Athira™ PHARMA

2023 ANNUAL REPORT

Enhancing Connections

To Our Shareholders,

In January 2024, we announced the completion of enrollment for the Phase 2/3 LIFT-AD clinical trial and now look forward to reporting topline data from LIFT-AD in the second half of 2024.

2023 marked an important year for Athira, as we continued to make significant progress in our pursuit to advance novel, first-in-class therapies to patients with neurodegenerative diseases in need of better treatment options.

Our approach to altering the course of neurological diseases is focused on the development of therapeutic candidates designed to modulate the neurotrophic hepatocyte growth factor (HGF) system. The HGF system plays a critical role in nervous system maintenance and repair, including stimulating neuron survival, increasing neuronal outgrowth and enhancing neuronal network repair.

Throughout 2023 and the first quarter of 2024, we presented and published preclinical and clinical data that further reinforce the potential of our small molecule approach targeting the neurotrophic HGF system across several neurodegenerative diseases including Alzheimer's disease (AD), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS).

We are approaching a critical inflection point toward achieving our mission with topline data from our Phase 2/3 LIFT-AD clinical trial of fosgonimeton in mild-to-moderate AD on the horizon. In 2023, we made meaningful strides advancing fosgonimeton through late-stage clinical development and have built on this momentum moving into 2024. In July 2023, we completed an end-of-phase 2 meeting with the U.S. Food and Drug Administration (FDA) to gain alignment on development plans for fosgonimeton in AD. Based on these interactions, we believe all registrational pathways remain viable.

In January 2024, we announced the completion of enrollment for the Phase 2/3 LIFT-AD clinical trial and now look forward to reporting topline data from LIFT-AD in the second half of 2024.

Findings to-date support the potential success of LIFT-AD, which include encouraging results from the exploratory Phase 2 ACT-AD and SHAPE trials, outcomes from the LIFT-AD unblinded interim efficacy and futility analysis, and continued high participation rates and long duration of investigational treatment in the ongoing open label extension trial (OLEX).

In parallel, we continue to advance ATH-1105, our next-generation, orally administered therapeutic candidate targeting the HGF system for the treatment of ALS. We are highly encouraged by the consistent benefit and neuroprotective effects ATH-1105 has shown in preclinical models, which have demonstrated statistically significant improvements in nerve and motor

function, biomarkers of inflammation and neurodegeneration, and survival in various animal models of ALS. We are filing our Investigational New Drug (IND) application with the FDA for ATH-1105 and are excited to initiate a first-in-human study of ATH-1105.

As always, we are extremely grateful to you, our loyal shareholders, for your continued support and encouragement as we execute on our strategy and advance our mission to transform the treatment paradigm for neurodegenerative diseases and bring new standards of care to the millions of patients who suffer from these debilitating diseases.

Importantly, we thank our clinical collaborators and their patients who participate in our clinical trials with the hope of improving not only their own outcomes, but also the outcomes of future patients. None of the progress we have made would be possible without their support.

Sincerely,

Mark J. Litton, Ph.D.
President and Chief Executive Officer
Athira Pharma, Inc.

Certain statements contained in this letter may constitute forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. A detailed discussion of such forward-looking statements and the related risks and uncertainties is included in our Annual Report on Form 10-K included herewith.

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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2023

OR

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

Commission File Number 001-39503

Athira Pharma, Inc.

(Exact name of registrant as specified in its charter)

Delaware **(State or other jurisdiction of incorporation or organization)**	**45-3368487** **(I.R.S. Employer Identification No.)**

18706 North Creek Parkway, Suite 104
Bothell, Washington 98011
(Address of principal executive officer)
(425) 620-8501
(Registrant's telephone number, including area code)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	ATHA	The Nasdaq Stock Market LLC (The Nasdaq Global Select Market)

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 15(d) of the 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, 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 §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 ☒

The aggregate market value of the common stock held by non-affiliates of the registrant, based on the closing price of the shares of common stock on June 30, 2023 (the last business day of the registrant's most recently completed second fiscal quarter) as reported by The Nasdaq Stock Market LLC on such date was approximately $96.3 million. Shares of the registrant's common stock held by each executive officer and director and by each other person who may be deemed to be an affiliate of the registrant have been excluded from this computation. This calculation does not reflect a determination that certain persons are affiliates of the registrant for any other purpose.

The number of shares of Registrant's Common Stock outstanding as of February 19, 2024 was 38,326,652.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive proxy statement to be delivered to stockholders in connection with the 2024 annual meeting of stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K. Such proxy statement will be filed with the Securities and Exchange Commission not later than 120 days following the end of the Registrant's fiscal year ended December 31, 2023.

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Summary Risk Factors

Our business is subject to numerous risks and uncertainties, including those highlighted in the section of this report captioned "Risk Factors." The following is a summary of the principal risks we face:

- We are a late clinical-stage biopharmaceutical company with a limited operating history.
- Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve a number of objectives.
- Our development of fosgonimeton may never lead to a marketable drug product.
- Our approach to targeting neurotrophic factors through the use of small molecules is based on a novel therapeutic approach, which exposes us to unforeseen risks. We have limited data from our Phase 1a/1b and Phase 2 clinical trials to date, and we cannot be certain that future trials will yield data in support of the safety, efficacy and tolerability of our drug candidates.
- We have concentrated our research and development efforts on the treatment of central and peripheral nervous system, or PNS, degenerative disorders, a field that has seen very limited success in product development.
- An independent special committee of our board of directors engaged in a review of papers co-authored by our former chief executive officer in connection with her doctoral research at Washington State University, or WSU. The special committee's findings included that (1) our former chief executive officer altered images in her 2011 doctoral dissertation and at least four research papers that she co-authored while a graduate student at WSU, and published from 2011 to 2014, (2) that we cited challenged research papers in certain communications and applications, and (3) that WSU's dihexa patent, exclusively licensed to us, incorporated certain of these altered images. WSU has undertaken a review of claims of potential research misconduct involving our former chief executive officer's doctoral research at WSU. We cannot predict when WSU's investigation will be completed or what conclusions WSU will reach.
- We are and may in the future be subject to claims, lawsuits, arbitration proceedings, government investigations and other legal, regulatory and administrative proceedings and face potential liability and expenses related thereto, which could have a material adverse effect on our business, operating results and financial condition.
- Any "topline", interim, initial, or preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.
- Clinical development involves a lengthy and expensive process with an uncertain outcome, and results of early, smaller-scale preclinical studies and clinical trials with a single or few clinical trial sites may not be predictive of eventual safety or effectiveness in large-scale potentially pivotal clinical trials across multiple clinical trial sites. We may encounter substantial delays in clinical trials, or may not be able to conduct or complete clinical trials on the expected timelines, if at all.
- Our success depends on our ability to protect our intellectual property and our proprietary technologies.
- If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical drug candidates would be adversely affected.
- We face significant competition, and if our competitors develop and market technologies or products more rapidly than we do or that are more effective, safer, or less expensive than the drug candidates we develop, our commercial opportunities will be negatively impacted.
- We may expend our limited resources to pursue a particular drug candidate or indication and fail to capitalize on drug candidates or indications that may be more profitable or for which there is a greater likelihood of success.

- The loss of any of our key personnel could significantly harm our business, results of operations and competitive position.
- We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.
- We will require substantial additional funding to finance our operations, complete the development and commercialization of fosgonimeton, and develop and commercialize other and future drug candidates. If we are unable to raise this funding when needed, we may be forced to delay, reduce, or eliminate our drug product development programs or other operations.
- The regulatory approval processes of the U.S. Food and Drug Administration, or FDA, and other comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our drug candidates, we will not be able to commercialize, or will be delayed in commercializing, our drug candidates, and our ability to generate revenue will be materially impaired.
- We rely on third parties to conduct our nonclinical studies and clinical trials. If these third parties do not properly and successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval of or commercialize our drug candidates.
- Even if approved, our drug candidates may not achieve adequate market acceptance among physicians, patients, healthcare payors and others in the medical community necessary for commercial success.
- We have never commercialized a drug candidate before and may lack the necessary expertise, personnel and resources to successfully commercialize any drug products on our own or together with suitable collaborators.
- If we experience delays or difficulties in the enrollment or retention of patients in clinical trials, our regulatory submissions or receipt of necessary marketing approvals could be delayed or prevented.
- Intellectual property discovered or developed through government funded programs may be subject to federal regulations such as “march-in” rights, certain reporting requirements and a manufacturing preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights and limit our ability to contract with non-U.S. manufacturers, which could adversely affect our ability to successfully develop and commercialize our drug products.
- The market price of our common stock has been and may continue to be volatile, which could result in substantial losses for investors.
- We and certain of our directors and executive officers have been, and may in the future be, named as defendants in lawsuits that could result in substantial costs and divert management’s attention.
- Actions by activist stockholders have in the past been, and may in the future be, disruptive and could cause uncertainty about the strategic direction of our business.

Our Risk Factors are not guarantees that no such conditions exist as of the date of this report and should not be interpreted as an affirmative statement that such risks or conditions have not materialized, in whole or in part.

PART I

Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements that are based on our management's beliefs and assumptions and on information currently available to our management. This section should be read in conjunction with our audited consolidated financial statements and related notes included in Part II, Item 8 of this report. The statements contained in this report that are not purely historical are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act.

In some cases, you can identify forward-looking statements by the following words: "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "ongoing," "plan," "possible," "potential," "predict," "project," "should," "target", "will," "would" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. You should read these statements carefully because they discuss future expectations, contain projections of future results of operations or financial condition, or state other "forward-looking" information. These statements relate to our future plans, objectives, expectations, intentions and financial performance and the assumptions that underlie these statements. These forward-looking statements include, but are not limited to, statements about:

- our financial performance;
- the sufficiency of our existing cash, cash equivalents and investments to fund our future operating expenses and capital expenditure requirements;
- our ability to obtain funding for our operations, including funding necessary to develop and commercialize our drug candidates;
- the ability of our nonclinical studies and clinical trials to demonstrate safety and efficacy of our drug candidates;
- the success, cost and timing of our development activities, nonclinical studies and clinical trials;
- the rate and degree of market acceptance of our drug candidates;
- the timing or likelihood of regulatory filings and approvals;
- the potential learnings from our ACT-AD and SHAPE trials and LIFT-AD independent unblinded interim efficacy and futility analysis and their ability to inform and improve future clinical development plans;
- the potential of LIFT-AD to show clinical benefits of fosgonimeton;
- the timing and focus of our future clinical trials, and the reporting of data from those trials;
- our plans relating to commercializing our drug candidates, if approved;
- our plans and ability to establish sales, marketing and distribution infrastructure to commercialize any drug candidates for which we obtain approval;
- our ability to attract and retain key managerial, scientific and clinical personnel;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the pricing and reimbursement of our drug candidates, if approved;

- our reliance on third parties to conduct clinical trials of our drug candidates, and for the manufacture of our drug candidates for nonclinical studies and clinical trials;
- the success of competing therapies that are or may become available;
- the beneficial characteristics, safety and efficacy of our drug candidates;
- regulatory developments in the United States and other jurisdictions;
- our ability to obtain and maintain regulatory approval of our drug candidates in the United States and other jurisdictions, and any related restrictions, limitations or warnings in the label of any approved drug candidate;
- future agreements with third parties in connection with the commercialization of our drug candidates;
- our plans, capacity and capability relating to the further development and manufacturing of our drug candidates, including additional indications for which we may pursue regulatory approval;
- our plans and ability to obtain or protect intellectual property rights, including extensions of existing patent terms where available;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our drug candidates and technology;
- the outcome of legal proceedings which have been or may in the future be instituted against us and certain of our directors and officers, including the legal proceedings discussed in Part I, Item 3 — "Legal Proceedings," and elsewhere in this report;
- the actions by activist stockholders, which have in the past been, and may in the future be, disruptive and could cause uncertainty about the strategic direction of our business;
- the size and growth potential of the markets for our drug candidates, if approved for commercial use, and our ability to serve those markets;
- the potential benefits of any strategic collaboration agreements we may enter into; and
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act.

These forward-looking statements are subject to certain risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. Factors that might cause such a difference include, but are not limited to, those discussed in this report in Part I, Item 1A — “Risk Factors,” and elsewhere in this report. These statements, like all statements in this report, speak only as of their date, and we undertake no obligation to update or revise these statements in light of future developments. Our Risk Factors are not guarantees that no such conditions exist as of the date of this report and should not be interpreted as an affirmative statement that such risks or conditions have not materialized, in whole or in part.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this report, and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to unduly rely upon these statements.

This report includes our trademarks and registered trademarks, including Athira, Athira Pharma, the Athira logo, and other trademarks, trade names, or service marks of Athira. Each other trademark, trade name or service mark appearing in this report belongs to its holder. Solely for convenience, trademarks, trade names, and service marks referred to in this report are listed without ® or TM symbols, but we will

assert, to the fullest extent under applicable law, our or the rights of the applicable licensors to these trademarks, trade names, and service marks.

In this report, “we,” “our,” “us,” “Athira,” and “the Company” refer to Athira Pharma, Inc. and its wholly-owned subsidiary.

Item 1. Business.

Overview

At Athira, our scientific philosophy is rooted in the need for a healthy neuronal network to help build, restore, and maintain connections. Loss of neuronal network connections can be an underlying cause for numerous neurological diseases, which in turn may result in the loss of personal connections for people afflicted by these diseases. Our mission is to restore these neuronal networks and, in turn, personal connections by advancing bold therapies for neuronal health, thoughtfully and urgently.

We are a late clinical-stage biopharmaceutical company focused on developing small molecules engineered to restore neuronal health and slow neurodegeneration. Our approach is designed to modulate the neurotrophic hepatocyte growth factor, or HGF, system, that is critical to normal brain function and may play a key role in maintaining the health and functioning of neuronal networks. We believe that by acting on the neurotrophic HGF system and its multiple downstream signaling pathways, we may be able to enhance the body’s natural ability to protect and repair neuronal networks by reducing inflammation, promoting regeneration, and reducing disease-specific protein pathologies, thereby positively impacting the course of disease. We aim to achieve these goals by advancing our pipeline of novel small molecule compounds which are designed to and have exhibited properties in enhancing the neurotrophic HGF system in either the central nervous system, or CNS, by crossing the blood brain barrier, or BBB, or the PNS.

Over time, the body’s innate ability to heal itself deteriorates due to a variety of factors associated with the normal aging process and other internal and external factors leading to various injuries and insults at the cellular and molecular level. In the case of neurodegenerative diseases, where neuronal networks may be damaged due to inflammation, oxidative stress, protein pathologies, excitotoxicity, or synaptic dysfunction, the neurotrophic HGF system function is often reduced, thereby limiting the body’s ability to protect and repair neurodegeneration. Hallmarks of neurodegeneration include neuronal damage, loss of network connectivity, loss of function and, ultimately, disease progression.

Scientific evidence supporting the neurotrophic HGF system as a naturally occurring repair mechanism is backed by over 30 years of research, which includes establishing its multimodal mechanism of action and critical role to healthy nervous system functioning. HGF’s receptor, known as MET, is one of the most stably expressed genes in the adult human brain and is a signature of a healthy, viable nervous system. In Alzheimer’s disease, or AD, neuronal MET expression is reduced in the brains of patients by approximately 25% and 75% in the frontal cortex and hippocampus, respectively. And although evidence supports the HGF/MET signaling system as an attractive target with its multimodal mechanism of action for combating neurodegenerative diseases, it has proven a difficult drug target. There are approved and in-development gene therapy approaches to increase HGF expression beyond normal physiological levels, but these are limited primarily due to challenges with delivery. Athira has chosen a different approach. Athira’s novel approach is to positively modulate the neurotrophic HGF system through our proprietary small molecules.

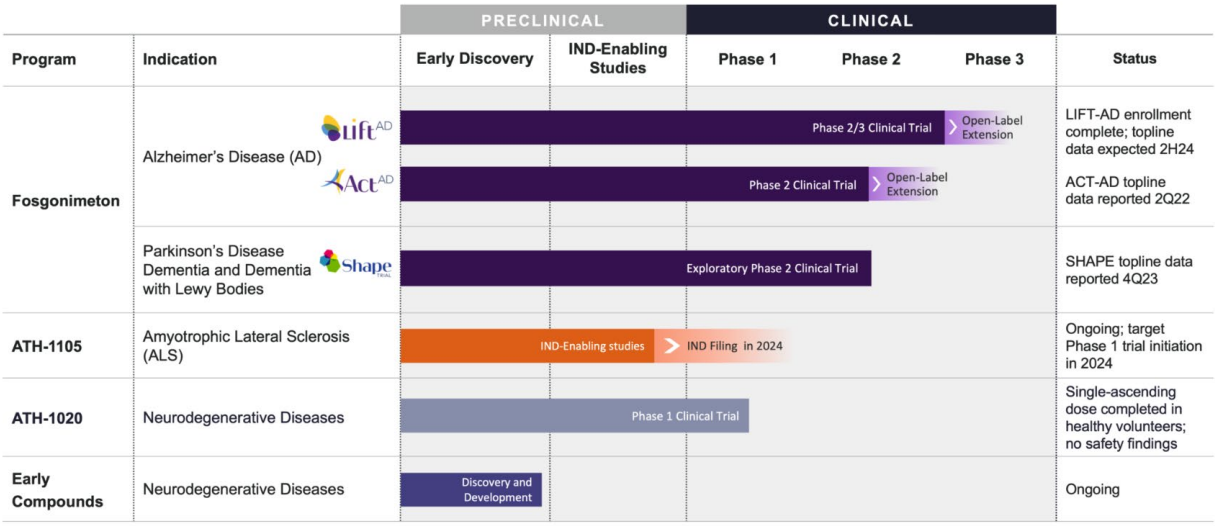
We have developed and tested preclinically a series of novel small molecule drug candidates, of which three candidates are in, or nearing, clinical phase, that we believe show promising evidence in modulating the neurotrophic HGF system and producing potential multimodal downstream effects. Our pipeline consists of both BBB permeable and peripherally restricted drug candidates for CNS, PNS and other indications. Today, our most advanced drug candidate is fosgonimeton (formerly known as ATH-1017), which is currently being evaluated in a Phase 2/3 clinical trial for mild-to-moderate AD, and has recently completed an exploratory Phase 2 clinical trial for Parkinson’s disease dementia, or PDD, and dementia

with Lewy bodies, or DLB. We are also evaluating other drug candidates for the potential treatment of neuropathic pain, amyotrophic lateral sclerosis, or ALS, Parkinson's disease, or PD, and other neurodegenerative diseases. For example, ATH-1020 completed a Phase 1 single ascending dose, or SAD, evaluation in healthy volunteers and is under consideration for further testing in neuropathic pain and/or neurodegenerative diseases and we expect to submit an Investigational New Drug, or IND, application for ATH-1105 in ALS and initiate a Phase 1 clinical trial in the first half of 2024.

Our Pipeline

Figure 1 below illustrates the current development stage of our proprietary drug candidates and early discovery and development programs. Our pipeline consists of both BBB permeable and peripherally restricted drug candidates for CNS, PNS and other indications. In addition, we are exploring the use of our proprietary ATH compounds in additional indications in the CNS and PNS as we aim to improve neuronal health in multiple neurodegenerative diseases. Our drug discovery efforts are focused on designing and testing new early compounds to enhance the neurotrophic HGF system for a variety of clinical applications.

Figure 1. Summary of Our Preclinical and Clinical ATH Programs.



Fosgonimeton (ATH-1017)

Our lead drug candidate, fosgonimeton, is a potentially first-in-class small molecule designed to positively modulate the neurotrophic HGF system for potential treatment of CNS disorders.

Alzheimer's Disease

The effects of fosgonimeton in its primary target indication, AD, are currently being evaluated in multiple clinical trials:

- In vitro studies in primary neuron cultures with fosgonimeton active metabolite, or fosgo-AM, showed enhanced synaptogenesis and neurite outgrowth, supporting the neurotrophic effects of positively modulating the neurotrophic HGF system. Treatment of primary neuron cultures with fosgo-AM prevented neuron death when exposed to several neurotoxic insults, supporting the neuroprotective effects of positively modulating the neurotrophic HGF system. In an animal model of cognitive deficit and dementia, treatment with fosgo-AM rescued this cognitive impairment. In a separate inflammation-induced animal model of cognitive impairment, fosgonimeton also reversed cognitive deficits. These study results were published in Neurotherapeutics in December 2022 and support the therapeutic potential of fosgonimeton to promote neuroprotective and anti-inflammatory effects and procognitive benefits in animal models of dementia.

