanetap, is a small molecule administered orally that is designed to attack neurodegeneration by entering the brain and inhibiting the translation of multiple neurotoxic proteins thereby impeding the toxic cascade.

Going Concern

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 has a history of incurring net losses and 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 common stock and warrants to purchase common stock.

Since the Company's inception, the Company has incurred losses and negative cash flows from operations. At December 31, 2024, the Company had cash and cash equivalents of $10.6 million and an accumulated deficit of $134.8 million. The Company's net loss was $24.6 million and $56.2 million for the years ended December 31, 2024 and 2023, respectively. In addition, the Company's operating loss was $26.7 million and $45.0 million for the years ended December 31, 2024 and 2023, respectively. The Company follows the provisions of Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 205-40, Presentation of Financial Statements-Going Concern, or ASC 205-40, which requires management to assess the Company's ability to continue as a going concern for one year after the date the financial statements are issued. The Company expects that its existing balance of cash and cash equivalents as of December 31, 2024, combined with cash raised in the first quarter of 2025 in connection with its December 2024 ATM with OpCo and February 2025 stock offering with ThinkEquity, is not sufficient to fund operations for the period through one year after the date of this filing and therefore management has concluded that substantial doubt exists about the Company's ability to continue as a going concern. Management's plans to mitigate this risk include raising additional capital through equity financings, debt or other potential alternatives. Management's plans may also include the deferral of certain operating expenses unless and until additional capital is received. However, there can be no assurance that the Company will be successful in raising additional capital or that such capital, if available, will be on terms that are acceptable to the Company, or that the Company will be successful in deferring certain operating expenses. As such, management concluded that such plans do not alleviate the substantial doubt. If the Company is unable to raise sufficient additional capital or defer sufficient operating expenses, the Company may be compelled to reduce the scope of its operations.

The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business, and do not include any adjustments relating to recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might be necessary should the Company be unable to continue as a going concern.

(2) Summary of Significant Accounting Policies

(a) Basis of Presentation

The accompanying financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("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

In preparing the financial statements in conformity with GAAP, management is required to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported amounts of expenses during the reporting period. Due to the inherent uncertainty involved in making estimates, actual results reported in future periods may be affected by changes in these estimates. On an ongoing basis, the Company evaluates its estimates and assumptions. These estimates and assumptions include those used in the accounting for research and development contracts, including clinical trial accruals, common stock warrant liabilities, derivative liabilities and the accounting and fair value measurement of equity awards.

(c) Segment Information

As of December 31, 2024, the Company viewed its operations and managed its business as one operating segment consistent with how the Company's chief operating decision-maker, the Company's Chief Executive Officer, makes decisions regarding resource allocation and assesses performance. As of December 31, 2024, substantially all of the Company's assets were located in the United States. Refer to Note 11 for additional information

(d) Basic and Diluted Net Income per Share

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

(e) Cash and Cash Equivalents

The Company considers all highly-liquid investments with original maturities of three months or less to be cash equivalents. Cash equivalents may include bank demand deposits and money market funds that invest primarily in certificates of deposit, commercial paper, and U.S. government agency securities and treasuries. The Company records interest income received on cash and cash equivalents to other income (expense), net in the statements of operations. The Company has significant cash balances at financial institutions which throughout the year regularly exceed the federally insured limit of $250,000. Any loss incurred or a lack of access to such funds could have a significant adverse effect on the Company's financial condition, results of operations, and cash flows.

(f) Issuance Costs Associated with Equity Issuances

Issuance costs incurred in connection with the Company's equity issuances, which primarily consist of direct incremental legal, printing, listing and accounting fees, are offset against proceeds received in the issuances and charged to additional paid-in capital in the period the equity issuance is completed. Issuance costs related to the Equity Line of Credit ("ELOC") Purchase Agreement are expensed as incurred as prescribed by ASC 815.

(g) Derivative Liability

The Company evaluates all features contained in financing agreements to determine if there are any embedded derivatives that require separate accounting from the underlying agreement under ASC 815 – *Derivatives and Hedging*. An embedded derivative

that requires separation is accounted for as a separate liability or asset from the host agreement. The separated embedded derivative is accounted for at fair market value, with changes in fair value recognized in the statements of operations within the other financing costs line item. The Company determined that certain features under the ELOC Purchase Agreement (See Note 7 — Stockholders' Equity (Deficit)) collectively qualified as an embedded derivative. The derivative was accounted for separately from the underlying ELOC Purchase Agreement and is accounted for at fair value. As of December 31, 2024, the liability balance was zero because the ELOC facility had been exhausted and all shares from the equity line had been sold.