- Fosgonimeton was assessed in a Phase 1a/b clinical trial and was well tolerated in healthy young and elderly volunteers and AD subjects, without serious adverse events. This clinical trial recruited a total of 88 participants, including 11 with mild to moderate AD, who were randomly assigned to active and placebo groups. Findings from the Phase 1 trial provided safety data, as well as translational and supportive evidence of fosgonimeton crossing the BBB and improving brain network activity by significantly improved event-related potential, or ERP, P300 latency. P300 latency is a functional measure that is highly correlated with cognition; however, we have not yet established a connection between these ERP P300 latency results and improved cognition. Trial results were published in the Journal of Alzheimer's Disease in April 2022, and helped inform the study design of our exploratory Phase 2 ACT-AD and Phase 2/3 LIFT-AD trials.

- ACT-AD* was a randomized, double-blind, placebo-controlled, parallel-group 26-week exploratory Phase 2 clinical trial in mild-to-moderate AD, with ERP P300 latency as the primary endpoint. Initiated in November 2020, the trial was designed to better characterize the overall effects of fosgonimeton on working memory processing speed and cognitive measures and inform the Phase 2/3 LIFT-AD trial. Topline results for this exploratory Phase 2 ACT-AD trial were announced in June 2022, and the primary and all secondary endpoints were not met by protocoled analysis. However, a post hoc analysis of results from ACT-AD in a pre-specified subgroup suggested positive effects on measures of cognition, function and neurodegeneration in participants taking fosgonimeton alone without background acetylcholinesterase inhibitors, or AChEIs. Additionally, data from post hoc analysis of plasma biomarkers from participants on fosgonimeton without background AChEIs showed descriptive improvements (non-statistically significant) in markers of neuroinflammation and AD-specific protein pathologies when compared to placebo. Fosgonimeton was generally well tolerated in the ACT-AD study, with a favorable safety profile, and there were no treatment related serious adverse events or deaths observed.

- LIFT-AD is a randomized, double-blind, placebo-controlled, parallel-group 26-week Phase 2/3 clinical trial with fosgonimeton for the treatment of mild-to-moderate AD. In September 2020, we began site initiation and patient screening for LIFT-AD. The primary endpoint for the Phase 2/3 LIFT-AD trial will be measured by the Global Statistical Test, or GST, which is a composite score that combines the scores from cognition (Alzheimer's Disease Assessment Scale-Cognitive Subscale, or ADAS-Cog11), and function (Alzheimer's Disease Cooperative Study-Activities of Daily Living, or ADCS-ADL23). Guided by the results from the completed exploratory ACT-AD Phase 2 trial, in September 2022, we proactively amended LIFT-AD to focus on participants not on background AChEIs. In October 2022, we announced that following an unblinded interim efficacy and futility analysis, an independent data monitoring committee, or DMC, recommended continuation of the LIFT-AD trial. The committee also determined that, with the additional enrollment of fewer than 150 participants for a total enrollment of less than 300 participants without background AChEIs, the amended trial will be well powered for the primary endpoint given the preliminary effect size observed. In May 2023, we further amended LIFT-AD to focus on 40 mg dosing, which we have selected for further development and as the potential dose for regulatory approval of fosgonimeton in this indication. This selection was based on a review of the totality of the preclinical and clinical data, biomarker results, observations from the open label extension study and in consultation with independent regulatory and biostatistical consultants based on patients treated with 40 mg fosgonimeton without concomitant AChEIs. In January 2024 we announced the completion of enrollment with a total of approximately 315 patients randomized. We expect to report topline LIFT-AD results in the second half of 2024. In July 2023, we completed an end of Phase 2 meeting with the FDA to gain alignment on our plans for the continued clinical development of fosgonimeton as a treatment for mild-to-moderate AD. During this meeting we provided an update and discussed with the FDA the ongoing LIFT-AD trial, including use of the 40 mg dose, concomitant AChEIs use, biomarker analyses including neurofilament light chain, or NfL, and the statistical analysis plan, or SAP. The FDA noted the importance of showing effects on both cognition (ADAS-Cog11) and function (ADCS-ADL23) in the trial population. The FDA is open to ongoing dialogue with us regarding the LIFT-AD trial once completed as well as other aspects of our program to develop fosgonimeton as a potential treatment for mild-to-moderate AD.

- In July 2021, we announced that we are enrolling participants into a 26-week open-label extension trial*, or OLEX*, for our LIFT-AD and ACT-AD clinical trials, allowing us to collect up to a total of one year of safety data with fosgonimeton. In May 2022, we announced that we extended the 26-week OLEX for our LIFT-AD and ACT-AD clinical trials for an additional 12 months, enabling eligible participants who have completed either trial and elect to participate in the ongoing OLEX to receive up to 18 months of open-label treatment with fosgonimeton. In May 2023, we amended the OLEX to further extend the trial by an additional 12 months. Eligible participants who have completed the LIFT-AD or ACT-AD trials and elect to participate in the ongoing OLEX may now receive up to 30 months of open-label treatment, which allows us to collect up to 36 months total of long-term exposure data.

  **The ACT-AD trial and the related OLEX for ACT-AD participants have been supported by a grant from the National Institute on Aging of the National Institutes of Health under Award Number R01AG06268. The information presented is solely the responsibility of Athira and does not necessarily represent the official views of the National Institutes of Health.*

Parkinson's Disease

In PD-relevant cellular and animal models, treatment with fosgonimeton or fosgo-AM resulted in significant neuroprotective and neurotrophic effects as well as improvements in motor function. Fosgo-AM significantly protected against neurotoxic insults and reduced PD-related toxic protein (α-synuclein) aggregation in neuron-based models of disease. Neurotrophic effects, with or without neurotoxic insults, were significantly enhanced following fosgo-AM treatment. Cellular effects translated to improvements in motor function in an animal model, including improved coordination, balance and strength. These data were presented at the Society for Neuroscience Annual Conference in November 2022, the American Society for Experimental Neurotherapeutics Annual Meeting in March 2023, and at the AD/PD Conference in March 2023.

In December 2023, we announced the completion of the 28-patient exploratory Phase 2 SHAPE trial, which tested 40 and 70 mg fosgonimeton doses versus placebo in PDD and DLB. The primary endpoint of the trial, a composite score of the change in ERP P300 latency and cognitive assessment (ADAS-Cog13), was not met by protocoled analysis compared with placebo. Directionally positive results were observed for the 40 mg fosgonimeton dose group with improvements in cognitive, functional and biomarker measurements. In particular, the five patients in the modified intent to treat (mITT) population treated with fosgonimeton 40 mg once daily saw improvement in ADAS-Cog13 individually, and collectively improved compared with placebo (n=7 mITT, one-sided p=0.0321). Results for patients in the 70 mg dose group were inconsistent.

ATH-1105

ATH-1105 is a novel, orally available, next generation, small molecule drug candidate designed to positively modulate the neurotrophic HGF system.

Amyotrophic Lateral Sclerosis

In preclinical models of ALS, treatment with ATH-1105 resulted in improvements in motor neuron survival and function. In vitro, ATH-1105 treatment protected spinal motor neurons from glutamate toxicity and prevented accumulation of toxic protein aggregates. In a preclinical mouse model of ALS, treatment with ATH-1105 significantly prevented loss of body weight, and improved motor function including balance, coordination and muscle strength. We additionally reported that treatment with ATH-1105 significantly improved electrophysiological measures of functional nerve signaling and protected against motor neuron axon degeneration and demyelination. ATH-1105 treatment also significantly reduced biomarkers of inflammation and neurodegeneration and prolonged survival. Study results were presented at the Motor Neurone Disease Association International Symposium in December 2022 and 2023. Weight loss, motor deficits, inflammation, loss of functional nerve signaling, and motor neurondegeneration and demyelination are all hallmarks of ALS disease; treatment with ATH-1105 significantly improved all of these aspects in the preclinical models tested. We expect to submit our IND application for ATH-1105 and initiate a Phase 1 clinical trial in the first half of 2024.

ATH-1020

ATH-1020 is a novel, orally available, next generation, small molecule drug candidate designed to positively modulate the neurotrophic HGF system. We filed an IND application with the FDA for ATH-1020 at the end of 2021 and received notice of acceptance in January 2022. This compound was originally assessed for neuropsychiatric indications in preclinical models as presented at the American Society for Experimental Therapeutics Annual Conference in February 2022.

Neuropathic Pain

In preclinical models of diabetic neuropathic pain, we demonstrated significant improvements in two aspects of disease that are prominent symptoms in people suffering from neuropathic pain: increased sensitivity to mechanical and thermal stimulation. The significant improvements in neuropathic pain were partially sustained after seven days of not receiving ATH-1020, suggesting persistent and potentially disease-modifying effects. Data from these studies were presented at the Society for Neuroscience Annual Conference in November 2022 and the American Society for Experimental Neurotherapeutics in March 2023. We have completed the SAD escalation portion of our Phase 1 trial, in which ATH-1020 demonstrated a favorable safety profile and which was well-tolerated in healthy volunteers. We plan to evaluate options with this compound and will consider its advancement in relation to other opportunities and resources.

Early Compounds

In addition to the compounds described above, we have several other compounds in preclinical discovery and development for neurodegenerative diseases and other indications where we believe positive modulation of the neurotrophic HGF system may have therapeutic potential.

Upcoming Pipeline Milestones

- For AD, we anticipate reporting topline data for our Phase 2/3 LIFT-AD trial in the second half of 2024. At the end of 2023, our ongoing OLEX trial for completers of ACT-AD and LIFT-AD had a greater than 85% participation rate. As with any voluntary clinical trial, participant dropout in the OLEX has also been observed. In 2024, we anticipate continuation of the OLEX trial and continued collection of long-term fosgonimeton safety data.

- We plan to file an IND application and initiate first-in-human studies of ATH-1105 as a treatment for ALS in the first half of 2024.

Our Strategy

Our strategic imperative and responsibility to people with neurological diseases is to advance our pipeline of small molecule drug candidates designed to target and enhance this naturally occurring repair mechanism to help build, restore, and maintain healthy neuronal connections. The multimodal mechanism of action of the neurotrophic HGF system has the potential to address complex multifactorial neurological diseases. We are encouraged by the scientific evidence we have generated thus far and will continue adding to the scientific foundation behind this neuroprotective and reparative approach with the potential to transform the treatment paradigm and provide meaningful therapeutic options for AD, PD, ALS, neuropathic pain, and other neurodegenerative diseases and neurological disorders, where limited effective options exist today. Key aspects of our business strategy to achieve these goals are to:

- *Advance fosgonimeton through clinical development for mild-to-moderate AD.* We believe fosgonimeton has the potential to rapidly improve cognition and function to help improve the lives of the millions of people suffering from AD who currently have limited therapeutic options. We initiated both the exploratory Phase 2 ACT-AD trial and the ongoing Phase 2/3 LIFT-AD trial in 2020 and have applied learnings from the completed ACT-AD trial to help inform the LIFT-AD trial. The topline results for our ACT-AD trial were announced in June 2022 and are discussed in further detail in the section of this Annual Report on Form 10-K titled "Business—Our Pipeline." While the primary and secondary endpoints were not achieved, encouraging results from our post hoc analyses of a subgroup in the ACT-AD trial informed our decision to proactively amend LIFT-AD to focus on participants not on background AChEIs and the independent unblinded interim analysis further supported our decision. We announced completed enrollment for the LIFT-AD trial in January 2024 and anticipate reporting topline data in the second half of 2024.

- *Expand the development of fosgonimeton to maximize opportunities in AD.* We are developing fosgonimeton as a treatment for mild-to-moderate AD, but over time we aim to expand development of fosgonimeton to cover more stages of AD, either delivered alone or in combination with other approved therapies.

- *Advance innovative research to expand and develop our ATH pipeline of small molecule drug candidates.* Our strategy is to advance drug candidates that show both strong pharmacokinetics and pharmacodynamics, or PK/PD, translation and early predictive clinical data. We plan to continue growing our discovery organization across neurological disorders in general, but with a near-term focus on neurodegenerative diseases, by building upon the strong foundational knowledge of our ATH positive modulators and enhancing the multimodal mechanism of action through the neurotrophic HGF system. It is our goal to advance our pipeline of next generation ATH positive modulators, designed to enhance the body's naturally occurring repair mechanism. With several drug candidates in development, we will prioritize development to potentially address a wide range of clinical applications ranging from CNS and PNS diseases to other indications. Our ATH-1105 program targeting ALS is our next priority beyond fosgonimeton, with an IND application and first-in-human studies expected to be initiated in the first half of 2024.

- *Optimize the value of fosgonimeton and next-generation positive modulators of the neurotrophic HGF system in major markets.* We own worldwide rights to fosgonimeton as well as our pipeline of next generation, proprietary small molecule drug candidates. We plan to develop and pursue approval of fosgonimeton and other future drug candidates across major markets. Where appropriate, we may use strategic collaborations or partnerships to accelerate development and maximize the commercial potential of our programs.

Mechanism of Disease

Causes of neurodegenerative diseases are not fully understood as these diseases are complex with several contributing factors including inflammation, oxidative stress, neurotoxicity, excitotoxicity, synaptic dysfunction, and protein pathologies that ultimately lead to neuronal damage, neuronal network degeneration and a decline in function. Intrinsic to these diseases is the disruption of a healthy neuronal network that can be overcome and repaired or maintained when the body's natural repair mechanisms are intact. However, a loss of or reduction in ability of the body to repair itself can lead to dysregulation that then manifests as symptoms and overall functional decline. One such naturally occurring repair mechanism is the neurotrophic HGF system.

Scientific evidence supporting the neurotrophic HGF system as a naturally occurring repair mechanism is backed by over 30 years of research. MET is one of the most stably expressed genes in the adult human brain and is a signature of a healthy, viable nervous system, In AD, neuronal MET expression is reduced in the brains of participants by approximately 25% and 75% in the frontal cortex and hippocampus, respectively. And although evidence supports the neurotrophic HGF system as an attractive target for combating neurodegenerative diseases with its multimodal mechanism of action, it has proven a difficult drug target. There are approved and in-development gene therapy approaches to increase HGF expression beyond normal physiological levels, but these are limited as potentially viable treatment options for neurological disorders due to more invasive delivery requirements, such as intrathecal or intravenous, or locally restricted to the periphery, such as via intramuscular routes of administration.

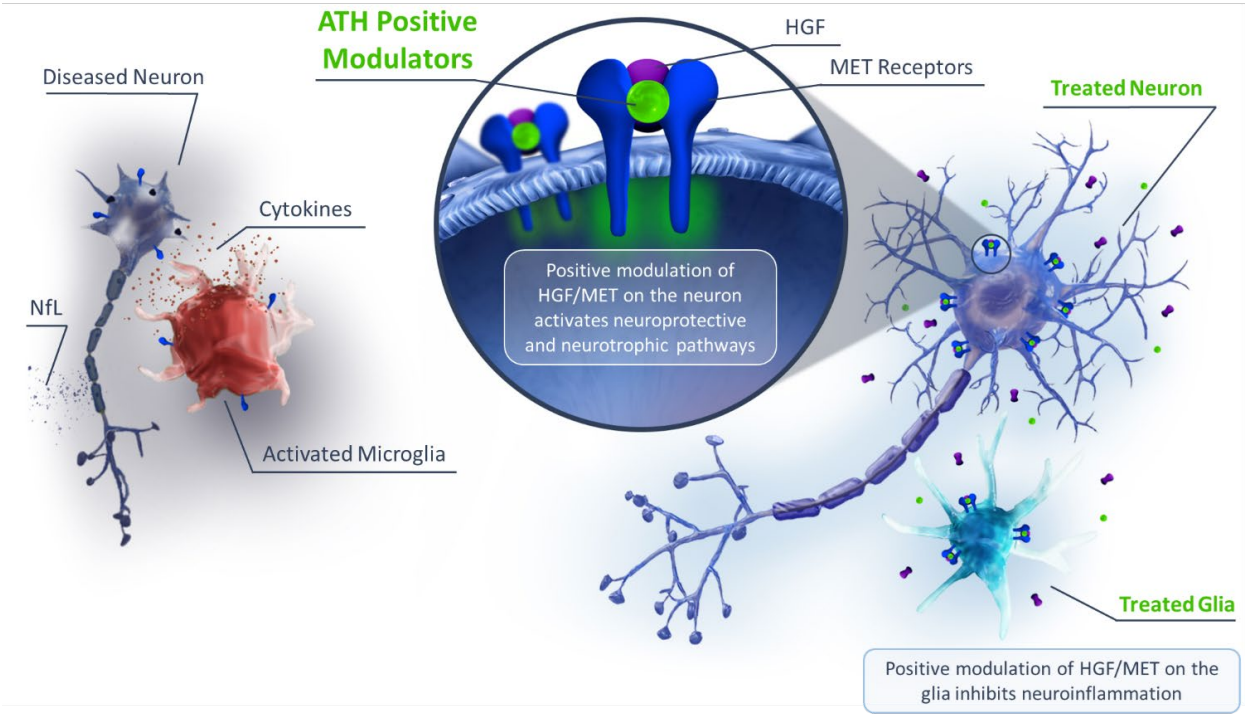
To date, drug developers have been deploying approaches that typically address only a single factor of the cascade of pathologies that lead to neurodegeneration, yet translating early successful results to meaningful clinical benefit has been mixed if not elusive. We believe that to address such complex and multifactorial diseases requires a novel multimodal approach, such as targeting the neurotrophic HGF system through non-invasive or minimally invasive small molecules that enhance innate levels of HGF system activation to protect and repair neuronal networks.

Mechanism of Action

We have developed a pipeline of proprietary small molecule compounds, or ATH positive modulators, designed to enhance the neurotrophic HGF system and promote its neuroprotective, neurotrophic and anti-inflammatory effects, including protection of neurons from a variety of insults. Our novel small molecules are designed to cross the blood-brain barrier for CNS disorders or remain in the periphery for PNS and other indications, and mechanistically produce a series of multimodal effects that support their therapeutic promise to: reduce inflammation, promote regeneration, provide neuroprotection, and, ultimately, slow disease progression.

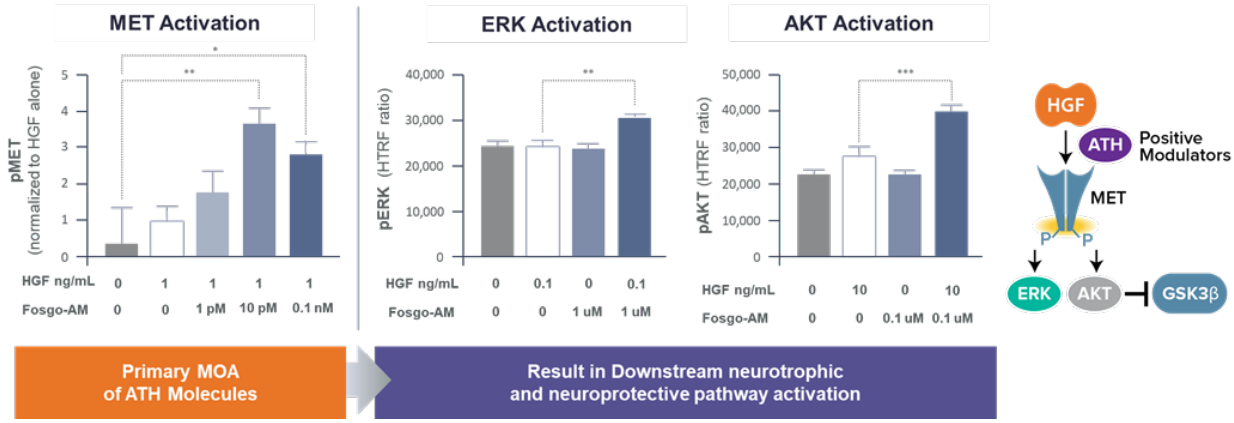
Figure 2 below illustrates the hypothesized mechanism of action of ATH positive modulators and the cellular disease state where diseased neurons generate a biomarker of neurodegeneration, NfL, as well as other signature markers of neuronal damage. Contributing to a diseased neuron are also proinflammatory cytokines produced by activated microglia. In the treated neuron state where ATH positive modulators are designed to enhance HGF/MET signaling to promote neuroprotective and neurotrophic pathways, reduced neuron degeneration and NfL production occur while the treated glia show reduced activation and production of proinflammatory cytokines, illustrating the potential reduction in neurodegeneration and inhibition of neuroinflammation through the enhancement of the neurotrophic HGF system.

Figure 2. Hypothesized Mechanism of Action of ATH Positive Modulators.



As ATH positive modulators interact with the HGF system, neurotrophic and neuroprotective pathways are activated downstream, including the activation of the extracellular-signal regulated kinase, or ERK and protein kinase B, or AKT pathways, which play critical roles in protecting neurons from damage and death, including from oxidative stress, excitotoxicity, and apoptosis. Figure 3 below shows cell culture data demonstrating that one of the key mechanisms of action of ATH positive modulators is through activation of ERK and AKT via MET activation.