(h) Common Stock Warrants

On October 31, 2023, the Company completed an underwritten offering whereby the Company sold (i) 1,250,000 shares of common stock and (ii) warrants to purchase an aggregate of 1,250,000 shares of common stock at an exercise price of $9.00 per share ("Canaccord Warrants"). The warrants are liability classified as they contain certain cash settlement adjustment features that are outside of the Company's control or not deemed to be indexed to the Company's stock. The warrant liabilities are recorded at fair value regardless of the timing of the redemption feature, the redemption price, or the likelihood of redemption. These warrants are subject to re-measurement at each balance sheet date and any change in fair value is recognized as a component of change in fair value of warrant liability in the statements of operations. The Company will continue to adjust the liability for changes in fair value until the earlier of the exercise, expiration, or other settlement of the warrants. The warrants are classified as Level 3 liabilities.

(i) Research and Development

Research and development costs are either expensed as incurred, or recorded separately as a prepaid asset where expense is recognized when the service is performed. These costs 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. Prepaid clinical expenses represent valid future economic benefits based on the Company's contracts with its vendors and are realized in the ordinary course of business.

(j) Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses.

(k) Stock-Based Compensation

The Company accounts for its stock-based compensation awards in accordance with FASB ASC Topic 718, *Compensation—Stock Compensation* ("ASC 718"). The Company has issued stock-based compensation awards, including stock options. ASC 718 requires all stock-based payments, including grants of stock options, to be recognized in the financial statements based on their grant date fair values. The Company uses the Black-Scholes option-pricing model to determine the fair value of stock options granted. The Company recognizes forfeitures as they occur.

Expense related to stock-based compensation awards granted with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term. Stock options have a contractual term of 10 years. Expense for stock-based compensation awards with performance-based vesting conditions is only recognized when the performance-based vesting condition is deemed probable to occur. Expense related to stock-based compensation awards are recorded in research and development expense or general and administrative expense based on the underlying function of the individual that was granted the stock-based compensation award.

Estimating the fair value of stock options requires the input of subjective assumptions, including the expected term of the stock option, stock price volatility, the risk-free interest rate, and expected dividends. The assumptions used in the Company's Black-Scholes option-pricing model represent Management's best estimates and involve a number of variables, uncertainties, assumptions,

and the application of Management's judgment, as they are inherently subjective. If any assumptions change, the Company's stock-based compensation expense could be materially different in the future.

The assumptions used in the Company's Black-Scholes option-pricing model for stock options are as follows:

Expected Term. As Annovis does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate expected term, the expected term of employee stock options subject to service-based vesting conditions is determined using the "simplified" method, as prescribed in SEC's Staff Accounting Bulletin No. 107, whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the stock option.

Expected Volatility. The expected volatility is based on historical volatilities of Annovis and similar entities within the Company's industry for periods commensurate with the assumed expected term.

Risk-Free Interest Rate. The risk-free interest rate is based on the interest rate payable on U.S. Treasury securities in effect at the time of grant for a period that is commensurate with the assumed expected term.

Expected Dividends. The expected dividend yield is 0% because Annovis has not historically paid, and does not expect for the foreseeable future to pay, a dividend on its common stock.

(l) 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, 2024 and 2023, 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 as of December 31, 2024 or 2023.

(m) Recently Adopted Accounting Pronouncements

Effective January 1, 2024, the Company retrospectively adopted Accounting Standards Update ("ASU") 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures* ("ASU 2023-07") on an annual basis, which requires public entities to disclose information about their reportable segments' significant expenses and other segment items. ASU 2023-07 also requires public entities with a single reportable segment to apply the disclosure requirements in ASU 2023-07, as well as all existing segment disclosures and reconciliation requirements in FASB ASC Topic 280, *Segment Reporting*. This guidance is effective for fiscal years beginning after December 15, 2023 and interim periods within fiscal years beginning after December 15, 2024. See Note 11 for additional disclosures made as a result of adopting ASU 2023-07.

(n) Recent Accounting Pronouncements

In December 2023, the FASB issued ASU No. 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures* ("ASU 2023-09"), which improves income tax disclosures by requiring: (1) consistent categories and greater disaggregation of information in the rate reconciliation, and (2) income taxes paid disaggregated by jurisdiction. It also includes certain other amendments to improve the effectiveness of income tax disclosures. ASU 2023-09 is effective for annual periods beginning after December 15, 2024. Early adoption is permitted. The ASU indicates that all entities will apply the guidance prospectively with an option for retroactive application to each period presented in the financial statements. The Company has not determined the impact ASU 2023-09 may have on the Company's financial statement disclosures, but it does not anticipate material impacts.

In November 2024, the FASB issued ASU 2024-03, *Income Statement — Reporting Comprehensive Income — Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses (*"ASU 2024-03"*)*, which requires public entities, at annual and interim reporting periods, to disclose in a tabular format additional information about specific expense categories in the notes to the financial statements. ASU 2024-03 is effective for annual reporting periods beginning after December 15, 2026, and interim reporting periods beginning after December 15, 2027, with early adoption permitted. The Company is still evaluating the impacts of this ASU on its future financial statements and disclosures.

(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 tables 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, 2024 and 2023:

		Fair Value Measurement at December 31, 2024		
	Carrying Value	Level 1	Level 2	Level 3
Assets:				
Cash equivalents	$ 491,006	$ 491,006	$ —	$ —
Total assets measured and recorded at fair value	$ 491,006	$ 491,006	$ —	$ —
Liabilities:				
Warrant liability	$ 737,000	$ —	$ —	$ 737,000
Total liabilities measured and recorded at fair value	$ 737,000	$ —	$ —	$ 737,000

		Fair Value Measurement at December 31, 2023		
	Carrying Value	Level 1	Level 2	Level 3
Assets:				
Cash equivalents	$ 5,136,677	$ 5,136,677	$ —	$ —
Total assets measured and recorded at fair value	$ 5,136,677	$ 5,136,677	$ —	$ —
Liabilities:				
Warrant liability	$ 13,680,000	$ —	$ —	$ 13,680,000
Total liabilities measured and recorded at fair value	$ 13,680,000	$ —	$ —	$ 13,680,000

The Company did not transfer any financial instruments into or out of Level 3 classification, during the year ended December 31, 2024 or 2023.

(a) Canaccord Warrants

The common stock warrants issued in connection with the Company's equity financing in November 2023 ("Canaccord Warrants") were classified as liabilities at the time of issuance due to certain cash settlement adjustment features that are outside of the Company's control or not deemed to be indexed to the Company's stock. The Canaccord Warrant liability is remeasured each reporting period with the change in fair value recorded to other income (expense), net in the statements of operations until the warrants are exercised, expired, reclassified, or otherwise settled. From their date of issuance until the period ended June 30, 2024, the fair value of the Canaccord Warrants was estimated using a Monte Carlo simulation model, given the performance conditions outlined further below. However, during the quarter ended September 30, 2024, the Company determined that certain performance conditions could not be met and that going forward, their use as inputs for determining fair value was no longer appropriate. As such, after the period ended June 30, 2024, the fair value of the Canaccord Warrants is estimated using a Black-Scholes option-pricing model.

The estimated fair value of the Canaccord Warrants is determined using Level 3 inputs. Inherent in both a Monte Carlo simulation model and a Black-Scholes option-pricing model are assumptions related to expected stock-price volatility, expected life, risk-free interest rate and other inputs. The Company estimates the volatility of its warrants based on an implied asset volatility calculated and believed to be reasonable for the Company over the holding period remaining. The risk-free interest rate is based on the market yield of U.S. Treasuries over a term commensurate with the remaining term to expiration. Any changes in these assumptions can change the associated valuation significantly.

The following tables provide quantitative information regarding Level 3 fair value measurements inputs as of their respective measurement dates. The table for the year ending December 31, 2024 presents inputs used under a Black-Scholes option-pricing model. The table for the year ending December 31, 2023 presents inputs used under a Monte Carlo simulation model:

	December 31, 2024	December 31, 2023
Exercise price	$ 9.00	$ 9.00
Closing stock price	$ 5.03	$ 18.70
Number of warrants outstanding	308,333	1,200,000
Phase III data probability of success	— %	60 %
Volatility	80 %	55 %
Term (time to expiration in years)	3.84	4.84
Redemption hurdle price	$ —	$ 14.25
Risk-free rate	4.3 %	3.9 %

The Canaccord Warrants were exercisable immediately at an exercise price of $9.00 per unit, and redeemable at the Company's option, in whole or in part, at a redemption price equal to $0.001 per Warrant upon 30 days' prior written notice, at any time after:

- the Company's public announcement of Positive Topline Data (as defined in the Warrant Agreement) from its Phase 3 in patients with Parkinson's Disease; and

- the date on which (a) the closing price of the Company's common stock on the principal exchange or trading facility on which it is then traded has equaled or exceeded $14.25 and (b) the average daily trading value ("ADTV") of the Company's common stock is equal to or exceeds $2,000,000, for two consecutive Trading Days.