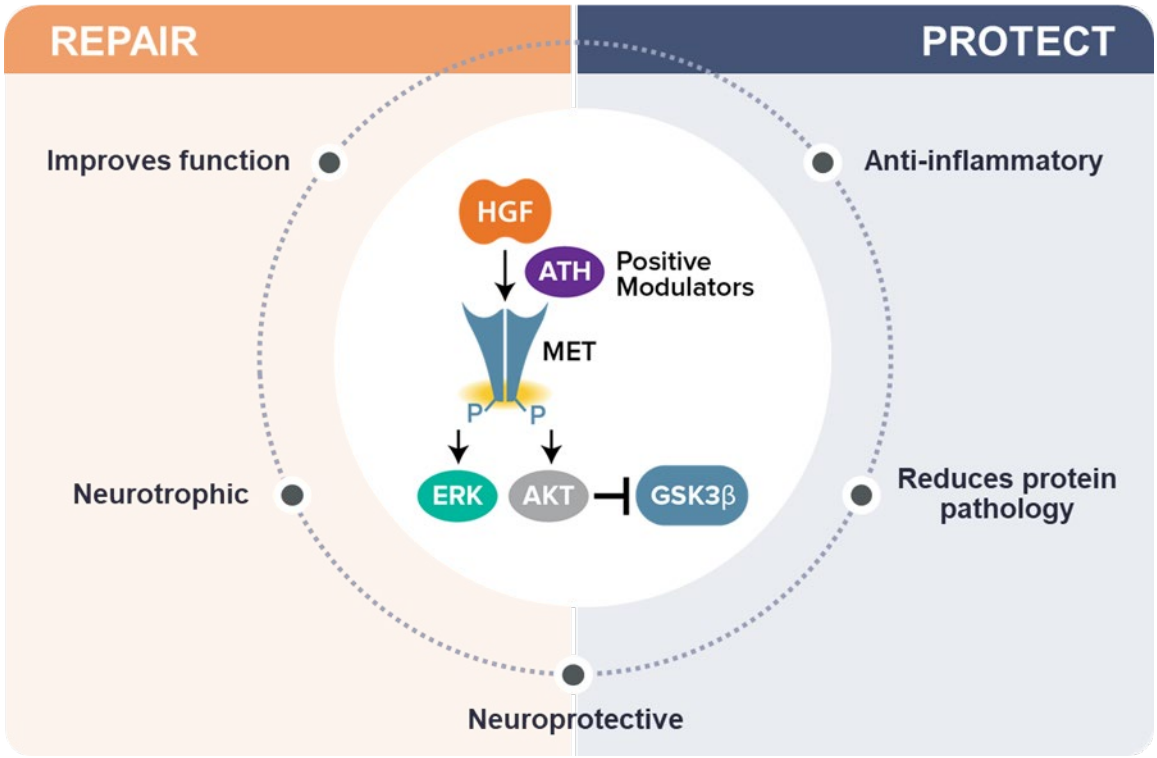
Figure 3. Enhancement of HGF/MET by Fosgo-AM Activates ERK and AKT Signaling Pathways.



Data presented as mean + SEM. Statistics applied: One-way ANOVA with Tukey's multiple comparisons.
** p<0.01; *** p<0.001 vs. HGF only.
AKT, protein kinase B; ERK, extracellular-signal regulated kinase; Fosgo-AM, fosgonimeton active metabolite; GSK3b, glycogen synthase kinase-3 beta; HGF, hepatocyte growth factor.

Positively modulating the neurotrophic HGF system promotes its multimodal effects, which we believe can potentially address the complex pathology in neurodegenerative diseases. These positive multimodal effects taken together may lead to improvement in function. Figure 4 below illustrates the therapeutic potential of enhancing the neurotrophic HGF system to protect and repair neurons.

Figure 4. ATH Compounds are Designed to Protect and Repair Neuronal Networks.



Fosgonimeton

Fosgonimeton is being assessed in multiple preclinical and clinical studies of neurodegenerative diseases, including AD and PD.

Fosgonimeton for AD - Clinical Trials and FDA Interaction

Phase 1 Clinical Trial

The IND application for fosgonimeton in AD was submitted in September 2017. Since then, we have completed our Phase 1 clinical trial, which enrolled a total of 88 participants, including 48 healthy young male participants (mean age = 33.4 ± 6.3), 29 healthy elderly participants (mean age = 63.8 ± 4.0; 14 male, 15 female), and 11 AD participants (mean age = 69.2 ± 7.1; 5 male, 6 female, median [range] Mini-Mental State Exam, or MMSE, = 20 [5–29]) was completed in 2019. In both the SAD and multiple ascending dose, or MAD, parts of the trial, fosgonimeton was well tolerated, without serious adverse events. All participants were randomly assigned to active and control groups. Findings from the Phase 1 trial provided safety data, as well as translational and supportive evidence in the form of quantitative electroencephalography, or qEEG, measures to evaluate effects of fosgonimeton on brain activity in study participants. Results from qEEG measures demonstrated fosgonimeton crossing the BBB and improving brain network activity by significantly improved ERP P300 latency, a measure of working memory processing speed, over 8-days. Trial results were published in the Journal of Alzheimer's Disease in April 2022, and helped inform the study design of our exploratory Phase 2 ACT-AD and Phase 2/3 LIFT-AD trials.

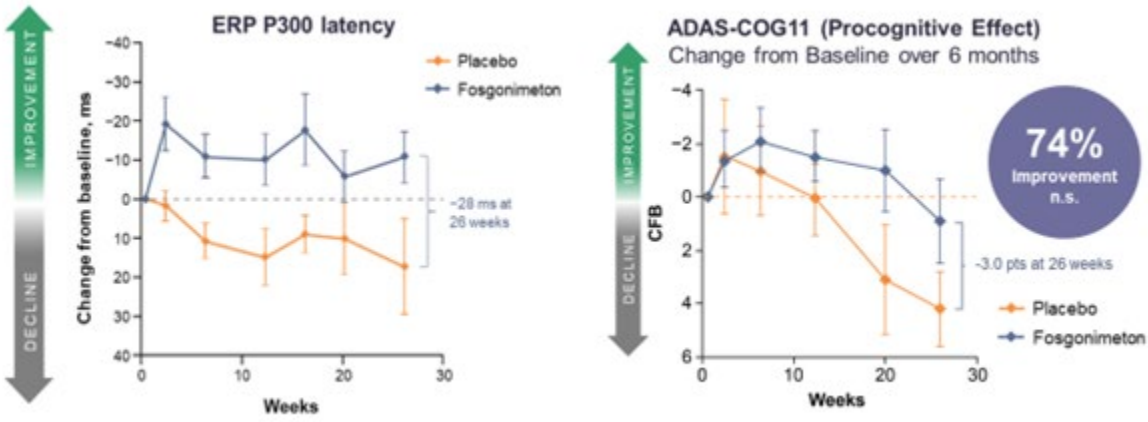
*Phase 2 ACT-AD Trial**

ACT-AD was a randomized, double-blind, placebo-controlled, parallel-group 26-week trial evaluating fosgonimeton in participants with mild-to-moderate AD. The trial enrolled 77 participants in the United States and Australia (age 55 to 85 years, MMSE score of 14-24 and Clinical Dementia Rating, or CDR, scale global score of 1 or 2). Participants were allowed to continue receiving background AChEIs; 60% remained on stable doses of AChEIs and 40% were not receiving AChEIs during the study. Participants were randomized 1:1:1 to receive placebo or fosgonimeton at either 40 mg/day or 70 mg/day. The primary endpoint for ACT-AD was ERP P300 latency, a measure of working memory processing speed, measured by change from baseline, or CFB, averaged over Weeks 12, 16, 20, and 26. Secondary endpoints included correlation of CFB in ERP P300 latency with a composite score of cognition and executive memory defined by ADAS-Cog11, and the Controlled Oral Word Association Test, or COWAT; various composite scores of clinical assessments as measured by the GST, Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change, or ADCS-CGIC, a measure of global clinical change; and ADCS-ADL23, a measure of functional change as well as measures of caregiver burden, quality of life, resource utilization, and psychiatric symptoms. Plasma samples were also bio banked for future analysis. Safety data was evaluated throughout.

ACT-AD was completed in 2022; topline data was reported in June 2022, later presented at the Alzheimer's Association International Conference in August 2022, and in early 2023 was finalized. The finalized data show some numerical differences from the previously reported preliminary topline data, which we had reported were not statistically significant (n.s.). As reported previously, we did not meet the primary endpoint of a statistically significant change in ERP P300 latency by protocoled analysis nor did we meet the secondary endpoints. However, the data showed a numerical improvement in the functional measure of ADCS-ADL23, which evaluates participants' activities of daily living as assessed by their caregivers, compared to placebo at 26 weeks (41% or +1.7 points improvement, n.s.). Although not statistically significant, a post hoc analysis of results from ACT-AD in a pre-specified subgroup suggested positive effects on measures of working memory processing speed and cognition, plus improvements in plasma biomarkers of neurodegeneration, inflammation and AD-specific protein pathologies in participants taking fosgonimeton alone without background AChEIs. All data and analyses presented are from pooled 40mg and 70mg of fosgonimeton. During the ACT-AD trial, fosgonimeton, at either dose, was generally well tolerated with a favorable safety profile, and there were no treatment related serious adverse events or deaths observed.

In participants treated with fosgonimeton alone, a potentially beneficial change in ERP P300 latency (-28 milliseconds, n.s.), as well as cognitive improvement, as measured by ADAS-Cog11 (74% or -3.0 points, n.s.), compared with placebo at 26 weeks was observed post hoc (Figure 5).

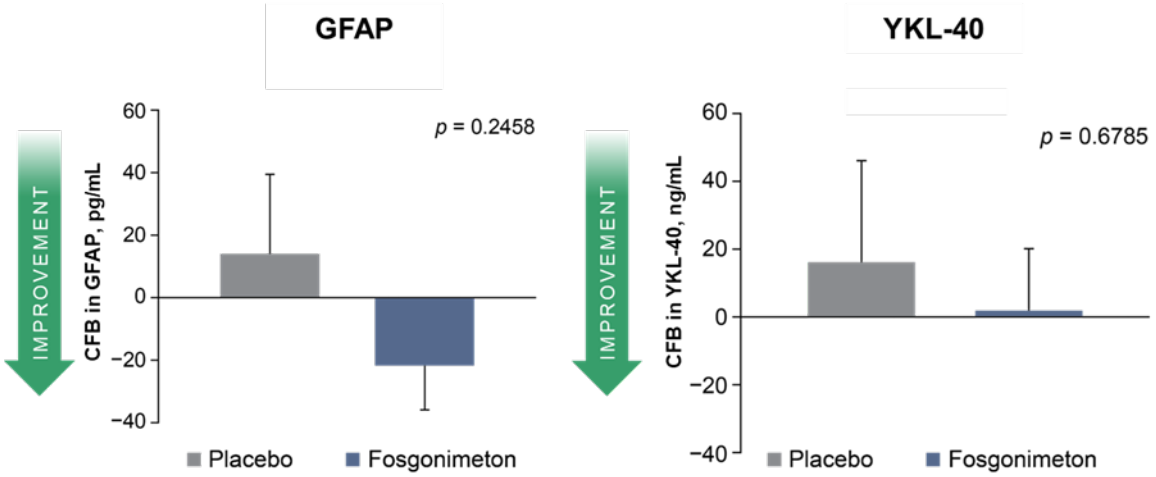
Figure 5. Treatment with Fosgonimeton Results in Consistent Directional Improvements in Working Memory Processing Speed and Cognition.



Data from ACT-AD were additionally analyzed post hoc for effects across plasma biomarkers in participants treated with fosgonimeton without background AChEIs. In concert with the multimodal mechanism of action, targeting the neurotrophic HGF system with fosgonimeton resulted in directional improvements across plasma biomarkers of inflammation and AD-specific protein pathologies, and a statistically significant improvement in neurodegeneration, all of which are pending further analysis and clinical investigation in our ongoing Phase 2/3 LIFT-AD clinical trial.

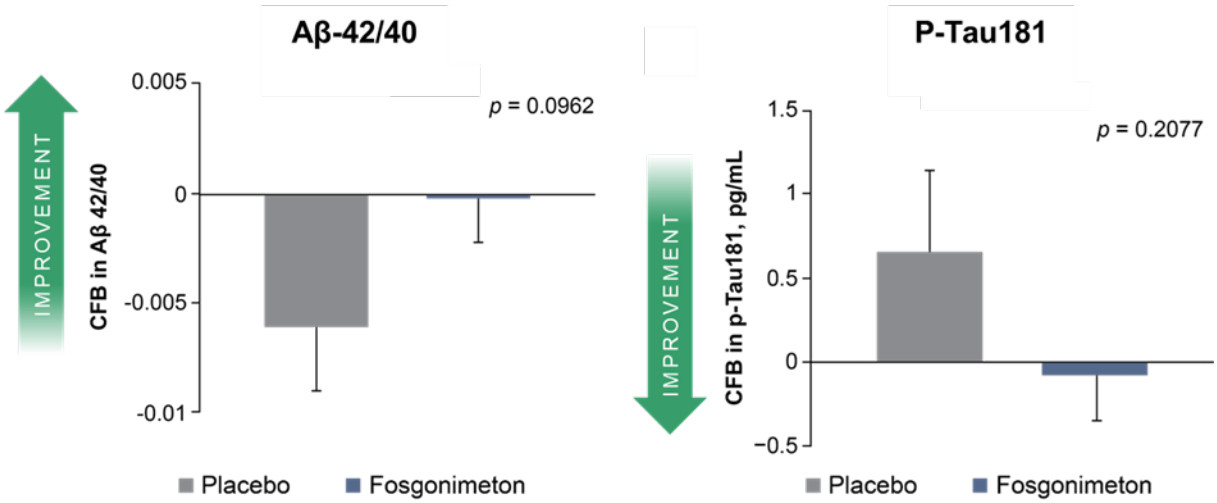
Figure 6 below shows that treatment with fosgonimeton appears to improve neuroinflammation in mild-to-moderate AD as measured by glial fibrillary acidic protein, or GFAP, and chitinase-3-like protein 1, or YKL-40. The observed nominal GFAP improvement and statistical trend in YKL-40 improvement, plus the magnitude of decrease below baseline for those on active treatment is encouraging in this continuously progressive condition and indicates the translation of the anti-inflammatory effects of fosgonimeton.

Figure 6. Treatment with Fosgonimeton Appears to Improve Neuroinflammation.



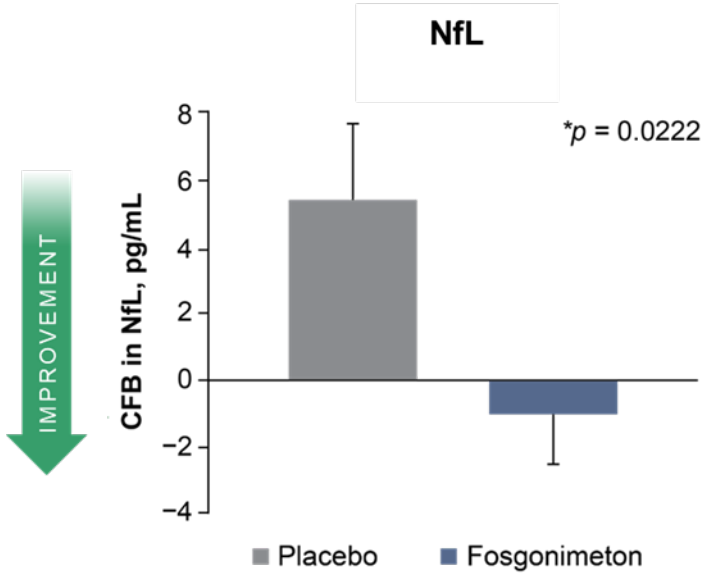
Treatment with fosgonimeton additionally resulted in a statistical trend and directional improvements in plasma biomarkers of AD-specific protein pathologies, Aβ and pTau, respectively. The changes observed, as shown in Figure 7, continue to support the relevance of targeting the neurotrophic HGF system and its relevance to AD, with a potentially disease-modifying effect by impacting these protein pathologies.

Figure 7. Treatment with Fosgonimeton Induces Directional Improvements in Protein Hallmarks of AD.



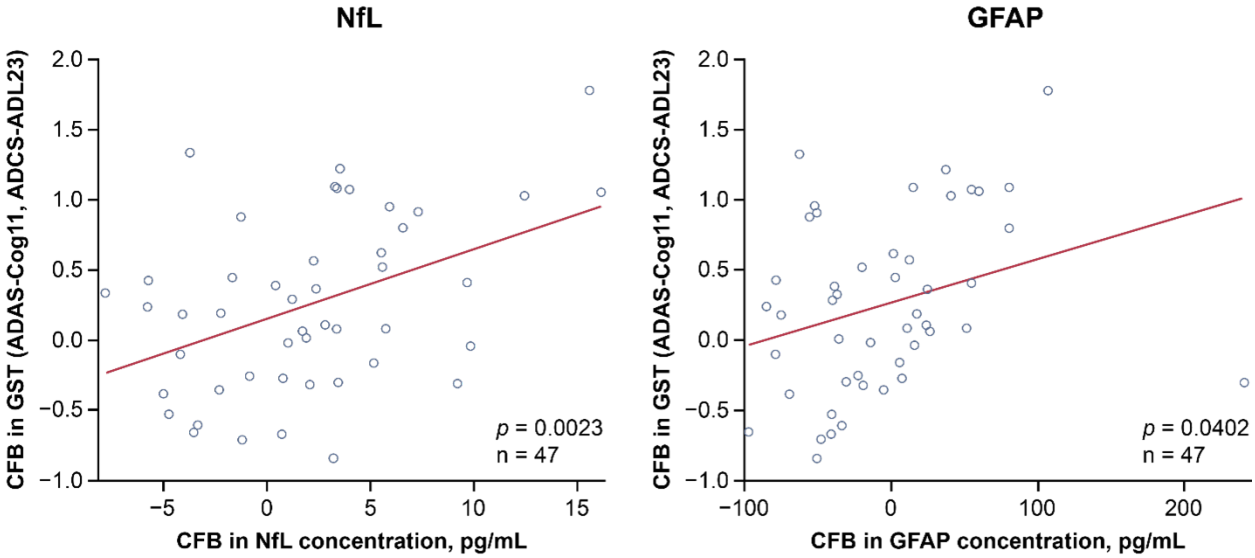
Supportive of the potentially neuroprotective mechanism of action of the neurotrophic HGF system, treatment with fosgonimeton showed a statistically significant improvement in NfL (an objective marker of neurodegeneration) levels, even to the extent of improvement below baseline (Figure 8). This decrease of NfL below baseline levels (-6.49 pg/mL, p=0.0241), is suggestive of repair in this continuously progressive condition.

Figure 8. Treatment with Fosgonimeton Shows Neuroprotective Effects.



With the potential of fosgonimeton to be both neuroprotective and anti-inflammatory for AD, we assessed the relevance or predictive value of these biomarkers potentially translating to clinical effects. A correlation analysis of NfL and GFAP with the GST, a composite endpoint of cognition (ADAS-Cog11), and function (ADCS-ADL23), and the primary endpoint of our ongoing Phase 2/3 LIFT-AD trial was performed. In Figure 9, scatterplots from the full ACT-AD trial population are shown with the CFB in the GST on the Y axis and on the X axis, CFB in NfL on the left and GFAP on the right, respectively. From this analysis, we showed the statistically significant correlation between clinical and plasma biomarker improvements, and despite the limited trial size, these data support the interpretation of the clinical results.

Figure 9. Decreases in Disease-State Biomarkers Significantly Correlate with Improvements in Cognitive and Functional Measures.



The consistent clinical effects and plasma biomarker data from this exploratory Phase 2 ACT-AD trial clinical effects and plasma biomarkers continue to support the multimodal mechanism of action by enhancing the neurotrophic HGF system through fosgonimeton and suggests that fosgonimeton may have potential benefit for Alzheimer's patients.

Phase 2/3 LIFT-AD Trial

LIFT-AD is a randomized, double-blind, placebo-controlled, parallel-group 26-week Phase 2/3 clinical trial with fosgonimeton for the treatment of mild-to-moderate AD. In September 2020, we began site initiation and patient screening. The primary endpoint for LIFT-AD will be measured by the GST, which is a composite score of cognition (ADAS-Cog11) and function (ADCS-ADL23). Guided by the results from the completed exploratory Phase 2 ACT-AD trial, in September 2022, we proactively amended LIFT-AD to focus on participants not on background AChEIs. An unblinded adjudication of drug safety was performed by the drug safety monitoring board, which resulted in no serious adverse findings to date for both participants on or off background AChEIs.