During the year ended December 31, 2024, the Company released topline data from its Phase 3 study in patients with Parkinson's Disease. It was determined that based on the data, both criteria required for redemption of the Canaccord Warrants were not met. As such, the probability of success and redemption hurdle price inputs were no longer used in the Black-Scholes option-pricing model outlined above for the year ending December 31, 2024.

The Warrants were exercisable immediately and will expire on November 2, 2028, five years from the date of issuance. See Note 7 – Stockholders' Equity (Deficit) for additional background.

(4) Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following:

	As of December 31,	
	2024	2023
Prepaid clinical expenses	$ 2,998,811	$ 4,391,219
Prepaid other	346,313	23,455
Prepaid insurance	21,098	18,074
Security deposits	7,495	20,796
Total prepaid expenses and other current assets	$ 3,373,717	$ 4,453,544

(5) Accrued Expenses

Accrued expenses consisted of the following:

	As of December 31,	
	2024	2023
Accrued clinical expenses	$ 948,695	$ 2,645,589
Payroll and related benefits	364,717	96,848
Accrued professional fees and other	261,601	243,836
Total accrued expenses	$ 1,575,013	$ 2,986,273

(6) Commitments and Contingencies

(a) Research & Development

The Company has entered contracts with CROs and CMOs related the Company's clinical trials. The contracts require upfront payments, milestone payments, and pass-through cost reimbursements, to be made. While the contracts are generally cancellable with (written) notice, the Company is obligated to make payments for services rendered through the termination date of the project with any applicable CRO/CMO.

(b) Leases

The Company maintains one short-term lease associated with occupying its corporate headquarters. Total rental expense was $0.1 million and $0.1 million for the years ended December 31, 2024 and 2023, respectively.

(c) Employment Agreements

The Company has an agreement with its Chief Executive Officer that provides for severance payments 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 agreement was estimated to be $1.1 million at December 31, 2024.

(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.

For both the years ended December 31, 2024 and December 31, 2023 the Company did not have any pending legal actions deemed to be material.

(7) Stockholders' Equity (Deficit)

(a) Overview

The Company's Amended and Restated Certificate of Incorporation was adopted on January 31, 2020, in conjunction with the closing of the Company's initial public offering (the "IPO") and amended on June 15, 2023 to increase the authorized number of shares. Currently, there are two classes of stock authorized which are designated, respectively, common stock and preferred stock. The total number of shares which the Company is authorized to issue is 72,000,000, each with a par value of $0.0001 per share. Of these shares, 70,000,000 is designated as common stock and 2,000,000 is preferred stock.

(b) Common Stock

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 of Directors.

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.

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. There was no preferred stock issued or outstanding as of December 31, 2024 or December 31, 2023.

(d) IPO Warrants

In conjunction with the closing of the Company's Initial Public Offering ("IPO"), the Company granted its underwriters 0.1 million warrants to purchase shares of Company common stock ("IPO Warrants") at an exercise price of $7.50 per share, which was 125% of the IPO price. The IPO Warrants have a five-year term and were exercisable as of January 29, 2021 and have been classified by the Company as a component of stockholders' equity. At both December 31, 2024 and December 31, 2023, 2,400 of the IPO Warrants were outstanding. No IPO Warrants were exercised during the years ended December 31, 2024 or 2023.

(e) March 2023 ATM

On March 31, 2023, the Company, entered into an At the Market ("ATM") Equity Offering Sales Agreement (the "Sales Agreement" or "March 2023 ATM") with BofA Securities, Inc. ("BofA") and ThinkEquity LLC ("ThinkEquity" and, together with BofA, the "Sales Agents"), as sales agents, pursuant to which the Company could offer and sell, from time to time through the Sales Agents, shares of the Company's common stock, par value $0.0001 per share (the "Common Stock"), having an aggregate offering price of up to $50.0 million.

On April 4, 2023, the Company delivered written notice to BofA and ThinkEquity to terminate the Sales Agreement, effective April 9, 2023. The Company was not subject to any termination penalties related to the termination of the Sales Agreement.

Prior to termination of the Sales Agreement, the Company sold 0.7 million shares of Common Stock pursuant to the Sales Agreement at a price of $10.88 per share, for gross proceeds of $7.6 million before commissions. As a result of the termination of the Sales Agreement, the Company will not offer or sell any additional shares of Common Stock under the Sales Agreement.

(f) April 2023 Private Placement

On April 7, 2023, the Company sold 0.1 million shares of its common stock in a private placement to individual members of its Board of Directors and management at a price of $12.61 per share, for aggregate proceeds of $1.1 million.

(g) November 2023 Equity Offering and Warrant Issuance

On October 31, 2023, the Company entered into an underwritten offering with a Canaccord Genuity LLC whereby the Company sold (i) 1,250,000 shares of common stock and (ii) warrants ("Canaccord Warrants") to purchase an aggregate of 1,250,000 shares of common stock at an exercise price of $9.00 per share. The offering closed on November, 2, 2023. The warrants were exercisable immediately on the date of issuance and will expire five years after the date of issuance. The Company received $6.8 million in net cash proceeds after deducting underwriter discount and fees, as well as other third-party costs. The Canaccord Warrants are liability classified as they contain certain cash settlement adjustment features that are outside of the Company's control or not deemed to be indexed to the Company's stock.

The following is a roll forward of the Common Stock Warrant Liability during the years ended December 31, 2023 and 2024, respectively:

Issuance of Canaccord Warrants	$ 2,449,001
Exercise of 50,000 warrants	(606,201)
Change in fair value of warrant liabilities	11,837,200
Warrant liability at December 31, 2023	13,680,000
Change in fair value of warrant liabilities	(3,625,893)
Exercise of 891,667 warrants	(9,317,107)
Warrant liability at December 31, 2024	$ 737,000

(h) Warrant Summary

As of December 31, 2024, the Company had the following common stock warrants outstanding:

	Classification	Outstanding December 31, 2023	Granted	Exercised or Expired	Outstanding December 31, 2024	Exercise price per share	Expiration date
IPO warrants	Equity	2,400	—	—	2,400	$ 7.50	January 29, 2026
Canaccord warrants	Liability	1,200,000	—	(891,667)	308,333	$ 9.00	November 2, 2028

(i) November 2023 Private Placement

On November 27, 2023, the Company sold 0.2 million shares of its common stock in a private placement to individual members of its Board of Directors and management at a price of $6.10 per share, for aggregate proceeds of $1.3 million.

(j) March 2024 Registered Direct Offerings

On March 15, 2024 and March 21, 2024, the Company entered into two separate securities purchase agreements with the same institutional investor. When aggregating the results of both purchase agreements, the Company issued 0.4 million shares for net proceeds of $3.9 million in registered direct offerings.

(k) April 2024 ELOC Purchase Agreement

On April 25, 2024, the Company entered into an ELOC Purchase Agreement with an ELOC Purchaser, whereby we could offer and sell, from time to time at our sole discretion, and whereby the ELOC Purchaser committed to purchase, up to 2.0 million shares of shares of the Company's common stock. The term of the agreement was until the expiration of the Company's active S-3 Registration Statement, unless earlier terminated or exhausted. Due to certain pricing and settlement provisions, the ELOC Purchase Agreement qualified as a standby equity purchase agreement and included an embedded put option and embedded forward option. The Company therefore accounted for the ELOC Purchase Agreement as a derivative measured at fair value, with changes in the fair value recognized in the statements of operations within other financing costs. The Company initially recognized a derivative liability of $1.7 million related to the purchased put option at inception of the ELOC Purchase Agreement. The Company then expensed the difference between the discounted purchase price of the settled forward and the fair value of shares on the date of settlement as a noncash financing issuance cost. The Company recognized $1.3 million of noncash financing costs during the year ended December 31, 2024 related to the discounted purchase price of the settled forward and the underlying fair value of the shares issued.

Upon execution of the ELOC Purchase Agreement, the Company agreed to issue to the ELOC Purchaser 33,937 shares of Common Stock as commitment shares (the "Commitment Shares"). The fair value of the Commitment Shares was $0.5 million, which was expensed within other financing costs in the statements of operations during the year ended December 31, 2024. The Company also incurred issuance costs of $0.1 million, consisting of legal costs incurred in connection with the ELOC Purchase Agreement, which were expensed within other financing costs in the statements of operations during the year ended December 31, 2024. The ELOC Purchaser agreed that during the term of the Purchase Agreement, neither it nor any of its affiliates would engage in any short sales or hedging transactions involving the Company's common stock.

Under the ELOC Purchase Agreement, on any business day (the "Purchase Date"), if the Company's stock price is greater than or equal to $5.00 per share, the Company could direct the ELOC Purchaser to purchase common stock. The ELOC Purchaser's committed obligation under any single Fixed Purchase could not exceed the lower of 25,000 shares of Common Stock or $250,000 ("Fixed Purchases").

In addition, the Company could also direct the ELOC Purchaser, on any trading day in which the Company submitted a Fixed Purchase notice for the maximum amount allowed for such Fixed Purchase, to purchase an additional amount of the Company's common stock (a "VWAP Purchase"). The ELOC Purchaser's committed obligation under any single VWAP Purchase could not exceed a number of shares of Common Stock equal to the lesser of (i) 300% of the number of Shares directed by the Company to be purchased by the Investor pursuant to the corresponding Fixed Purchase Notice and (ii) 30% of the trading volume in the Company's Common Stock on the NYSE during the applicable VWAP Purchase Period on the applicable VWAP Purchase Date ("VWAP Purchase Maximum Amount").