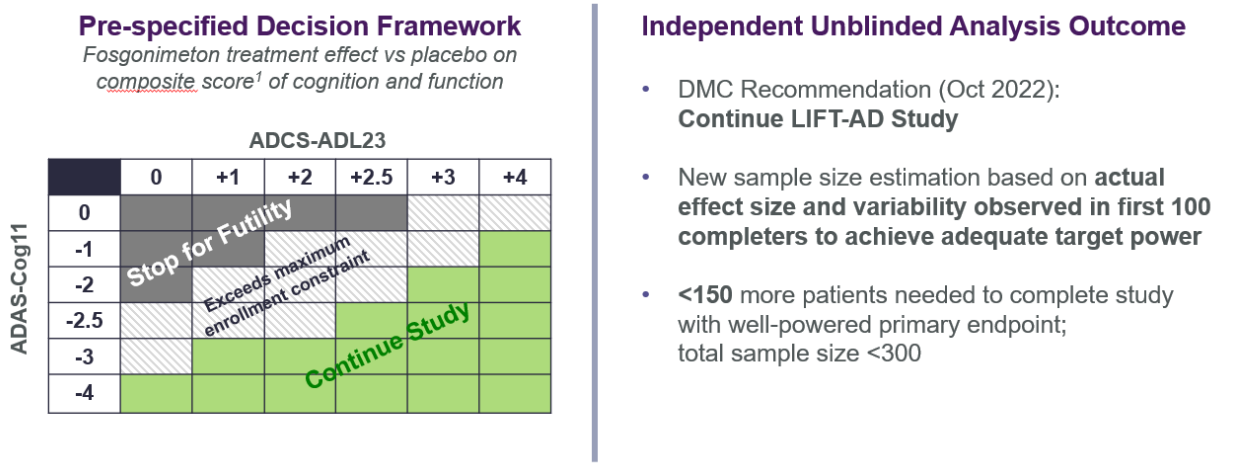
An independent DMC consisting of one neurologist and two biostatisticians, performed an unblinded efficacy and futility interim analysis using a 2011 published method by Mehta and Pocock. This adaptive method enables a sample-size re-estimation using actual observed interim data based on our co-key secondary endpoints, ADAS-Cog11 and ADCS-ADL23, which these two endpoints inform our primary endpoint, GST.

Pre-specified constraints were protocolled in the interim SAP which consisted of a sample size range with a maximum enrollment limit, and a minimum target power. The formal efficacy analysis was then based on approximately 100 completers at week 26 (end of the double-blind treatment period) without background AChEIs. The primary analysis used was a mixed model for repeated measures, or MMRM, to compare the CFB in the GST between fosgonimeton treatment and placebo. Two potential outcomes were also pre-specified: 1) to stop the study for futility or 2) to continue the enrollment within the pre-specified range to achieve an adequate target power for the primary endpoint.

Following this interim analysis, the DMC recommended to "continue LIFT-AD study" and also determined that, with the additional enrollment of fewer than 150 participants for a total enrollment of less than 300 participants without background AChEIs, the study will be well-powered for the primary endpoint given the preliminary effect size observed.

Figure 10 below shows the pre-specified decision framework and potential outcomes for the primary GST composite endpoint of cognition (ADAS-Cog11) and function (ADCS-ADL23). The shaded area in grey was pre-determined as the futility zone where the recommended sample size would exceed Athira's pre-specified maximum and shaded in green are the GST combinations resulting in a recommendation from the DMC to continue the study.

Figure 10. Independent DMC Recommends to Continue LIFT-AD after Unblinded Interim Analysis Using a Published Methodology and Pre-Specified Decision Framework.



Conducted by DMC: Chair neurologist (MD) and two biostatisticians (PhD); [1]Primary endpoint is the global statistical test, an unweighted composite of ADAS-Cog11 and ADCS-ADL23. AD, Alzheimer's disease; ADAS-Cog11, Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADCS-ADL23, Alzheimer's Disease Cooperative Study–Activities of Daily Living; DMC, data monitoring committee.

The results from the DMC unblinded analysis give us confidence in a potentially positive outcome for LIFT-AD. Stringent evaluation criteria were applied based on validated and clinically meaningful cognitive and functional outcomes, which support the potential clinical benefits and underscores the rationale for continued development of fosgonimeton.

In May 2023, we amended the LIFT-AD trial to focus ongoing enrollment and the primary analysis on the 40 mg dose versus placebo. Enrollment of the 70 mg arm of the trial was discontinued. The dose selection was based on a review of the totality of the data across preclinical and clinical studies, observations from the OLEX and in consultation with independent regulatory and biostatistical experts based on patients treated with 40 mg fosgonimeton without concomitant AChEIs.

In July 2023, we completed an end of Phase 2 meeting with the FDA to gain alignment on our plans for the continued clinical development of fosgonimeton as a potential treatment for mild-to-moderate AD. We provided an update and discussed with the FDA the ongoing LIFT-AD trial including use of the 40 mg dose, concomitant AChEI use, biomarker analyses including NfL, and the SAP.

The LIFT-AD trial is ongoing with the completion of enrollment announced in January 2024 and topline data expected in the second half of 2024.

Open Label Extension Trial*

In July 2021, we announced that we are enrolling patients into an optional 26-week OLEX for our LIFT-AD and ACT-AD clinical trials. In May 2022 and again in May 2023, we announced extensions of the 26-week OLEX for our LIFT-AD and ACT-AD clinical trials for a total of 24 additional months. These extensions enable eligible participants who have completed either trial, and elect to participate in the ongoing OLEX, to now receive up to 30 months of open-label treatment with fosgonimeton, which will allow us to collect up to a total of three years of safety data with fosgonimeton. As of year-end 2023, greater than 85% of patients who have completed either study have elected to participate in the OLEX and currently more than 60 patients have continued on OLEX beyond 18 months of investigational treatment.

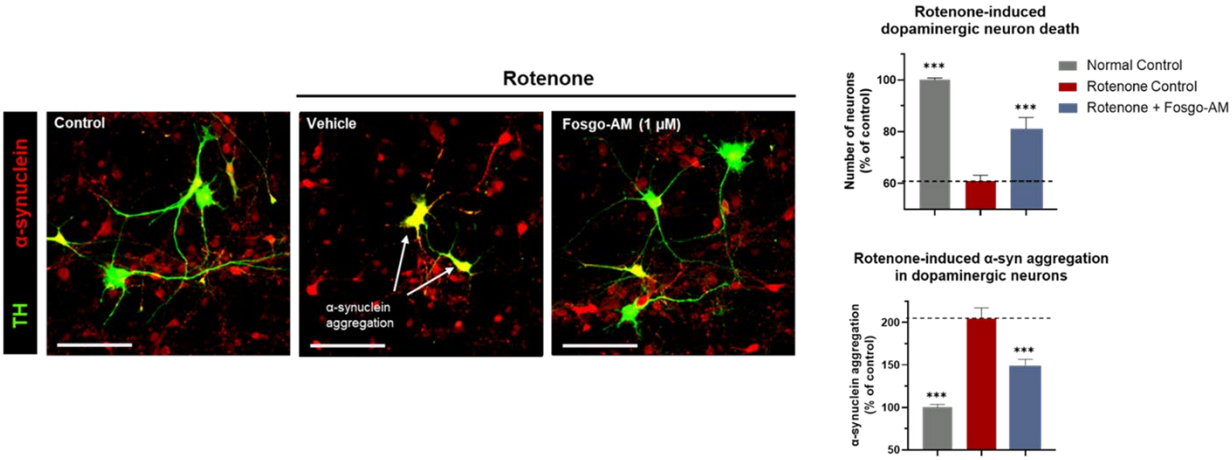
**The ACT-AD trial and the related OLEX for ACT-AD participants have been supported by a grant from the National Institute on Aging of the National Institutes of Health under Award Number R01AG06268. The information presented is solely the responsibility of Athira and does not necessarily represent the official views of the National Institutes of Health.*

Fosgonimeton for PD

In PD-relevant cellular and animal models, treatment with fosgonimeton or fosgo-AM demonstrated significant neuroprotective, neurotrophic and motor function improvements. Data supporting these findings were presented at the Society for Neuroscience Annual Conference in November 2022, the American Society for Experimental Neurotherapeutics Annual Meeting in March 2023, and at the AD/PD Conference in March 2023.

Fosgo-AM significantly protected against neurotoxic insults and minimized PD-related toxic protein buildup in neuron-based models of disease. Figure 11 below shows results from cell models of PD exposed to the neurotoxin rotenone. Tyrosine hydroxylase, or TH+, staining in green identifies dopaminergic neurons, the neurons primarily affected in PD, and α-synuclein staining in red identifies the toxic aggregates found in PD pathology. The leftmost image shows cultures not exposed to rotenone toxin where TH+ dopaminergic neurons are abundant with robust neurites and minimal accumulation of α-synuclein within the cell. In the rightmost image, treatment with fosgo-AM significantly preserved the number of healthy dopaminergic neurons and reduced toxic α-synuclein aggregation in rotenone-toxic conditions, compared to the middle image showing cultures exposed to rotenone but treated with vehicle only. Quantification of fosgo-AM effects on reducing rotenone-induced dopaminergic neuron death and α-synuclein aggregation are shown in the bar charts.

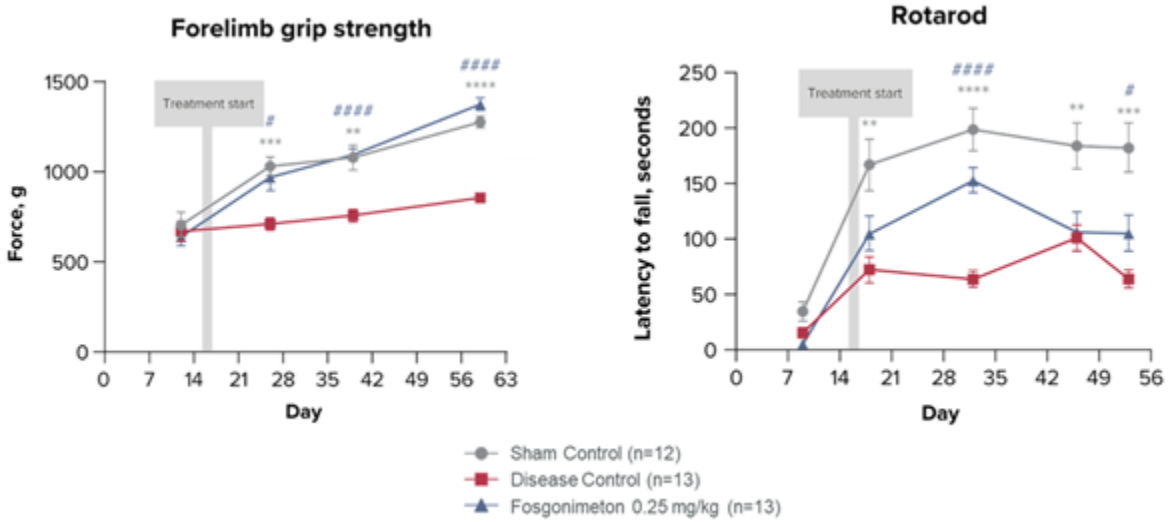
Figure 11. Fosgo-AM Reduces α-synuclein Aggregation and Protects Dopaminergic Neurons from Degeneration Induced by the Neurotoxin Rotenone in Primary Mesencephalic Neurons.



Data presented as mean + SEM. Statistics applied: 1-way ANOVA with Fisher least significant difference test. ***p<0.001 versus Rotenone Control. Scale bar = 100 μm. n=5-6 per group
α-syn; alpha synuclein; fosgo-AM, fosgonimeton active metabolite; TH, tyrosine hydroxylase.

Cellular improvements translated to improvements in motor function in several behavioral assessments, including improved coordination, balance and strength. Figure 12 below are two examples of improved motor function in a 6-hydroxydopamine, or 6-OHDA, rat model of PD, where treatment with fosgonimeton rescues muscular strength in the grip test, balance and coordination deficits in the rotarod test.

Figure 12. Fosgonimeton Rescues Grip Strength and Balance and Coordination Deficits in a Rat Model of PD.

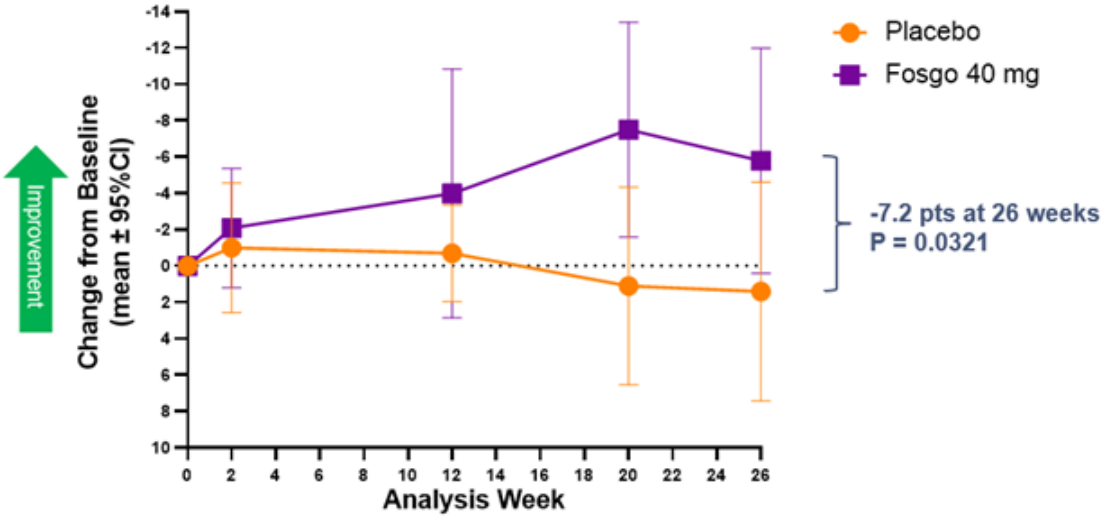


Data presented as means ± SEM. Statistics applied: 2-way ANOVA with Dunnett test. Statistical significance indicated with * represent sham control versus disease control; # represent fosgonimeton versus disease control. For all symbols: *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001 versus disease control.
6-OHDA, 6-hydroxydopamine.

Exploratory Phase 2 SHAPE Trial

The exploratory Phase 2 clinical trial, SHAPE, tested 40 and 70 mg fosgonimeton doses versus placebo in PDD and DLB. The trial enrolled 28 participants and we reported topline results in December 2023. The primary endpoint of the trial, a composite score of the change in ERP P300 latency and cognitive assessment (ADAS-Cog13), was not met by protocoled analysis compared with placebo. Directionally positive results were observed for the 40 mg fosgonimeton dose group with improvements in cognitive, functional and biomarker measurements. In particular (see Figure 13 below), the five patients in the mITT population treated with fosgonimeton 40 mg once daily saw improvement in ADAS-Cog13 individually, and collectively improved compared with placebo (n=7 mITT, one-sided p=0.0321). Results for patients in the 70 mg dose group were inconsistent.

Figure 13. ADAS-Cog13 Score Change from Baseline in mITT Population.



n size per visit

	BL	W2	W12	W20	W26
Placebo	9	9	9	8	7
40 mg	7	7	7	6	5

ADAS-Cog13: Alzheimer's Disease Assessment Scale – Cognitive Subscale 13-item version; CI: Confident Interval; Baseline is defined as the mean of the pre-dose measurements. Multiple efficacy assessments are averaged if they fall at the same visit.

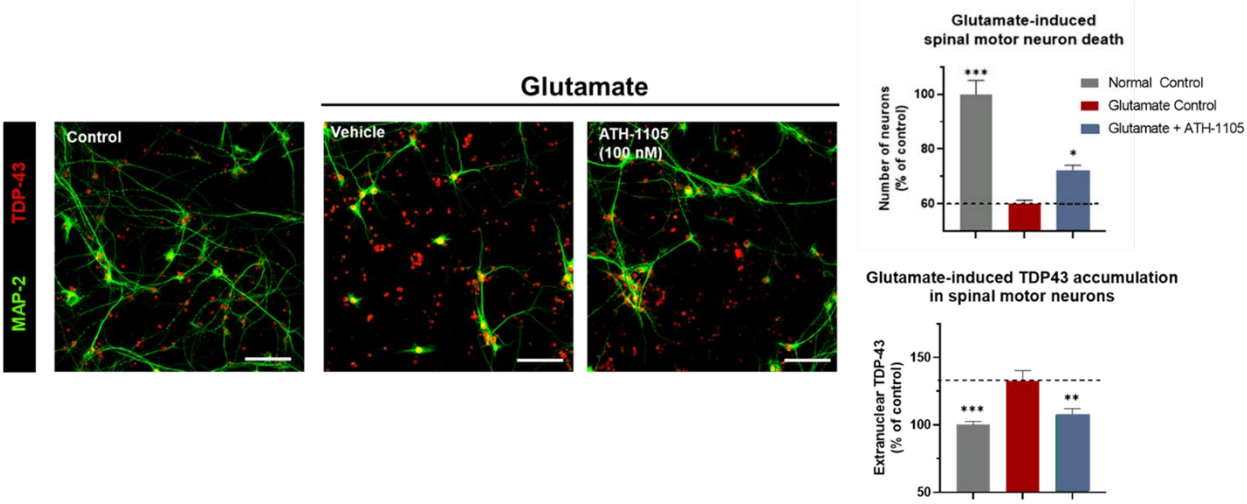
We believe the totality of the preclinical and clinical evidence supports continued testing of neurotrophic HGF system modulators in PD. In the future we will consider how best to progress fosgonimeton or another of our neurotrophic HGF system modulators in clinical testing for this complex disease.

ATH-1105

ATH-1105 Preclinical Evidence for ALS

ATH-1105 is a novel oral small molecule drug candidate being assessed as a potential treatment for ALS. In a spinal motor neuron model, ATH-1105 significantly protected against neuron death by glutamate-induced excitotoxicity, while reducing pathological aggregation of TAR DNA-binding protein 43, or TDP-43. Figure 14 summarizes the data with images of microtubule-associated protein-2, or MAP-2-labeled spinal motor neurons in green, and extranuclear TDP-43 in red. In the control image on the left with no excitotoxic insult (glutamate), there is minimal overlap of MAP-2 neurons with extranuclear TDP-43. When glutamate is applied to the motor neuron cultures, there's an overall reduction in the number of neurons and increased extranuclear TDP-43 as shown by overlapping red-green staining in the middle image. When cell cultures were treated with ATH-1105, the effect of glutamate-induced excitotoxicity on the overall number of motor neurons and extranuclear TDP-43 protein aggregation was significantly reduced, as seen in the rightmost image and as quantified in the bar graphs.

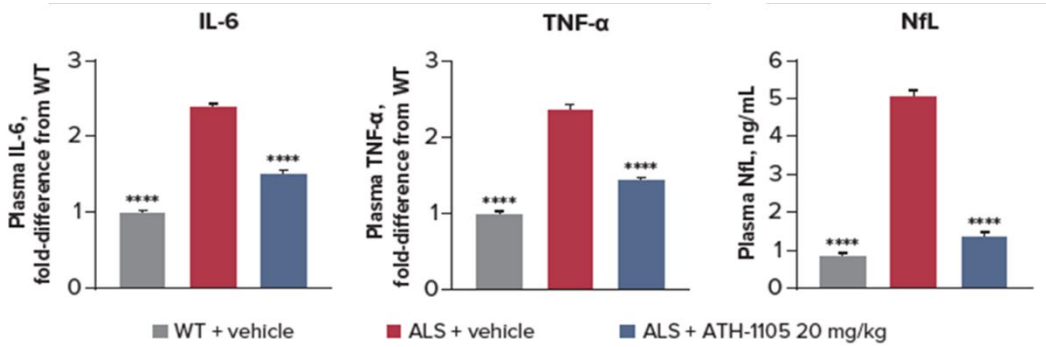
Figure 14. ATH-1105 is Neuroprotective Against Excitotoxic Insult and Reduces Extranuclear TDP-43 Levels in Spinal Motor Neurons.



Data presented as mean + SEM. Statistics applied: 1-way ANOVA with Fisher least significant difference test. *p<0.05; **p<0.01; ***p<0.001 versus Glutamate Control. Scale bar: 100 µm. n=5-6 per group.
MAP-2, microtubule-associated protein-2; TDP-43, TAR DNA-binding protein 43.

Plasma biomarkers of inflammation and neurodegeneration were significantly reduced following treatment with ATH-1105 in a transgenic TDP-43-driven mouse model of ALS (Figure 15). These results support the anti-inflammatory and neuroprotective effects of ATH-1105 through enhancement of neurotrophic HGF system signaling. In the TDP-43-driven ALS model, significant increases in the proinflammatory cytokines tumor necrosis factor alpha, or TNF-alpha, and interleukin 6, or IL-6, were observed compared to healthy wild-type, or WT, control animals. When ALS-model mice, or ALS mice, were treated with ATH-1105 significant reductions in both TNF-alpha and IL-6 were observed, demonstrating anti-inflammatory activity. Consistent with the neuroprotective effects demonstrated in cell-based models, a significant reduction in plasma levels of the neurodegeneration biomarker, NfL, was observed in ALS mice treated with ATH-1105, which is indicative of neuroprotection.