The Company could also direct the ELOC Purchaser, on any trading day for which a VWAP Purchase had been completed and all of the shares had been placed, to purchase an additional amount of the Company's common stock (an "Additional VWAP Purchase"). The ELOC Purchaser's committed obligation under any single Additional VWAP Purchase was the lesser of (i) 300% of the number of Shares directed by the Company to be purchased by the Investor pursuant to the corresponding Fixed Purchase Notice and (ii) a number of Shares equal to (A) the Additional VWAP Purchase Share Percentage multiplied by (B) the trading volume of shares of Common Stock traded during the applicable Additional VWAP Purchase Period on the applicable Additional VWAP Purchase Date for such Additional VWAP Purchase ("Additional VWAP Purchase Maximum Amount"). The applicable pricing structure for each purchase type is outlined below:

The purchase price per share for Fixed Purchases ("Fixed Purchase Price") equals 95% of the lesser of:

- the daily volume weighted average price ("VWAP") of the Company's Common Stock on the NYSE for the five (5) Trading Days immediately preceding the applicable Fixed Purchase Date for such Fixed Purchase; and
- the Closing Sale Price of a share of Common Stock on the applicable Fixed Purchase Date.

The purchase price per share for VWAP Purchases ("VWAP Purchase Price") equals 95% of the lesser of:

- the VWAP during the applicable VWAP Purchase Period during the applicable VWAP Purchase Date.
- the Closing Sale Price of the Common Stock on the applicable VWAP Purchase Date.

The purchase price per share for Additional VWAP Purchases ("Additional VWAP Purchase Price") equals 95% of the lesser of:

- the VWAP for the applicable Additional VWAP Purchase Period during the applicable Additional VWAP Purchase Date; and
- the Closing Sale Price of the Common Stock on such applicable Additional VWAP Purchase Date.

In addition to the commitment shares referenced above, a total of 2.0 million shares of the Company's common stock were issued under the ELOC Purchase Agreement during the year ended December 31, 2024, for net proceeds of $14.6 million. The facility was fully exhausted during 2024 and no further shares are available to issue as of December 31, 2024.

The following is a roll-forward of the ELOC derivative liability from date of execution to December 31, 2024:

Fair value at April 25, 2024	1,697,500
Settlements and changes in fair value of ELOC derivative liability	(1,192,500)
Fair value at June 30, 2024	505,000
Settlements and changes in fair value of ELOC derivative liability	(62,500)
Fair value at September 30, 2024	442,500
Settlements and changes in fair value of ELOC derivative liability	(442,500)
Fair value at December 31, 2024	—

(l) December 2024 ATM

On December 11, 2024, the Company entered into an Equity Distribution Agreement ("Distribution Agreement") with Oppenheimer & Co. Inc., ("OpCo") relating to the sale of shares of the Company's common stock. In accordance with the terms of the Distribution Agreement, The Company may offer and sell shares of its common stock having an aggregate offering price of up to $50.0 million from time to time through or to OpCo, acting as agent or principal.

During the year-ended December 31, 2024, the Company sold 26,788 million shares of common stock pursuant to the Distribution Agreement for gross proceeds of $0.2 million before commissions.

(8) Stock-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. 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. Effective June 12, 2024, the 2019 Plan was amended to increase the number of shares authorized from 2,000,000 to 3,000,000. As of December 31, 2024, the 2019 Plan contained 354,299 shares 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, except when they are below previously approved thresholds allowing the Company's CEO to grant awards on a discretionary basis. The Company's stock options generally carry a maximum term of 10 years after date of grant and are exercisable in cash, or as otherwise determined by the Board.

Stock-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, 2024 and 2023 was as follows:

	Year Ended December 31,	
	2024	2023
General and administrative	$ 2,510,444	$ 2,414,867
Research and development	1,326,326	2,213,539
	$ 3,836,770	$ 4,628,406

The following table summarizes the Company's stock option activity:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (In Thousands)
Outstanding at December 31, 2023	1,954,774	$ 13.41	6.1	$ 17,863
Granted	870,494	6.01		—
Exercised	(300,000)	3.13		570
Forfeited	(189,248)	20.61		—
Outstanding at December 31, 2024	2,336,020	$ 11.39	7.3	$ 1,298
Exercisable at December 31, 2024	1,824,122	$ 12.80	6.8	$ 1,298

The weighted average grant date fair value of stock options granted during the years ended December 31, 2024 and 2023 was $5.16 and $7.39, respectively. During the year ended December 31, 2024 the Company received no cash proceeds from the exercises of stock options. For the year ended December 31, 2023, the Company received $8,385 cash proceeds from the exercises of stock options. As of December 31, 2024, there was unrecognized stock-based compensation expense related to unvested stock option awards, related to service-based options of $2.4 million, which will be recognized over a remaining weighted-average period of 1.0 years.

During the years ended December 31, 2024 and 2023, the Company issued 870,494 and 367,329 options, respectively. Under the grant agreements for the 2024 stock option grants, 382,282 of the options vested immediately and 468,212 of the options vest in substantially equal quarterly installments over two years from the date of grant. There are also 20,000 stock option grants that vest as consulting services are performed and awards are earned. Under the grant agreements for the 2023 stock option grants, 94,624 of the options vested immediately, and 272,705 of the options vest in substantially equal quarterly installments over two years from the date of grant. All of the options have a 10-year term prior to expiration.

The assumptions utilized in the fair value calculations for stock options granted during the years ended December 31, 2024 and 2023, respectively, were as follows:

	Year Ended December 31, 2024	Year Ended December 31, 2023
Weighted average risk-free interest rate	4.18 %	4.17 %
Weighted average expected option term (years)	5.3	5.5
Weighted average expected volatility	123 %	120 %
Expected dividend yield	—	—

Related Party Transaction

During the year ended December 31, 2024, the Company issued 20,000 non-qualified stock options to a member of its Board of Directors in consideration for the member's agreement to serve as a consultant to the Company. The options were issued in one tranche, at a grant price of $5.27 per share. 8,069 of the awards became vested during the year ended December 31, 2024.

(9) Net Loss Per Share

The Company has reported a net loss for the years ended December 31, 2024 and 2023, and the basic and diluted net loss per share attributable to common stockholders are the same for both years because all warrants 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 common share for the years ended December 31, 2024 and 2023:

	Year Ended December 31,	
	2024	2023
Net loss per share – Basic:		
Numerator		
Net loss	$ (24,590,375)	$ (56,204,313)
Denominator		
Weighted-average common shares outstanding, basic	12,182,475	9,023,138
Basic net loss per common share	$ (2.02)	$ (6.23)
Net loss per share – Diluted:		
Numerator		
Net loss	$ (24,590,375)	$ (56,204,313)
Less: gain from change in fair value applicable to dilutive liability-classified warrants	(3,625,893)	—
Numerator for diluted net loss per share	$ (28,216,268)	$ (56,204,313)
Denominator		
Denominator for basic net loss per share	12,182,475	9,023,138
Plus: incremental shares underlying “in the money” liability-classified warrants outstanding	52,969	—
Denominator for diluted net loss per share	12,235,444	9,023,138
Diluted net loss per common share	$ (2.31)	$ (6.23)

Potentially dilutive securities, whose effect would have been antidilutive, were excluded from the computation of diluted earnings per share for each of the years ended December 31, 2024 and 2023. Total antidilutive securities that were excluded from the computation of diluted weighted-average shares outstanding were as follows:

	December 31,	
	2024	2023
Stock options	2,336,020	1,954,774
Warrants	2,400	1,202,400

(10) Income Taxes

The federal and state provision (benefit) for income taxes was $0 for the years ended December 31, 2024 and 2023.

A reconciliation of income tax provision (benefit) computed at the statutory federal income tax rate to income taxes as reflected in the financial statements for the years ended December 31, 2024 and 2023 is as follows:

	Year Ended December 31,	
	2024	2023
Federal income tax benefit at statutory rate	21.0 %	21.0 %
State and local tax, net of federal benefit	4.0 %	3.1 %
State and local tax, change in rates	0.0 %	(3.5)%
Permanent differences	(1.9)%	(0.4)%
Research and development credit	4.3 %	4.5 %
Stock-based compensation	0.0 %	0.4 %
Change in fair value of warrants	1.5 %	(4.4)%
Change in valuation allowance	(28.9)%	(20.7)%
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,	
	2024	2023
Net operating loss carryforwards	$ 13,634,896	$ 9,607,158
Stock compensation	4,390,635	4,245,472
Capitalized R&D	1,137,406	1,334,494
Section 174	12,802,738	10,793,442
R&D credit carryforwards	5,198,123	4,132,475
Other	76,757	14,553
Total deferred tax assets	37,240,555	30,127,594
Less valuation allowance	(37,240,555)	(30,127,594)
Net deferred taxes	$ —	$ —

As of December 31, 2024, the Company had U.S. federal net operating loss ("NOL") carryforwards of $54.1 million which may be available to offset future income tax liabilities. Federal NOL carryforwards generated in 2017 and prior of $2.8 million will expire beginning in 2032. The remaining federal NOL carryforwards generated in 2018 and later do not expire. As of December 31, 2024, the Company also had U.S. state NOL carryforwards of $56.6 million 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, 2024 and 2023 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 recorded a net change in valuation allowance of $7.1 million and $11.7 million in the years ended December 31, 2024 and 2023, respectively.