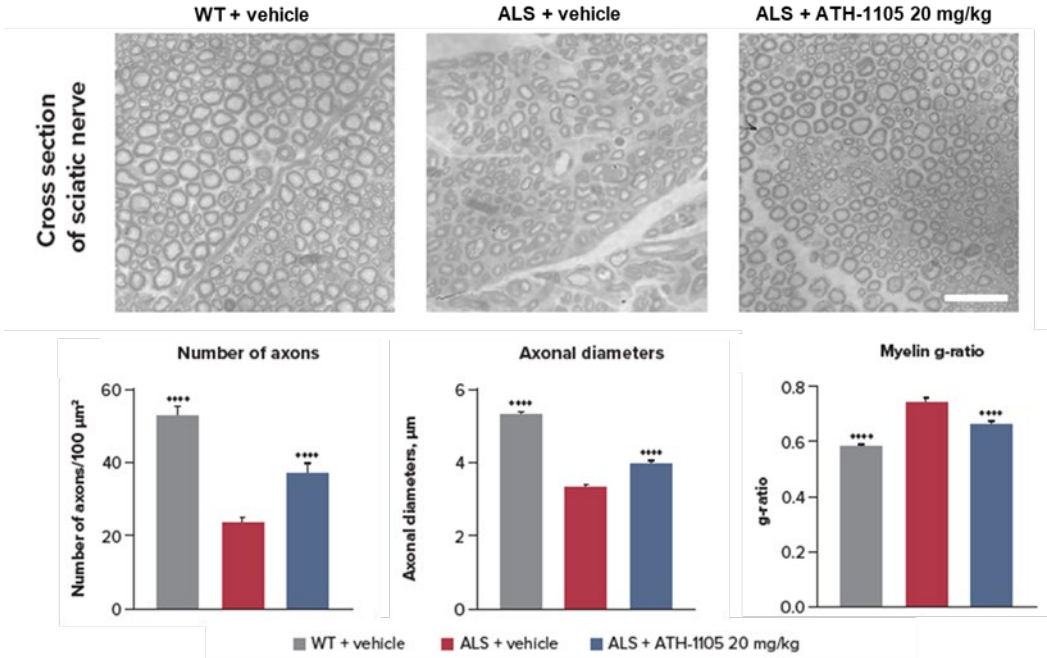
Figure 15. ATH-1105 Improves Biomarkers of Inflammation and Neurodegeneration in a Mouse Model of ALS.



Graphical representation of plasma IL-6, TNF-α in fold-difference over the WT + vehicle group, and NfL levels in ng/ml at two months of treatment. N=10 per group. Data presented as mean ± SEM. Statistical significance was determined by 1-way ANOVA with the Dunnett's test versus ALS + vehicle. ****p<0.0001.
ALS, amyotrophic lateral sclerosis; IL-6, interleukin 6; NfL, neurofilament light chain; TNF-α, tumor necrosis factor alpha; WT, wild-type.

Treatment with ATH-1105 in a mouse model of ALS protected against axon degeneration and demyelination as observed from histological examination of cross-sections of the sciatic nerve. Figure 16 below includes an image of the sciatic nerve from a WT healthy control animal, on the left, featuring a large number of large diameter axons surrounded by a consistent and highly regular coating of myelin sheath. In the middle, a sciatic nerve image from an ALS disease control animal is shown, where a marked reduction in the number of axons, a decrease in average axon diameter, and irregular myelination is observed. On the right, when ALS animals are treated with ATH-1105, sciatic nerve integrity is preserved with a greater population of large diameter axons and preservation of regular myelination. Graphs below the images are quantified data showing these effects of ATH-1105 in a mouse model of ALS.

Figure 16. Treatment with ATH-1105 Protected Against Axon Degeneration and Demyelination in a Mouse Model of ALS.

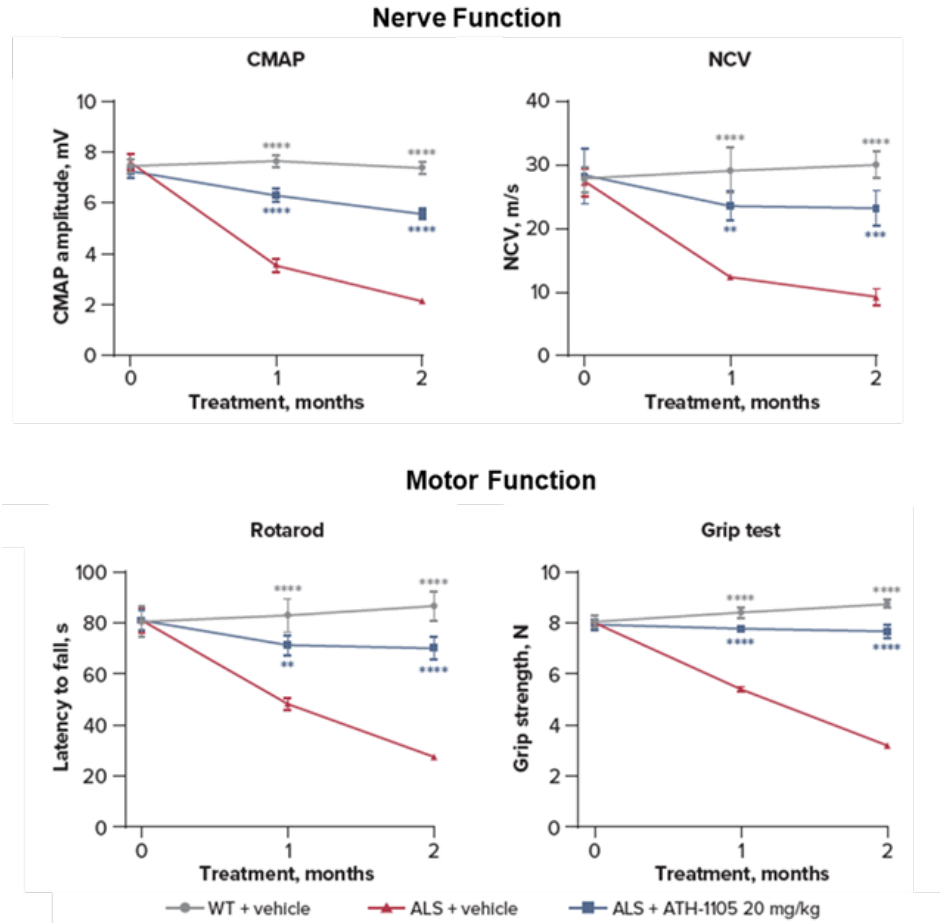


Histology images of sciatic nerve cross-sections stained with toluidine blue to label myelin. Scale is 10 µm (all panels). Graphical representation of the number of axons (per 100 µm2), axonal diameter (in micrometers), and mean of myelin g-ratio, defined as the ratio of the inner axonal diameter to the total axonal diameter, following two months of treatment. Data presented as mean + SEM. Statistical significance was determined by 1-way ANOVA with the Dunnett's test versus ALS + vehicle. ****p<0.0001.
ALS, amyotrophic lateral sclerosis; WT, wild-type.

Further analyses of electrophysiological and behavioral assessments indicated the protection of the motor neurons with ATH-1105 translated to improved nerve and motor function (Figure 17). Compound muscle action potential, or CMAP, and nerve conduction velocity, or NCV, are two electrophysiological measures of functional nerve signaling. Treatment with ATH-1105 in a mouse model of ALS demonstrated consistent and significant improvements of nerve function compared to ALS disease control animals.

Two examples of motor function improvements are shown by the rotarod, an assessment of balance and coordination, and the grip test, an assessment of strength. ALS disease control animals showed significant motor impairments compared to WT healthy control animals. ATH-1105 treatment in this mouse model of ALS led to significant improvements in both the rotarod and grip tests compared to the vehicle treated ALS disease control animals, demonstrating preservation of motor function. Other motor behavior tests assessing balance, coordination and muscle strength were the balance beam and Kondziela screen tests. Across all motor function measures, significant improvements were seen in ALS animals treated with ATH-1105 compared to ALS animals treated with vehicle.

Figure 17. Treatment with ATH-1105 Improves Nerve and Motor Function in a Mouse Model of ALS.

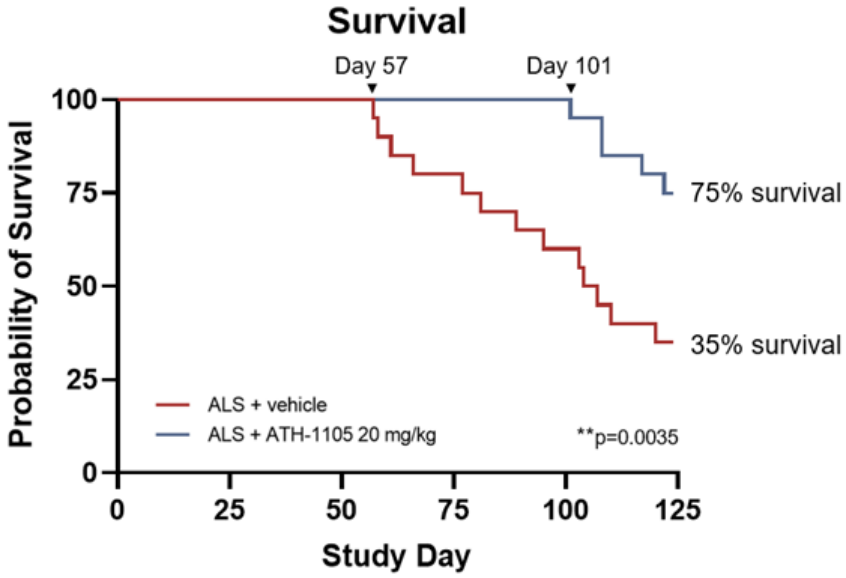


Graphical representation of CMAP amplitude, NCV, rotarod latency, and grip strength at baseline and after one and two months of treatment. Data presented as mean ± SEM. Statistical significance was determined by 2-way ANOVA with the Dunnett's test versus ALS + vehicle. **p<0.01; ***p<0.001; ****p<0.0001. N=10 per group.
ALS, amyotrophic lateral sclerosis; CMAP, compound muscle action potential; NCV, nerve conduction velocity; WT, wild-type.

The above study results, depicted in Figure 17, were presented at the American Academy of Neurology, or AAN, in April 2023, and the ALS Drug Development Summit in May 2023.

Treatment with ATH-1105 in a mouse model of ALS extends survival and improves other disease-related measures. Figure 18 below compares ALS mice treated with oral ATH-1105 20 mg/kg once daily in blue with oral vehicle once daily treated ALS mice in red. Mice were treated from one month of age to a humane endpoint maximum of five months of age, for a total of up to four months of treatment. ATH-1105 increased time to first mortality and significantly prolonged survival compared to ALS disease control animals (p=0.0035). ATH-1105 also significantly protected against body weight reduction (p<0.01). These findings were reported at the AAN 2023 Annual Meeting in April 2023.

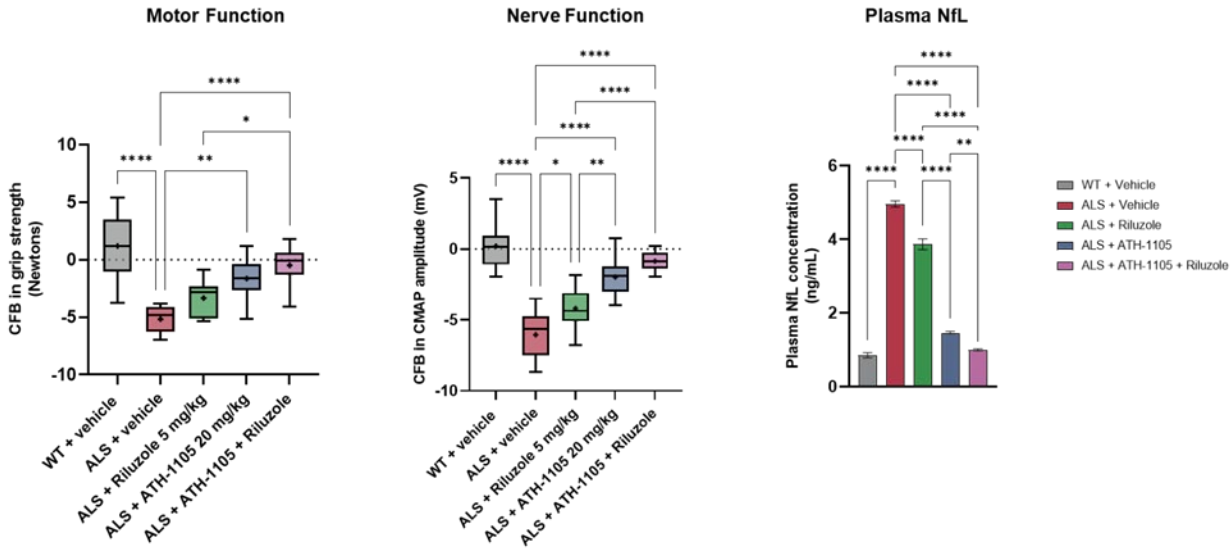
Figure 18. ATH-1105 Significantly Improved Survival in a Mouse Model of ALS.



Data presented as Kaplan-Meier curve
Statistics applied: Log-rank (Mantel-Cox) test for survival curve comparison, **p<0.01. n=20 mice per group at start

Treatment with ATH-1105 in a mouse model of ALS outperforms treatment with riluzole under the conditions tested in assessments of motor function, nerve function, and in reducing disease-related plasma biomarkers. Figure 19 below compares performance in the grip test of WT mice (grey) and transgenic ALS mice treated daily with vehicle (red), intraperitoneal riluzole 5 mg/kg (green), oral ATH-1105 20 mg/kg (blue), or both ATH-1105 and riluzole (purple). Mice treated with ATH-1105 alone and co-administration of riluzole and ATH-1105 consistently outperformed the vehicle-treated ALS disease control group. In both the ATH-1105 and the co-administration of ATH-1105 and riluzole groups, performance on the test approached that of the WT healthy control group. ATH-1105 treatment outperformed riluzole treatment in tests of motor function including the grip, rotarod, Kondziela screen, and balance beam tests. ATH-1105 also outperformed riluzole in tests of nerve function preservation including CMAP amplitude and NCV. ATH-1105 treatment further reduced plasma levels of IL-6 and TNF-alpha compared to riluzole, which are biomarkers of inflammation. ATH-1105 treatment also more greatly reduced plasma levels of NfL compared to riluzole, which is a biomarker of neurodegeneration. These findings were reported at the Northeast ALS Consortium meeting in October 2023, and the Motor Neurone Disease Association conference in December 2023.

Figure 19. ATH-1105 Preserves Motor and Nerve Function and Reduces Plasma NfL Compared with Riluzole in a Mouse Model of ALS.



Graphical representation of change from baseline following two months of treatment in grip test, CMAP amplitude, and Plasma Nfl. Data presented as mean ± SEM, or box-and-whisker plots
Statistics applied: One-way ANOVA with Dunnett's test. *p<0.05; **p<0.01; *** p<0.001; **** p<0.0001. n=10 mice per group;
Abbreviations: CFB, change from baseline, CMAP, compound muscle action potential, NfL, neurofilament light chain

Clinical Development Plan for ATH-1105 in ALS

Weight loss, motor deficits, inflammatory effects, loss of muscle integrity, nerve degeneration and demyelination are all classical hallmarks of disease in people with ALS; treatment with ATH-1105 significantly improved all of these deficits preclinically. We expect to submit an IND application to the FDA and commence ATH-1105 clinical testing in healthy volunteers in the first half of 2024. In this single ascending dose and multiple ascending dose, or SAD/MAD, Phase 1 trial, we expect to evaluate and establish safety and determine one or more doses for further potential testing in ALS patients.

ATH-1020

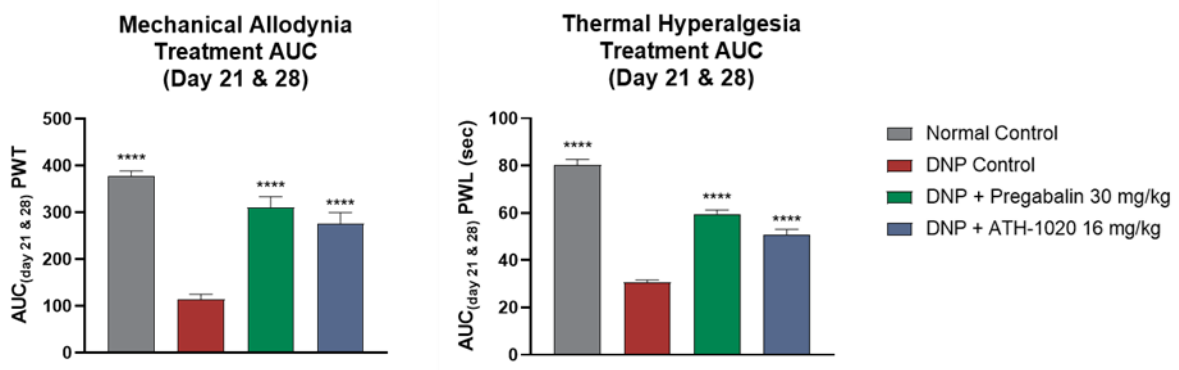
ATH-1020 Preclinical Evidence for Neuropathic Pain

ATH-1020 is a novel, orally available, next generation, small molecule drug candidate designed to positively modulate the neurotrophic HGF system. Enhancing HGF/MET signaling promotes neuroprotective, neurotrophic, and anti-inflammatory effects, and as neuropathic pain disorders, including diabetic neuropathy, or DNP, have components of oxidative stress, nerve damage, and inflammation, positive modulation of the HGF/MET pathway may provide therapeutic benefit in these disease areas. Data below were presented at the Society for Neuroscience Annual Conference in November 2022.

This compound was originally assessed for neuropsychiatric indications in preclinical models as presented at the American Society for Experimental Therapeutics Annual Conference in February 2022.

In animal models of DNP hypersensitivity to mechanical and thermal pain are commonly experienced, which are also representative of symptoms in people with neuropathic pain. Shown in Figure 20 below, treatment with ATH-1020 significantly reduced pain behaviors over the testing period compared to DNP controls alone.

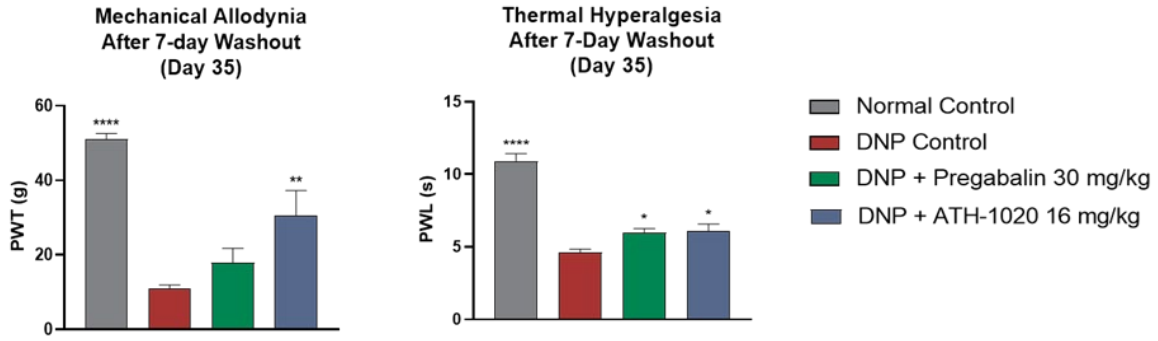
Figure 20. Reduced Mechanical and Thermal Pain-Related Behaviors Following ATH-1020 Treatment in a Rat Model of Diabetic Neuropathic Pain.



Data presented as means + SEM. ****p<0.0001 using one-way ANOVA with Dunnett test vs DNP control.
ANOVA, analysis of variance; AUC, area under the curve; DNP, diabetic neuropathic pain; PWL, paw withdrawal latency; PWT, paw withdrawal threshold.

Persistence of reduced pain behaviors following ATH-1020 treatment were assessed after a short-term (23-hour) or a long-term (7-day) washout period. Study results demonstrated that even after short- and long-term washout periods, where no drug is present, the effects of ATH-1020 reduction of pain behaviors remained persistent, suggesting a potential disease modifying effect (Figure 21).

Figure 21. Persistent Pain Reduction after 7-day Washout Following ATH-1020 Treatment.



Data presented as means + SEM. *p<0.05; **p<0.01; ****p<0.0001 using one-way ANOVA with Dunnett test vs DNP control. ANOVA, analysis of variance; AUC, area under the curve; DNP, diabetic neuropathic pain; PWL, paw withdrawal latency; PWT, paw withdrawal threshold.

ATH-1020 Clinical - Phase 1 Trial in Healthy Volunteers

We filed an IND application with the FDA for ATH-1020 at the end of 2021 and received notice of acceptance in January 2022. In September 2022, we completed the single-ascending dose escalation portion of the Phase 1 trial. ATH-1020 demonstrated a favorable safety profile and was well-tolerated in healthy volunteers. We plan to evaluate options with this drug candidate for future testing in either neuropathic pain or other neurodegenerative diseases.

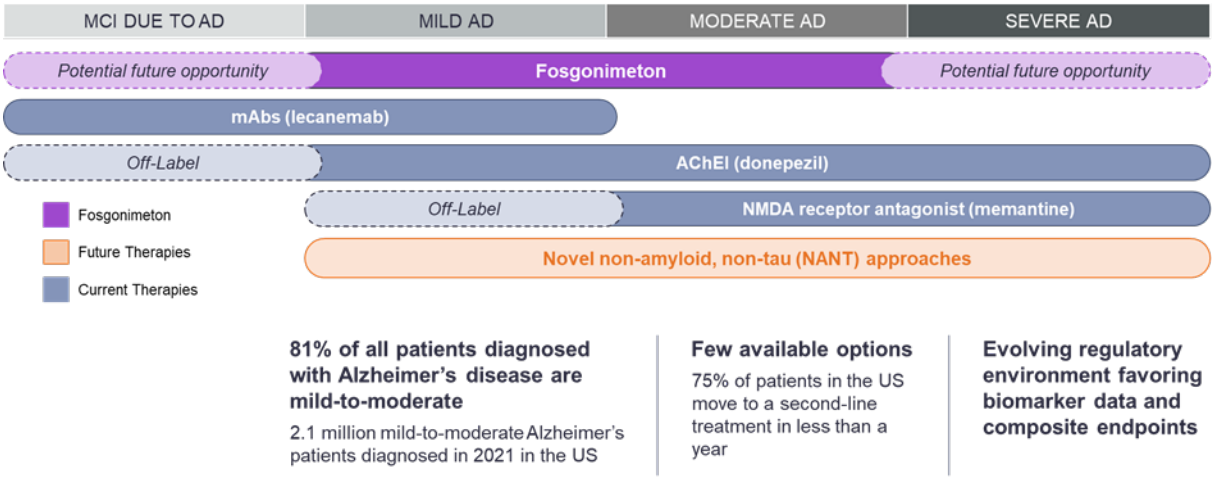
Market Opportunity

AD and Dementia

We believe fosgonimeton has the potential as a viable treatment option across all stages of AD but is initially being developed for mild-to-moderate stage of disease. Stages of this progressive disorder start with mild cognitive impairment, or MCI, mild AD, moderate AD, and finally severe AD. The AD dementia market, as last reported in 2023, consists of approximately 6.7 million Americans age 65 and older and is projected to reach nearly 13 million by 2050 in the U.S. alone. Worldwide, as many as 55 million people are estimated to have AD and other dementias, and this number is projected to grow to nearly 140 million by 2050. AD may account for an approximate 60-70% of all diagnosed dementia cases, however, with the continued innovation of diagnostic approaches coupled with better understanding of the disease pathology, diagnosis of AD and overall cases could continue to grow.

As shown in Figure 22 below, our initial focus is on mild-to-moderate AD as this stage has been identified where disease may progress rapidly and currently available therapies are few with only modest effects. Currently 81% of all diagnosed cases of AD are mild-to-moderate, and with many new therapies under development targeting earlier stages in AD, this is a highly underserved population with a high unmet need. Fosgonimeton is initially being developed for mild-to-moderate AD, but as we continue to advance fosgonimeton, and with our multimodal mechanism of action, we believe we will have the opportunity to address all stages of AD as well as expand into other dementias.

Figure 22. Significant Opportunity for Fosgonimeton in AD.



Other Target Indications

Our next potential target indications for our small molecule positive modulators include PD, ALS and neuropathic pain. PD is the second most common neurodegenerative disease after AD with a prevalence of nearly one million people and more than 10 million people in the United States and worldwide living with PD, respectively. Growth projections of United States cases of PD are expected to reach 1.2 million in the United States by 2030.

An estimated 16,000 Americans are affected with ALS while global estimates exceed 150,000 (1.9 per 100,000 to 6 per 100,000). Currently, there are only four approved drugs that are specifically indicated for the treatment of ALS, of which none target neurotrophic factor systems with a multimodal mechanism of action with the potential to offer neuroprotective, anti-inflammatory and potentially disease modifying effects.

Potential Commercialization Plan

Fosgonimeton is our proprietary, potentially first-in-class small molecule drug candidate designed to promote the neurotrophic HGF system, which activates neuroprotective, neurotrophic and anti-inflammatory pathways in the CNS, and is initially being developed in mild-to-moderate AD. For this patient population, our commercialization strategy will consider the following key elements:

- potential first-line therapy;
- an add-on therapy for patients on existing therapies;
- a therapeutic option for patients who are not suitable for AChEIs; and
- a therapeutic option for patients who have stopped AChEIs due to loss of effect or side effects.

We will initially target launching fosgonimeton in the US with plans to expand into the European Union, or EU, and Asian markets as part of our global strategy. Beyond our regional launch plans, and because of our multimodal mechanism of action, we also expect to advance fosgonimeton beyond the mild-to-moderate AD stage into both earlier and later stages of disease.

We aim to establish the potential value of fosgonimeton by demonstrating improvement in cognition, independence, and markers of neurodegeneration, inflammation and AD protein pathology, which could result in improved outcomes and reduced total healthcare costs for this progressive and potentially fatal disease.

Manufacturing

We are focused on the development of small molecule therapeutics which enables us to use well-established and widely available manufacturing processes and infrastructure, formulation compositions, and drug administration technologies or devices. We do not currently operate our own facilities for manufacturing, storing, or distributing our drug candidates. We utilize third-party contract development and manufacturing organizations, or CDMOs, to manufacture and supply our preclinical and clinical materials during the development of our drug candidates. We and various regulatory bodies have audited the CDMOs we contract with, and they have a proven track record of FDA-compliant manufacturing with an infrastructure to support both clinical supplies and subsequent large and commercial scale manufacturing.

We have a robust fosgonimeton clinical supply chain to ensure sufficient supply for our LIFT-AD Phase 2/3 clinical trial in AD and the open-label extension of our LIFT-AD and ACT-AD clinical trials. We believe the synthesis of fosgonimeton is reliable and reproducible and the synthetic routes can be further optimized to enable large-scale production that continues to avoid use of toxic materials or specialized equipment or handling during the manufacturing process. We continue to optimize the manufacturing process to support future large-scale and commercial supply. Fosgonimeton is purified as a stable solid and then released to additional CDMOs for formulation and packaging into final drug product for use in clinical testing.

The final drug product profile is a ready-to-use pre-filled syringe with a clear, non-viscous aqueous solution of fosgonimeton. The syringes utilize materials and components that are readily available commercially. The fosgonimeton drug product has shown extended stability (at least two years) in the proposed prefilled syringe supporting use of the drug product under refrigerated conditions as well as short-term dispensation and at-home storage in ambient conditions. Room temperature short-term storage allows patients to avoid cumbersome storage requirements and reduces overall burden.

We plan to maintain our focus to identify and develop small molecule drug candidates that are expected to have cost-effective manufacturing using third party CDMOs.

We expect to use similar contract resources for commercialization of our drug candidates, at least until our resources and operations are at a scale that potentially justifies investment in internal manufacturing capabilities.

Competition

The biotechnology and biopharmaceuticals industries are characterized by rapid technological advancement, significant competition, and an emphasis on intellectual property. As a late clinical-stage biopharmaceutical company developing small molecules to restore neuronal health and slow neurodegeneration, with our most advanced drug candidate focused on the treatment of AD, we face, and in the future may face, increased competitive pressures from both large and small pharmaceutical companies and from established and emerging biotechnology companies, as well as academic, government, and public and private research institutions. Any drug candidates that we successfully develop and commercialize will compete with current treatments and new treatments that may become available in the future. With the advancement of fosgonimeton as a novel small molecule therapeutic that positively modulates the neurotrophic HGF system, we must consider companies as competitors who are developing other novel approaches, including those that target other neurotrophic systems to address AD and other neurological diseases. Additionally, because fosgonimeton is being advanced as a once daily liquid formulation for subcutaneous delivery, we must also consider as competitors companies developing AD therapies as subcutaneous or other routes of administration, including oral formulations, and dosing frequency.

Because of the range of potential competitors, many of our competitors, alone or with strategic partners, have greater access to financial resources, market presence, and resources and expertise in development, preclinical and clinical testing, manufacturing, commercialization, the regulatory approval process, or marketing and sales than we do. In addition, these same competitors, who may be in a clinical development stage, could also be competing with us for patient recruitment, clinical research organization, and operational resources. These entities also compete with us in the recruitment and retaining of qualified scientific and management personnel, as well as the acquisition of enabling or complementary technologies for advancing fosgonimeton across all competitors. Merger and acquisition activity in the biotechnology and biopharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Our commercial opportunity could be substantially limited if our competitors develop and commercialize products that are more effective, safer, more convenient or less expensive than our comparable drug products. In geographies that are critical to our commercial success, competitors may also obtain regulatory approvals before us, resulting in our competitors building a strong market position in advance of the entry of our drug candidates. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of other treatments.

The AD market is experiencing a significant transformation where innovation and drug approvals have been limited for nearly 20 years. With the approval of two new monoclonal antibody therapies since 2021 (Biogen's Aduhelm and Biogen/Eisai's Leqembi), the potential approval of Eli Lilly's Donanemab this year, and the increased attention on novel approaches to AD, we are focused on strategically positioning ourselves in the evolving landscape to maximize our competitive advantage. Key competitive forces that could potentially affect the success of our drug candidates, if approved, are safety, efficacy, price, adoption, convenience, time-to-market, level of promotional activity, intellectual property protection, and reimbursement likelihood from government and private payors. Despite these forces, we view our competitive advantage in not only our lead drug candidate, fosgonimeton, but also our novel pipeline of therapeutics targeting the neurotrophic HGF system with a focus on overall neuronal health. In particular, the following summarizes certain categories of our potential competition.

Our direct competitors can potentially be viewed through two different lenses – stage of disease and mechanism of action, or MOA. While the AD space has just recently seen two new approvals specifically addressing earlier stages of disease, MCI and mild AD, limited options exist for the mild-to-moderate disease stage. Companies developing therapies for mild-to-moderate AD, such as AB Science, Annovis Bio, Biomed Industries, BioVie Pharma, or Cassava Sciences, may emerge as direct competitors if they are quicker to market, demonstrate superior clinical effects, are safe and offer treatment options to our same initial target patient population.

Monoclonal antibody therapies have been the focus of drug developers over the past several decades, and though the recent approval of Leqembi provides an option for those in early AD, more novel approaches and treatment options are needed. Through the MOA lens, companies developing non-amyloid, non-tau, or NANT, therapies may be direct competitors as well. Companies developing NANT therapies include those targeting other neurotrophic systems such as Alzecure, anti-inflammation such as AB Science, translational inhibitors such as Annovis Bio, and several other companies developing assets with novel targets like Cassava Sciences and BioVie Pharma.

Specific to targeting HGF/MET however, we are not aware of any direct competitors currently developing small molecules targeting the neurotrophic HGF system for neurological conditions. We are aware of several companies developing HGF/MET-directed therapies for other disease indications, including ANG-3777, an HGF mimetic, developed by Angion for the treatment of kidney injury; KP-100, a recombinant HGF protein, developed by Kringle Pharma for acute spinal cord injury and ALS; and Collategene developed by Mitsubishi Tanabe and AnGes as a gene therapy for the treatment of critical limb ischemia. Although ANG-3777 was reported to not have reached primary endpoints for their Phase 2 and 3 trials in 2021, the scientific basis remains unchanged, and the company is evaluating next steps for the program. KP-100 is currently in Phase 3 studies for acute spinal cord injury and Phase 2 studies for ALS. Collategene was launched in Japan in the third quarter of 2019. In addition, we are aware of VM-202, a regenerative plasmid DNA therapy candidate in Phase 3 development by Helixmith for the treatment of diabetic peripheral neuropathy and diabetic foot ulcers. VM-202 is in Phase 2 trials for Claudication and ALS.

Fosgonimeton has the potential to offer neuroprotective and anti-inflammatory effects by targeting the HGF/MET system. Our preclinical and clinical data have demonstrated this multimodal approach may have positive benefits across several biological and clinical measures. While several potential direct competitors may exist, we have not yet identified any competitive asset that has demonstrated consistent and congruent positive effects offering neuroprotection, anti-inflammation, reducing disease-specific protein pathologies, neurotrophic, and functional benefits. AD is a complex multifactorial disease, and we view our opportunity with fosgonimeton as potentially complementary to several approaches, including the recently approved monoclonal antibody therapies.

Intellectual Property

We own or have in-licensed numerous patents and patent applications and possess substantial know-how and trade secrets relating to the development and commercialization of our drug candidates, including related manufacturing processes and technologies.

As of December 31, 2023, our patent portfolio includes our exclusively owned intellectual property, including one issued U.S. patent, four pending U.S. patent applications, six issued patents in jurisdictions outside of the United States (not including certain European country validations or other registrations), forty-four pending patent applications in jurisdictions outside of the United States, and six pending international patent applications filed under the Patent Cooperation Treaty. The patents and patent applications issued and pending outside the United States are counterparts to the foregoing U.S. patents and patent applications and are generally held in Europe, Canada, Japan, Argentina, Australia, Brazil, China, Hong Kong, India, New Zealand, Singapore, South Africa, South Korea and Taiwan. Our owned patents and patent applications have claims directed to fosgonimeton and our other small molecule drug candidates, including ATH-1020 and ATH-1105, as compositions of matter and methods of use thereof. Our patent portfolio also includes seven issued U.S. patents and nine patents issued in jurisdictions outside of the United States (not including European country validations) that are exclusively licensed to us by WSU. Our in-licensed patents include, among others, claims directed to dihexa, the active metabolite of fosgonimeton, and its use.

Individual patents are in force for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance, and the legal term of patents in the countries in which they are obtained. Generally, patents issued for applications filed in the United States are in force for 20 years from the earliest nonprovisional filing date. In addition, in certain instances, a patent term can be adjusted or extended to recapture a portion of the term effectively lost as a result of the United States Patent and Trademark Office, or USPTO, delay or the FDA regulatory review period (a patent term adjustment or patent term extension, respectively). The restoration period for FDA delay cannot be longer than five years and the total patent term, including the restoration period, must not exceed 14 years following FDA approval. The duration of patents outside of the United States varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest nonprovisional filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related

extensions, the availability of legal remedies in a particular country, and the validity and enforceability of the patent. Our in-licensed issued patents will expire on dates ranging from 2027 to 2035, exclusive of any patent term adjustment or patent term extension. Our owned issued patents will expire in 2037, exclusive of any patent term adjustment or patent term extension. If patents are issued on our owned pending non-provisional patent applications, the resulting patents are projected to expire on dates ranging from 2037 to 2043, exclusive of any patent term adjustment or patent term extension.

When appropriate, we seek to protect aspects of our technology and business not amenable to, or that we do not consider appropriate for, patent protection as trade secrets. We seek to protect this intellectual property, in part, as trade secrets, by entering into confidentiality agreements with those who have access to our confidential information, including our employees, contractors, consultants, collaborators, and advisors. We also seek to preserve the integrity and confidentiality of our proprietary technology and processes by maintaining physical security of our premises and physical and electronic security of our information technology systems.

We seek trademark protection in the United States and in certain other jurisdictions where available and when we deem appropriate. Our trademark portfolio includes issued trademark registrations for Athira Pharma and other pending trademark applications in the United States and internationally.

Our Collaboration and Grant Agreements

Amended and Restated WSU License Agreement

We are party to an amended and restated exclusive license agreement with sublicensing terms with WSU that we entered into in 2015. Under this agreement, we have an exclusive license to make, use, sell, and offer for sale products covered by certain licensed patents, including dihexa, the chemical compound into which fosgonimeton metabolizes following administration.

The initiation of our first Phase 2 clinical trial in September 2020 triggered a $50,000 liability to WSU.

We may also be obligated to pay to WSU the following if the related milestones are reached:

- $300,000 – At initiation of the first Phase 3 clinical trial in the United States, European Union or Japan for the first licensed product.
- $600,000 – Marketing approval in the United States, European Union or Japan for the first licensed product.

We are obligated to pay WSU a royalty in the mid-single digits of net sales.

Additionally, under the agreement we have the right to sublicense the licensed rights, subject to additional payments to WSU for sublicense consideration received. Such amounts are dependent on the terms of the underlying sublicense, and range from the mid-single digits to mid tens of any non-sales based payments received, and low twenties of net sales-based sublicense royalties.

The term of the agreement will continue until the earlier of (1) the date that no valid claim in a licensed patent remains enforceable and (2) payment of earned royalties, once such payments begin, ceases for more than four consecutive calendar quarters. We have not yet commenced payment of royalties to WSU pursuant to the terms of the agreement, since, as of the date of this report, we do not have any approved products with respect to which we may generate revenue. If any of our drug candidates to which the patents relate are approved for commercial sale, our obligations to pay royalties would commence upon net sales of such approved drug candidates and cease no later than the date that no valid claim in a licensed patent remains enforceable. We may terminate this agreement with 90 days' prior written notice to WSU. WSU may terminate this agreement with 90 days' prior written notice if we fail to achieve certain performance milestones by the agreed upon dates. WSU may also terminate this agreement with 90 days' prior written notice (or thirty days' prior written notice in the case of our failure to make a timely payment owed to WSU) following our failure to conduct certain development activities for two consecutive calendar quarters or upon

our material breach of the agreement and our failure to cure any such breach within 90 days of our receipt of notice of such breach from WSU (or within 30 days in the case of our failure to make a timely payment owed to WSU).

National Institutes of Health Grant

In December 2020, we accepted a grant from the National Institute on Aging, or NIA, of the National Institutes of Health, or NIH, to support our ACT-AD Phase 2 clinical trial for fosgonimeton (then-named ATH-1017), our lead drug candidate being developed for the treatment of individuals with mild-to-moderate AD. Under the terms of the agreement and approval received from the NIH, we were awarded an aggregate of $15.2 million, all of which had been received as of December 31, 2023. Post award, we received approval from NIA to use these grant funds to support our open label extension of the ACT-AD trial. As this grant involves federally funded research, per the Bayh-Dole Act of 1980, or the Bayh-Dole Act, we are obligated to (1) report each new invention to the government, (2) decide whether to retain ownership, (3) file for patent protection to retain title, and (4) provide a license to the government to practice the invention. The "march-in" rights provided by the Bayh-Dole Act would apply to new subject matter arising from the use of the NIH funds, but would exclude pre-existing subject matter such as our drug candidates existing prior to the receipt of such grant. We also are expected to commercialize any inventions we file patent protection on for the benefit of public health. For more information see the section of this report titled "Risk Factors—Risks Relating to Our Intellectual Property. Intellectual property discovered or developed through government funded programs may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights and limit our ability to contract with non-U.S. manufacturers."

Government Regulation

Government authorities in the United States, at the federal, state, and local level, and other countries extensively regulate, among other things, the research, development, nonclinical and clinical testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing, and export and import of products such as those we are developing. Generally, before a new drug can be marketed, considerable data must be generated, which demonstrate the drug's quality, safety, and efficacy. Such data must then be organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, the approval process or after approval may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, 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. Any agency or judicial enforcement action could have a material adverse effect on us.

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

- completion of nonclinical laboratory tests, animal studies, and formulation studies in accordance with FDA's good laboratory practice, or GLP, requirements and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;

- approval by an independent institutional review board, or IRB, ethics committee, either centralized or with respect to each clinical site, before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice, or GCP, requirements to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of a New Drug Application, or NDA, after completion of all pivotal trials;
- determination by the FDA within 60 days of its receipt of an NDA to accept the filing for substantive review;
- 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 drug is produced to assess compliance with current good manufacturing practice, or cGMP, requirements to ensure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality, and purity, and of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the United States.