As of December 31, 2024, the Company had federal research and development tax credit carryforwards of $5.2 million 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 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 2021 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. To the extent the Company utilizes any tax attributes from a tax period that may otherwise be closed due to statute expiration, the tax authorities may adjust the tax attributes upon their examination of the future period in which the attribute was utilized. The Company will recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2024, 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.

Effective for tax years beginning after December 31, 2021, taxpayers are required to capitalize any expenses incurred that are considered incidental to research and experimentation (R&E) activities under IRC Section 174. While taxpayers historically had the option of deducting these expenses under IRC Section 174, the December 2017 Tax Cuts and Jobs Act mandates capitalization and amortization of R&E expenses for tax years beginning after December 31, 2021. Expenses incurred in connection with R&E activities in the US must be amortized over a 5-year period if incurred, and R&E expenses incurred outside the US must be amortized over a 15-year period. R&E activities are broader in scope than qualified research activities considered under IRC Section 41 (relating to the research tax credit). For the year ended December 31, 2024, the Company performed an analysis based on available guidance and determined that it will continue to be in a loss position even after the required capitalization and amortization of its R&E expenses. The Company will continue to monitor this issue for future developments, but it does not expect R&E capitalization and amortization to require it to pay cash taxes now or in the near future.

(11) Segment Information

The Company is a clinical-stage biopharmaceutical company and has not generated any revenue since commencing significant operations in 2008. The Company's operations are organized and reported as a single reportable segment, which includes all activities related to the discovery, development, and commercialization of our lead product candidate, buntanetap, which is designed to address AD, PD, and potentially other chronic neurodegenerative diseases. This presentation is consistent with how the Company's chief operating decision maker ("CODM"), its Chief Executive Officer, assesses the performance of the Company and makes operating decisions. The accounting policies of the segment are the same as those described in the summary of significant accounting policies (see Note 2). The CODM assesses performance and decides how to allocate resources based on net loss as reported on the statements of operations. The CODM uses net loss to monitor actual operating results, assess cash runway, and benchmark against the Company's competitors. The measure of segment assets is reported on the balance sheets as total assets. The Company's assets are held in the United States.

When evaluating the Company's financial performance, the CODM regularly reviews the following expense categories that comprise net loss. The table below sets forth the Company's segment information as reviewed by the CODM:

	Year Ended December 31,	
	2024	2023
Program expenses related to clinical-stage product candidates	$ (16,723,518)	$ (35,104,702)
Program expenses related to preclinical and discovery programs	(568,214)	(583,154)
Personnel-related expenses (including stock-based compensation)	(6,525,586)	(6,444,920)
General and administrative professional and consultant fees	(1,687,276)	(2,152,485)
Other segment items[1]	(1,190,333)	(749,750)
Interest income	331,849	667,898
Other non-cash income (expense) items[2]	1,772,704	(11,837,199)
Net Loss	$ (24,590,374)	$ (56,204,313)

[1] Other segment items included in net loss include insurance expense, information technology expenses, warrant commissions and other miscellaneous expenses.

[2] Other non-cash income (expense) items includes financing costs from our ELOC and change in fair value of our liability classified warrants.

(12) Subsequent Events

Subsequent to December 31, 2024, the Company sold 0.1 million shares of its common stock under its ATM with OpCo, which the Company entered into in December 2024. The Company received net proceeds of $0.5 million after deducting commissions and fees.

On February 3, 2025, the Company entered into an Underwriting Agreement with ThinkEquity LLC, acting as representative of the underwriters with respect to an underwritten public offering of 5.3 million units of the Company. Each unit sold consisted of one share of common stock and one warrant to purchase one share of common stock (the "ThinkEquity Warrants"), at a per unit price of $4.00 (the "Offering"). Aggregate gross proceeds from the Offering were $21.0 million before deducting underwriting discounts and other estimated offering expenses. The Warrants have an exercise price of $5.00 per share, are immediately exercisable and expire five years from the date of issuance. The shares of Common Stock and Warrants were issued separately. The Company has agreed to suspend sales of its Common Stock under the OpCo ATM Facility for a period of six months after the closing of the Offering.