Prior to beginning the first clinical trial with a product candidate in the United States, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacology, and PK/PD characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the clinical trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which may review data and endpoints at designated check points, make recommendations or halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

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

- *Phase 1*: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism, and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on

effectiveness. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

- *Phase 2*: The product candidate is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages, and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- *Phase 3*: The product candidate is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

Post-approval clinical trials, sometimes referred to as Phase 4 studies, may be conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. In addition, some clinical trials are overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a clinical trial may move forward at designated check points based on access to certain data from the clinical trial.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 clinical trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality, and purity of the final drug. In addition, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

While the IND is active and before approval, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or *in vitro* testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

NDA Review and Approval Process

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development nonclinical and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality, and purity. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes 12 months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision after the application is submitted. The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing.

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

Before approving an NDA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCPs. If the FDA determines that the application, manufacturing process, or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates an NDA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A Complete Response Letter usually describes the specific deficiencies in the NDA identified by the FDA and may require additional clinical data, such as an additional pivotal Phase 3 clinical trial or other significant and time-consuming requirements related to clinical trials, nonclinical studies, or manufacturing. If a Complete Response Letter is issued, the sponsor must resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the NDA with a risk evaluation and mitigation strategy, or REMS, to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use. It could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization

tools. The FDA also may offer conditional approval subject to, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may also require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies. In addition, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could impact the timeline for regulatory approval or otherwise impact ongoing development programs.

Expedited Development and Review Programs

The FDA has a fast track designation program that is intended to expedite or facilitate the process for reviewing new drug products that meet certain criteria. Specifically, new drugs are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. With regard to a fast track product, the FDA may consider for review sections of the NDA 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.

Any product submitted to the FDA for approval, including a product with a fast track designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. A product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis, or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date as compared to ten months for review of new molecular entity NDAs under its current PDUFA review goals.

In addition, a product may be eligible for accelerated approval. Drug products intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the 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, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, the FDA currently requires pre-approval of promotional materials as a condition for accelerated approval, which could adversely impact the timing of the commercial launch of the product.

The Food and Drug Administration Safety and Innovation Act established a category of drugs referred to as "breakthrough therapies" that may be eligible to receive breakthrough therapy designation. A sponsor may seek FDA designation of a product candidate as a "breakthrough therapy" if the product is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance. The breakthrough therapy designation is a distinct status from both accelerated approval and priority review, which can also be granted to the same drug if relevant criteria are met. If a product is designated as breakthrough therapy, the FDA will work to expedite the development and review of such drug.

Fast track designation, priority review, accelerated approval, and breakthrough therapy designation do not change the standards for approval, but may expedite the development or approval process. 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 drug product candidates as appropriate. On December 29, 2022, the Consolidated Appropriations Act, 2023, including the Food and Drug Omnibus Reform Act, or FDORA, was signed into law. FDORA made several changes to the FDA's authorities and its regulatory framework, including, among other changes, reforms to the accelerated approval pathway, such as requiring the FDA to specify conditions for post-approval study requirements and setting forth procedures for the FDA to withdraw a product on an expedited basis for non-compliance with post-approval requirements.

Post-Approval Requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There are continuing, annual program fees for any marketed products. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

The FDA may withdraw 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 revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions 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 untitled letters;
- clinical holds on post-approval or Phase IV clinical studies, if applicable;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- drug product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment, or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases, and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising, and promotion of drug products. A company can make only those claims relating to safety and efficacy that are approved by the FDA 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. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising, and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined companies from engaging in off-label promotion. The FDA and other regulatory agencies have also required that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labelling.

Marketing Exclusivity

Market exclusivity provisions authorized under the FDCA can delay the submission and approval of certain marketing applications for products containing the same active ingredient. The FDCA permits patent term restoration of up to five years as compensation for a patent term lost during product development and FDA regulatory review process to the first applicant to obtain approval of an NDA for a new chemical entity in the United States. Patent-term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application, or ANDA, or an NDA submitted under Section 505(b)(2) (505(b)(2) NDA), submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FDCA alternatively provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages, or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to any nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of marketing exclusivity available in the United States. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to another period of exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA. The issuance of a written request does not require the sponsor to undertake the described clinical trials. In addition, orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances.

Other Healthcare Laws

Pharmaceutical manufacturers are subject to additional healthcare laws, regulation, and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct

their business. Such laws include, without limitation, U.S. federal anti-kickback, anti-self-referral, false claims, transparency, including the federal Physician Payments Sunshine Act, consumer fraud, pricing reporting, data privacy, data protection, and security laws and regulations as well as similar foreign laws in the jurisdictions outside the U.S. Similar state and local laws and regulations may also restrict business practices in the pharmaceutical industry, such as state anti-kickback and false claims laws, which may apply to business practices, including but not limited to, research, distribution, sales, and marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, or by patients themselves; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the 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; state and local laws which require the tracking of gifts and other remuneration and any transfer of value provided to physicians, other healthcare providers and entities; and state and local laws that require the registration of pharmaceutical sales representatives; and state and local laws governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by the Health Insurance Portability and Accountability Act of 1996, or HIPAA, thus complicating compliance efforts.

The risk of our being found in violation of these or other laws and regulations is increased by the fact that many have not been fully interpreted by the regulatory authorities or the courts and their provisions are open to various interpretations. These laws and regulations are subject to change, which can increase the resources needed for compliance and delay drug approval or commercialization. Any action brought against us for violations of these laws or regulations, even successfully defended, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Also, we may be subject to private "qui tam" actions brought by individual whistleblowers on behalf of the federal or state governments. Actual or alleged violation of any such laws or regulations may lead to investigations and other claims and proceedings by regulatory authorities and in certain cases, private actors, and violation of any of such laws or any other governmental regulations that apply may result in penalties, including, without limitation, significant administrative, civil and criminal penalties, damages, fines, additional reporting obligations, and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, the curtailment or restructuring of operations, exclusion from participation in government healthcare programs and imprisonment.

Coverage and Reimbursement

Sales of any pharmaceutical product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance, and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Significant uncertainty exists as to the coverage and reimbursement status of any newly approved product. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. One third-party payor's decision to cover a particular product does not ensure that other payors will also provide coverage for the product. As a result, the coverage determination process can require manufacturers to provide scientific details, information on cost-effectiveness, and clinical support for the use of a product to each payor separately. This can be a time-consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

In addition, third-party payors are increasingly reducing reimbursements for pharmaceutical products and related services. The U.S. government and state legislatures have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Third-party payors are increasingly challenging the prices charged, examining the medical necessity and reviewing the cost effectiveness of pharmaceutical products, in addition to questioning their safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision

by a third-party payor not to cover a product could reduce physician usage and patient demand for the product.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Pharmaceutical products may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products and may also compete with imported foreign products. Furthermore, there is no assurance that a product will be considered medically reasonable and necessary for a specific indication, that it will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be established even if coverage is available, or that the third-party payors' reimbursement policies will not adversely affect the ability for manufacturers to sell products profitably.

Healthcare Reform

In the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system. In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, was signed into law, which substantially changed the way healthcare is financed by both governmental and private insurers in the United States. By way of example, the ACA increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1%; it required collection of rebates for drugs paid by Medicaid managed care organizations; imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell certain "branded prescription drugs" to specified federal government programs; it implemented a new methodology under which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected; it expanded the eligibility criteria for Medicaid programs; it created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and it established a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been executive, judicial and Congressional challenges to certain aspects of the ACA. For example, in June 2021 the U.S. Supreme Court held that Texas and other challengers had no legal standing to challenge the ACA, dismissing the case on procedural grounds without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and healthcare measures promulgated by the Biden administration will impact the ACA, our business, financial condition and results of operations. On January 28, 2021, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, effective April 1, 2013, which, due to subsequent legislative amendments, will stay in effect through 2032 with the exception of a temporary suspension implemented under various novel coronavirus disease, or COVID-19, relief legislation. Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several

Congressional inquiries and proposed and enacted legislation designed, among other things, to bring more transparency to product pricing, to review the relationship between pricing and manufacturer patient programs, and to reform government program reimbursement methodologies for pharmaceutical products. For example, under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business. In August 2022, Congress passed the Inflation Reduction Act of 2022, or IRA, which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high-priced single source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries, among other changes. Various industry stakeholders, including certain pharmaceutical companies and the Pharmaceutical Research and Manufacturers of America, have initiated lawsuits against the federal government asserting that the price negotiation provisions of the IRA are unconstitutional. The impact of these judicial challenges, legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the government on us and the pharmaceutical industry as a whole is unclear. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drug candidates if approved.

In addition, individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical 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, mechanisms to encourage importation from other countries and bulk purchasing. A number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our drug products. It is possible that additional governmental action may be taken to address the COVID-19 pandemic. Furthermore, there has been increased interest by third party payors and governmental authorities in reference to pricing systems and publication of discounts and list prices. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drug candidates.

Employees and Human Capital Resources

As of December 31, 2023, we had 67 employees, 65 of whom were full-time and 45 of whom were engaged in research and development activities. Twenty-five of our employees hold Ph.D. or M.D. degrees. None of our employees is represented by a labor union or covered under a collective bargaining agreement. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. The principal purposes of our equity and cash incentive plans are to attract, retain and reward personnel through the granting of stock-based and cash-based compensation awards, in order to increase stockholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

Corporate Information

We were incorporated in Washington as a corporation in March 2011 under the name M3 Biotechnology, Inc. In October 2015, we converted to a Delaware corporation and subsequently changed our name to “Athira Pharma, Inc.” Our principal executive office is located at 18706 North Creek Parkway, Suite 104, Bothell Washington 98011. Our telephone number is (425) 620-8501. Our website is www.athira.com. Information contained in, or that can be accessed through, our website is not a part of,

and is not incorporated into, this report, and the inclusion of our website address in this report is an inactive textual reference only.

We make available on or through our website certain reports and amendments to those reports that we file with or furnish to the SEC in accordance with the Exchange Act. These include our annual reports on Form 10-K, our quarterly reports on Form 10-Q, and our current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make this information available on or through our website free of charge as soon as reasonably practicable after we electronically file the information with, or furnish it to, the SEC.

Item 1A. Risk Factors.

You should carefully consider the *following risk factors, in addition to* the other information *contained in this Annual Report on Form 10-K*, including the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section *and our consolidated financial statements and related notes. If any of the events described in the following risk factors and the risks described elsewhere in this report occurs, our business, operating results and financial condition could be seriously harmed. This report also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described below and elsewhere in this report. Our Risk Factors are not guarantees that no such conditions exist as of the date of this report and should not be interpreted as an affirmative statement that such risks or conditions have not materialized, in whole or in part.*

Risks Relating to Our Business and the Development of Our Drug Candidates

We are a late clinical-stage biopharmaceutical company with a limited operating history.

We are a late clinical-stage biopharmaceutical company focused on developing small molecules engineered to restore neuronal health and slow neurodegeneration. Our limited operating history may make it difficult to evaluate the success of our business. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. To date, we have not completed a pivotal clinical trial, obtained marketing approval for any drug candidate, manufactured a commercial scale drug candidate, or conducted sales and marketing activities necessary for successful drug candidate commercialization. Our history as a company makes any assessment of our future success and viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by clinical-stage biopharmaceutical companies in rapidly evolving fields, and we have not yet demonstrated an ability to overcome such risks and difficulties successfully. If we do not address these risks and difficulties successfully, our business will suffer.

We may fail to or be unable to design and execute clinical trials to support marketing approval of fosgonimeton or any of our other drug candidates. We cannot be certain that our current or planned clinical trials or any other future clinical trials will be completed on time or be successful. We cannot guarantee that the FDA or foreign regulatory authorities will agree with our study design, protocol or protocol amendments, or statistical plan, or that they will interpret clinical trial results as we do, and more clinical trials could be required before we are able to submit applications seeking approval of our drug candidates. To the extent that the results of the clinical trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional clinical trials in support of potential approval of our drug candidates (including potential confirmatory or Phase 3 registrational trials). Even if regulatory approval is secured for any of our drug candidates, the terms of such approval may limit the scope and use of our drug candidate, which may also limit its commercial potential.

Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve a number of objectives.

Our business depends entirely on the successful discovery, development and commercialization of our drug candidates. We have no drug products approved for commercial sale and do not anticipate generating any revenue from drug product sales for the next several years, if ever. Our ability to generate drug product revenue will depend heavily on the successful clinical development and eventual commercialization of fosgonimeton and one or more of our other future drug candidates. Our ability to

generate revenue and achieve profitability depends significantly on our ability to achieve a number of objectives, including:

- successful and timely completion of nonclinical and clinical development of our drug candidates and any future drug candidates, as well as the associated costs, including any unforeseen costs;
- establishing and maintaining relationships with contract research organizations, or CROs, and clinical sites for the clinical development, both in the United States and internationally, of our drug candidates and any future drug candidates;
- timely submission of application for and receipt of marketing approvals from applicable regulatory authorities for any drug candidates for which we successfully complete clinical development;
- making any required post-marketing approval commitments to applicable regulatory authorities;
- developing an efficient and scalable manufacturing process for our drug candidates, including obtaining finished products that are appropriately packaged for sale;
- establishing and maintaining commercially viable supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and meet the market demand for drug candidates that we develop, if approved;
- successful commercial launch following any marketing approval, including the development of a commercial infrastructure, whether inhouse or with one or more collaborators;
- a continued acceptable safety profile following any marketing approval of our drug candidates;
- commercial acceptance of our drug candidates by patients, the medical community and third-party payors;
- identifying, assessing and developing new drug candidates;
- obtaining, maintaining and expanding patent protection, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- protecting our rights in our intellectual property portfolio;
- defending against third-party interference or infringement claims, if any;
- negotiating favorable terms in any collaboration, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize our drug candidates;
- obtaining coverage and adequate reimbursement by hospitals, government and third-party payors for drug candidates that we develop;
- addressing any competing therapies and technological and market developments; and
- attracting, hiring and retaining qualified personnel.

We may never be successful in achieving our objectives and, even if we are, may never generate revenue that is significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable may decrease the value of our company and could impair our ability to maintain or further our research and development efforts, raise additional necessary capital, grow our business and continue our operations.

We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners, which may prevent us from completing our clinical trials or commercializing our drug candidates on a timely or profitable basis, if at all. Changes in the manufacturing process or facilities will require further comparability analysis and approval by the FDA before implementation, which could delay our clinical trials and drug candidate development, and could

require additional clinical trials, including bridging studies and potential confirmatory or Phase 3 registrational trials, to demonstrate consistent and continued safety and efficacy.

We have not previously submitted an NDA to the FDA or similar approval filings to a comparable foreign regulatory authority, for any drug candidate. An NDA or other relevant regulatory filing must include extensive nonclinical and clinical data and supporting information to establish that the drug candidate is safe and effective for each desired indication. The NDA or other relevant regulatory filing must also include significant information regarding the chemistry, manufacturing and controls for the drug product. We cannot be certain that our current or future drug candidates will be successful in clinical trials. Further, even if they are successful in clinical trials, our drug candidates or any future drug candidates may not receive regulatory approval. If we do not receive regulatory approvals for current or future drug candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approval to market a drug candidate, our revenue will depend, in part, upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights, as well as the availability of competitive products, whether there is sufficient third-party reimbursement and adoption by physicians.

Our development of fosgonimeton may never lead to a marketable product.

We are developing fosgonimeton as a small molecule aimed at restoring neuronal health. We have not received regulatory approval for fosgonimeton and cannot be certain that our approach will lead to the development of an approvable or marketable product, alone or in combination with other therapies. The primary and all secondary endpoints of the ACT-AD and SHAPE trials were not met by protocoled analysis. While we are continuing with the LIFT-AD study, we may not succeed in demonstrating safety and efficacy of fosgonimeton in our LIFT-AD trial or in other clinical trials.

Advancing fosgonimeton as a small molecule aimed at restoring neuronal health creates significant challenges for us, including:

- obtaining marketing approval;
- if fosgonimeton is approved, educating medical personnel regarding the potential efficacy and safety benefits, as well as the challenges, of incorporating fosgonimeton into existing treatment regimens, including in combination with other treatments for AD or as a monotherapy; and
- establishing the sales and marketing capabilities upon obtaining any marketing approvals to gain market acceptance.

Our prospects are highly dependent on the successful development of fosgonimeton. If we do not demonstrate the safety and efficacy of fosgonimeton in our LIFT-AD trial, we may explore strategic alternatives to maximize stockholder value, which could involve, without limitation, exploring the potential for a possible merger, business combination, investment, a purchase, license or other acquisition of assets or return of capital to stockholders.

Our approach to targeting neurotrophic factors through the use of small molecules is based on a novel therapeutic approach, which exposes us to unforeseen risks. We have limited data from our Phase 1a/1b and Phase 2 clinical trials to date, and we cannot be certain that future trials will yield data in support of the safety, efficacy and tolerability of our drug candidates.

We have discovered and are developing a platform of small molecule drug candidates from which we have selected our lead drug candidate, fosgonimeton, which is under development to treat AD, PDD, and DLB. Our drug candidates target an endogenous neurotrophic factor which is expected to protect and repair neuronal networks, which we believe could ultimately result in improvements in clinical outcomes and disease-relevant biomarkers. The therapeutic promise of neurotrophic factors in neurodegenerative diseases had been hampered in earlier therapies by the lack of efficient and non-invasive delivery to the CNS. Our small molecule drug candidates are designed to penetrate the BBB and enhance the activity of a neurotrophic factor, but we cannot be certain of the safety and efficacy of our drug candidates in applicable

patients or that our clinical trials will provide sufficient evidence that our design approach results in the intended therapeutic effect.

Based on the results of our nonclinical and clinical studies to date, we believe fosgonimeton has the potential to rapidly improve cognition, function and restore the lives of patients suffering from AD. However, these ideas and this approach are novel, and we currently have limited data based on our Phase 1a/b and Phase 2 clinical trials to date.

The primary and all secondary endpoints of our Phase 2 ACT-AD clinical trial in AD were not met by protocoled analysis. A subsequent post hoc analysis of the data in a pre-specified subgroup from patients on fosgonimeton without background therapy, or AChEIs, showed a meaningful, but not statistically significant, improvement in both ERP P300 latency and cognitive performance compared to placebo at 26 weeks. Although post hoc analyses cannot be used to establish efficacy, these analyses can be helpful in informing the design of current and future clinical studies. Following an unblinded interim efficacy and futility analysis, an independent DMC recommended continuation of the LIFT-AD study of fosgonimeton in patients with mild-to-moderate AD. The committee also determined that, with the additional enrollment of fewer than 150 patients for a total enrollment of less than 300 patients without background therapy (AChEIs), the study will be well powered for the primary endpoint given the preliminary effect size observed. There is no assurance that the amendments to our ongoing LIFT-AD trial based on our findings from the ACT-AD trial and our interim analyses will ultimately result in a successful trial. For example, our biomarker data may not translate into a statistically significant clinical benefit, the FDA may not agree with our statistical plan or analyses, or the trial may not be sufficiently powered for our endpoint measures.

In addition, the primary endpoint of our Phase 2 SHAPE clinical trial in PDD and DLB was not met by protocoled analysis. Directionally positive results were observed for the 40 mg fosgonimeton dose group with improvements in cognitive, functional and biomarker measurements. In particular, the five patients in the mITT population treated with fosgonimeton 40 mg once daily saw improvement in ADAS-Cog13 individually, and collectively improved compared with placebo (n=7 mITT, one-sided p=0.0321). Results for patients in the 70 mg dose group were inconsistent.

Data from our Phase 1a/1b and Phase 2 clinical trials to date were obtained from a relatively small number of subjects and we cannot be certain that future trials involving a larger number of subjects and clinical sites will yield data in support of the safety, efficacy and tolerability of our drug candidates. We may ultimately discover that fosgonimeton, or any of our other small molecules, do not possess certain properties required for therapeutic effectiveness. We have limited evidence regarding the efficacy, safety and tolerability of fosgonimeton and other small molecules in our drug product platform. We may spend substantial funds attempting to develop these drug candidates and never succeed in doing so.

We have concentrated our research and development efforts on the treatment of central and peripheral nervous system degenerative disorders, a field that has seen very limited success in product development.

We have focused our research and development efforts on addressing CNS and PNS degenerative disorders. Collectively, efforts by pharmaceutical companies in the field of CNS and peripheral degenerative disorders have seen very limited successes in product development. The development of CNS therapies presents unique challenges, including an imperfect understanding of the biology, the presence of the BBB that can restrict the flow of drugs to the brain, a frequent lack of translatability of preclinical study results in subsequent clinical trials and dose selection, and the product candidate having an effect that may be too small to be detected using the outcome measures selected in clinical trials or if the outcomes measured do not reach statistical significance. There are few effective therapeutic options available for patients with AD and other CNS or peripheral disorders. Our future success is highly dependent on the successful development of our technology and our drug candidates for treating CNS and peripheral disorders. Developing and, if approved, commercializing our drug candidates for treatment of CNS and peripheral disorders subjects us to a number of challenges, including ensuring that we have selected the optimal

doses, executing an appropriate clinical trial to test for efficacy and obtaining regulatory approval from the FDA and other regulatory authorities.

An independent special committee of our board of directors engaged in a review of papers co-authored by our former chief executive officer in connection with her doctoral research at WSU. The special committee's findings included that (1) our former chief executive officer altered images in her 2011 doctoral dissertation and at least four research papers that she co-authored while a graduate student at WSU, and published from 2011 to 2014, (2) that we cited challenged research papers in certain communications and applications, and (3) that WSU's dihexa patent, exclusively licensed to us, incorporated certain of these altered images. WSU has undertaken a review of claims of potential research misconduct involving our former chief executive officer's doctoral research at WSU. We cannot predict when WSU's investigation will be completed or what conclusions WSU will reach.

An independent special committee of our board of directors engaged in a review of papers co-authored by our former chief executive officer, Dr. Leen Kawas, in connection with her doctoral research at WSU, including, among other things, an investigation of allegations that Dr. Kawas altered images used in research published by Dr. Kawas in connection with her doctoral studies.

The independent special committee's primary finding was that our former chief executive officer altered images in her 2011 doctoral dissertation and at least four research papers that she co-authored while a graduate student at WSU, and published from 2011 to 2014. While the conduct that was the subject of the allegations is not related to any of our current drug candidates or ongoing clinical research, this finding could have a material adverse effect on our reputation, our in-licensed patents and pending patent applications, licenses and grants, and could lead to further investigation from government agencies, including the FDA, any of which could have a material adverse impact on our business and prospects.

As disclosed elsewhere in this report, including in this "Risk Factors" section under the heading "*—We and certain of our directors and executive officers have been, and may in the future be, named as defendants in lawsuits that could result in substantial costs and divert management's attention*," and in "Part I, Item 3—Legal Proceedings," lawsuits have been filed against us and certain of our directors and officers, alleging violations of federal securities laws related to alleged false and misleading statements in connection with the alleged misconduct of Dr. Kawas and others associated with us. As a result of these allegations and the ongoing litigation against us and certain of our directors and officers and related matters, we have been the subject of negative publicity. This negative publicity may harm our credibility, reputation and relationships with current and future investors, government regulators, patent offices, courts, current and prospective employees, key opinion leaders, prospective collaborators, advocacy groups, current and future patients enrolled in our clinical trials, physicians and prospective patients and vendors. For example, this negative publicity may adversely affect our ability to recruit and hire talented employees, maintain existing business relationships with CROs, clinical trial sites and other parties, enter into new business relationships, enroll patients in our clinical trials, and maintain a viable business in the future. Also, it is possible that the negative publicity and its effect on our work environment could cause our employees to terminate their employment or, if they remain employed by us, result in reduced morale that could have a material adverse effect on our business. In addition, negative publicity has and may continue to adversely affect our stock price and, therefore, employees and prospective employees may be less inclined to seek or continue employment with us. As a result, our business, financial condition, results of operations and cash flows could be materially adversely affected.

WSU has undertaken a review of claims of potential research misconduct involving our former chief executive officer's doctoral research at WSU.

In addition to the investigation of the independent special committee of our board of directors noted above, WSU has also announced that it has undertaken a review of claims of potential research misconduct involving research conducted by Dr. Kawas during her doctoral studies at WSU. We understand this review is ongoing, and at this time we cannot predict what, if any, effect the investigation will ultimately have on

our business and reputation. We are also unable to predict with any certainty when WSU's investigation will be completed. It is possible that the ongoing investigation by WSU will come to different conclusions, or uncover additional or different information, than the investigation of the independent special committee of our board of directors, the conclusions of which are discussed under "*—An independent special committee of our board of directors engaged in a review of papers co-authored by our former chief executive officer in connection with her doctoral research at WSU. The special committee's findings included that (1) our former chief executive officer altered images in her 2011 doctoral dissertation and at least four research papers that she co-authored while a graduate student at WSU, and published from 2011 to 2014, (2) that we cited challenged research papers in certain communications and applications, and (3) that WSU's dihexa patent, exclusively licensed to us, incorporated certain of these altered images. WSU has undertaken a review of claims of potential research misconduct involving our former chief executive officer's doctoral research at WSU. We cannot predict when WSU's investigation will be completed or what conclusions WSU will reach*". The conclusions from WSU's investigation could have a material adverse impact on our business, reputation, scientific credibility, and prospects, as well as our in-licensed patents and pending patent applications, current grants and pending grant applications, and our relationship with WSU, from whom we in-license patents and patent applications underlying certain of our drug candidates.

We are and may in the future be subject to claims, lawsuits, arbitration proceedings, government investigations and other legal, regulatory and administrative proceedings and face potential liability and expenses related thereto, which could have a material adverse effect on our business, operating results and financial condition.

We are and may in the future be subject to claims, lawsuits, arbitration proceedings, government investigations and other legal, regulatory and administrative proceedings. In November 2022, we received a Civil Investigative Demand from the Civil Division of the Department of Justice, or the Demand. The Demand seeks documents and information relating to our relationship with WSU, certain of our grant applications in 2016 and 2019 with the NIH, and our receipt of a NIH grant in 2020. We are cooperating with the Department of Justice with respect to the Demand. In February 2023, the Securities and Exchange Commission, or SEC, sent us a subpoena seeking documents and information relating to, among other things, our former chief executive officer's alteration of images in certain research papers. We are cooperating with the SEC with respect to the subpoena.

The outcome of these or any other investigations, claims, or proceedings cannot be predicted with any degree of certainty. In the ordinary course of business we have been and may in the future be the subject of various legal claims. Any such claims, investigations or proceedings against us, whether meritorious or not, could be time-consuming, result in costly litigation, be harmful to our reputation, require significant management attention and divert significant resources, and the resolution of any such claims, investigations or proceedings could result in substantial damages, settlement costs, fines or penalties that could adversely affect our business, financial condition or operating results or result in harm to our reputation and brand, sanctions, consent decrees, injunctions or other remedies requiring a change in our business practices.

Further, under certain circumstances we may have contractual or other legal obligations to indemnify and to incur legal expenses on behalf of investors, directors, officers employees, customers, vendors or other third-parties. For example, our amended and restated bylaws provide that we will indemnify our directors and officers, and may indemnify our employees, agents and other persons, to the fullest extent permitted by the Delaware General Corporation Law. We have also entered into indemnification agreements with directors and officers that require us, among other things, to indemnify them against claims that may arise due to their service in those capacities. These indemnification agreements also require us to advance expenses reasonably and actually incurred by them in investigating or defending any such claims, and it may be difficult or impossible to recover any advanced expenses if it turns out the person was not entitled to indemnification. If we are required or agree to defend or indemnify, or advance expenses to, any of our investors, directors, officers, employees, customers, vendors or other third-parties, we could incur material costs and expenses that could adversely affect our business, results of operations or financial condition.

Clinical development involves a lengthy and expensive process with an uncertain outcome, and results of early, smaller-scale preclinical studies and clinical trials with a single or few clinical trial sites may not be predictive of eventual safety or effectiveness in large-scale potentially pivotal clinical trials across multiple clinical trial sites. We may encounter substantial delays in clinical trials, or may not be able to conduct or complete clinical trials on the expected timelines, if at all.

Our lead drug candidate, fosgonimeton, is in clinical development for the potential treatment of AD, PDD and DLB. Our additional early drug candidates, including ATH-1105 for ALS, are in preclinical development. It is impossible to predict when or if any of our drug candidates will prove to be effective and safe in humans or will receive regulatory approval.

Before obtaining regulatory approvals for the commercial sale of our drug candidates, we must demonstrate through lengthy, complex and expensive nonclinical studies and clinical trials that our drug candidates are both safe and effective for each target indication. Nonclinical and clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the nonclinical study and clinical trial processes, and, because our drug candidates are in an

early stage of development, there is a high risk of failure and we may never succeed in developing marketable products. The results of nonclinical studies and early clinical trials of our drug candidates may not be predictive of the results of later-stage clinical trials. Although product candidates may demonstrate promising results in nonclinical studies and early clinical trials, they may not prove to be safe or effective in subsequent clinical trials. For example, testing on animals occurs under different conditions than testing in humans and therefore, the results of animal studies may not accurately predict safety and effectiveness in humans. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through nonclinical studies and clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through nonclinical studies and initial clinical trials. For example, our Phase 1a/b clinical trial, which enrolled 88 patients, including only 11 patients with mild-to-moderate AD, of whom seven patients were treated with fosgonimeton and the other four patients were randomized to the control, suggested improvements in brain network activity including potentially positive effects on brain function. However, our Phase 2 ACT-AD clinical trial in AD, which included a larger patient population, approximately 60% of which were receiving standard-of-care AChEIs, did not meet its primary endpoint of a change in ERP P300 latency for the full study population nor did it meet the secondary endpoints. Although a post hoc analysis of results from ACT-AD in a pre-specified subgroup suggested positive effects on measures of cognition, function and neurodegeneration in patients taking fosgonimeton alone without background AChEIs, we cannot be sure that data from future trials will support our earlier findings or demonstrate the safety and effectiveness of fosgonimeton for treatment of AD to the satisfaction of the FDA and other regulatory authorities in order to support regulatory approval. Likewise, early, smaller-scale studies, biomarker analyses, and clinical trials with a single or relatively few clinical trial sites may not be predictive of eventual safety and effectiveness in large-scale pivotal clinical trials across multiple clinical trial sites. Even if data from a pivotal clinical trial are positive, regulators may not agree that such data are sufficient for approval and may require that we conduct additional clinical trials (including potential confirmatory or Phase 3 registrational trials), which could materially delay our anticipated development timelines, require additional funding for such additional clinical trials, and adversely impact our business. Our ability to achieve regulatory approval for fosgonimeton is further complicated by the nature of AD, which historically has been a challenging indication for drug development. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that commence nonclinical studies and clinical trials are never approved as products.

In some instances, there can be significant variability in safety or efficacy results between different nonclinical studies and clinical trials of the same product candidate due to numerous factors, including changes in clinical trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. For example, we believe the topline results of our Phase 2 ACT-AD clinical trial may have differed from the treatment data from our Phase 1a/b clinical trial at least in part due to differences in the patient population and treatment duration, and potential effects from background AChEI treatment. If future trials show that the effect of fosgonimeton when given in combination with add-on standard-of-care AChEIs is diminished, we may be required to seek a narrower indication or restrict our target population to those where fosgonimeton shows a greater effect, which could have a material adverse effect on our business and prospects.

On July 6, 2021, we announced the initiation of an open-label extension for the LIFT-AD and ACT-AD trials and in May 2022 we announced the extension of the open label extension for an additional 12 months. In May 2023, we amended the open-label extension trial to further extend the trial by an additional 12 months. Upon completion of the 26-week treatment period during the LIFT-AD or ACT-AD trials, patients may continue on the open-label extension and receive treatment with fosgonimeton for up to an additional 30 months. Investigators and patients remain blinded to treatment group assignment in the original trials. Such open-label extension studies are, and some of the clinical trials we conduct in the future may be, open-label in study design conducted at a limited number of clinical sites on a limited number of patients. An “open-label” clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most

typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a “patient bias” where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an “investigator bias” where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such clinical trials are being conducted, by a data safety monitoring board for such clinical trial or by the FDA or comparable foreign regulatory authorities. Clinical trials can be delayed or terminated or fail to meet endpoints for a variety of reasons, including delays or failures related to:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical trials;
- the FDA or comparable foreign regulatory authorities disagreeing with our ATH clinical development strategy or statistical plan;
- changes in governmental regulations or administrative actions;
- delays in our ability to commence a clinical trial;
- reaching 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 clinical trial sites;
- obtaining IRB approval at each clinical trial site;
- recruiting an adequate number of suitable patients to participate in a clinical trial on a timely basis;
- the number of patients required for clinical trials of our drug candidates may be larger than we anticipate;
- having subjects complete a clinical trial or return for post-treatment follow-up;
- clinical trial sites deviating from clinical trial protocol or dropping out of a clinical trial;
- protocol deviations or non-compliance with GCP requirements, or other data integrity reasons, that cause us or the FDA or other regulatory authorities to exclude data from non-compliant sites or investigators, which may cause the trial to be underpowered to meet the endpoints;
- delays by us or our CROs in qualifying or analyzing patient data at the completion of clinical trials;
- failure to demonstrate a benefit from using a drug candidate;
- addressing subject safety concerns that arise during the course of a clinical trial;
- adding a sufficient number of clinical trial sites; or
- obtaining sufficient supply of drug candidate for use in nonclinical studies or clinical trials from third-party suppliers.

Further, conducting clinical trials in foreign countries, as we intend to do for our drug candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our drug candidates. If we experience delays in the completion of, or termination of, any clinical trial of our drug candidates, the commercial prospects of our drug candidates will be harmed, and our ability to generate product revenues from any of these drug candidates will be delayed. Moreover, any delays in completing our clinical trials will increase our costs, slow down our drug candidate development and approval process and jeopardize our ability to commence product sales and generate revenues.

If the results of our current and future clinical trials are inconclusive with respect to the efficacy of our drug candidates, if we do not meet the clinical endpoints with statistical and clinically meaningful significance, or if there are safety concerns associated with our drug candidates, we may:

- incur unplanned costs;
- be delayed in or prevented from obtaining marketing approval for our drug candidates;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings including boxed warnings;
- be subject to changes in the way the drug candidate is administered;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw their approval of the drug product or impose restrictions on its distribution in the form of a modified REMS;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

Any "topline", interim, initial, or preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or topline data from our nonclinical studies and clinical trials, 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 or clinical trial. 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 fully and carefully evaluate all data. As a result, the topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline 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, topline data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our nonclinical studies and clinical trials. For example, in October 2022 we announced that an independent DMC had conducted an unblinded interim efficacy and futility analysis with respect to our Phase 2/3 LIFT-AD clinical trial. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. 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.

Additionally, we rely on data received from clinical trials, whether preliminary or final, to inform decisions on future clinical trials, including trial design, trial size, and whether or not to initiate additional clinical trials (including any potential confirmatory or Phase 3 registrational trials). For example, in November 2020, we initiated ACT-AD, an exploratory Phase 2 clinical trial, to better understand the overall effects of fosgonimeton on working memory processing speed and cognitive measures. Topline results of ACT-AD were announced in June 2022. We used these data to help inform strategic decisions around LIFT-AD and expect to use these data to help inform strategic decisions in the future around current clinical trials and any additional trials that we may initiate. Topline results are based on a preliminary analysis of then-available data, and a more comprehensive and full review of the data may result in different conclusions, which could have a negative impact on our decisions regarding any additional trials for fosgonimeton. There is no assurance that the amendments to our ongoing LIFT-AD trial based on our findings from the ACT-AD trial and our interim analysis of the LIFT-AD trial will ultimately result in a successful trial. For example, our biomarker data may not translate into a statistically significant clinical benefit, the FDA may not agree with our statistical plan or analyses, or the trial may not be sufficiently powered for our endpoint measures.

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 program, the approvability or commercialization of the particular drug candidate or drug 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 you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. 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, our drug candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

If we experience delays or difficulties in the enrollment or retention of patients in clinical trials, our regulatory submissions or receipt of necessary marketing approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our drug candidates if we are unable to recruit and enroll a sufficient number of eligible patients to participate in these clinical trials through completion of such trials as required by the FDA or other comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials. Our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. Patient enrollment may also be affected if our competitors have ongoing clinical trials for programs that are under development for the same indications as our drug candidates, and patients who would otherwise be eligible for our clinical trials instead enroll in clinical trials of our competitors' programs. Additionally, publicly reported results of our completed clinical trials may impact enrollment of our trials in progress. If we are unable to locate a sufficient number of such patients, our clinical trial and development plans could be delayed.

If we are delayed or unsuccessful in enrolling the desired number of subjects in our trials, whether as a result of the outcomes of prior trials conducted by us, competing clinical trials, overly stringent eligibility requirements, or other factors, our clinical trial results could be delayed, the costs of our clinical trials could materially increase, and the overall development timeline for fosgonimeton could be negatively impacted. For example, enrollment in our ongoing clinical trials had slowed due to the effects of the COVID-19 pandemic, including governmental restrictions imposed in Australia, where certain of our clinical trial sites are located. In our ACT-AD clinical trial, this slowed recruitment resulted in a change in the timing of topline

results from our Phase 2 ACT-AD clinical trial, which were announced in June 2022. We cannot ensure that similar enrollment issues will not occur again in the future. Even if we are successful in enrolling the targeted number of subjects in our trials, the FDA and other regulators may request additional clinical trials with larger numbers of subjects (including potential confirmatory or Phase 3 registrational trials) as a condition to any regulatory approval.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Further, to the extent any of our clinical trial sites fail to comply with the approved study protocol, good clinical practices, or FDA regulations, we may be required to exclude such sites, participants such sites may have enrolled, as well as the data collected by such sites. If any of these events were to occur, or if we are required to exclude any data for any reason, we may be required to recruit more sites or more participants than we initially thought. Enrollment delays or other delays in our clinical trials may result in increased development costs for our drug candidates and jeopardize our ability to obtain marketing approval for the sale of our drug candidates. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining participation in our clinical trials through the treatment and any follow-up periods.

We face significant competition, and if our competitors develop and market technologies or products more rapidly than we do or that are more effective, safer, or less expensive than the drug candidates we develop, our commercial opportunities will be negatively impacted.

The biotechnology and pharmaceutical industries utilize rapidly advancing technologies and are characterized by intense competition. While we believe that our scientific knowledge, platform technology and development expertise provide us with competitive advantages, we face competitive pressures from both large and small pharmaceutical companies, emerging biotechnology companies, as well as academic, government and private research institutions. Many of our competitors have access to greater financial resources, market presence, expertise in development, preclinical and clinical testing, manufacturing, commercialization, regulatory approval process, or marketing and sales than we do. Our competitors may compete with us in patient recruitment, clinical research organization, and operational resources. As a result, our competitors may discover, develop, license or commercialize products before or more successfully than we do.

Drug candidates that we may successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. For example, the FDA recently granted traditional approval for lecanemab, a drug developed by Biogen Inc. and Eisai Co., Ltd., and Eli Lilly and Company is also developing drug candidates for AD. Key product features that would affect our ability to effectively compete with other therapeutics include the efficacy, safety and convenience of our drug products. Our competitors may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our drug candidates. The availability of reimbursement from government and other third-party payors will also significantly affect the pricing and competitiveness of our drug products. For example, CMS announced a two-part National Coverage Determination, or NCD, under which Medicare will cover monoclonal antibodies that target amyloid (or plaque) for the treatment of AD that receive traditional approval from the FDA under coverage with evidence development. Additionally, for drugs that FDA has not determined to have shown a clinical benefit or that received an accelerated approval, Medicare will provide coverage in FDA or NIH approved clinical trials. In June 2023, CMS announced that Medicare will cover new Alzheimer's drugs with traditional FDA approval when a physician and clinical team participate in CMS' registry to collect evidence about how these drugs work in the real world. Current and future CMS coverage restrictions on classes of drugs that encompass our drug candidates could have a material adverse impact on our ability to commercialize our drug candidates, if approved, generate revenue and attain profitability. It is unclear how future CMS coverage decisions and policies will impact our business. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. For additional information regarding our competition, see the section of this report titled "Part I, Item 1 – Business—Competition".

We may expend our limited resources to pursue a particular drug candidate or indication and fail to capitalize on drug candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs, therapeutic platforms and drug candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other therapeutic platforms or drug candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs, therapeutic platforms and drug candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights.

We may develop drug candidates in combination with other therapies, which exposes us to additional risks.

We may develop drug candidates in combination with one or more other approved or unapproved therapies. Even if any drug 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 risks that the FDA or comparable foreign regulatory authorities outside of the United States could revoke approval of the therapy used in combination with our drug product or that safety, efficacy, manufacturing or supply issues could arise with any of those existing therapies. If the therapies we use in combination with our drug candidates are replaced as the standard of care for the indications we choose for any of our drug candidates, the FDA or comparable foreign regulatory authorities may require us to conduct additional clinical trials. The occurrence of any of these risks could result in our own drug products, if approved, being removed from the market or being less successful commercially.

We also may choose to evaluate drug candidates in combination with one or more therapies that have not yet been approved for marketing by the FDA or comparable foreign regulatory authorities. We will not be able to market and sell any drug candidate we develop in combination with an unapproved therapy for a combination indication if that unapproved therapy does not ultimately obtain marketing approval either alone or in combination with our drug product. In addition, unapproved therapies face the same risks described with respect to our drug candidates currently in development and clinical trials, including the potential for serious adverse effects, delay in their clinical trials and lack of FDA approval. If the FDA or comparable foreign regulatory authorities do not approve these other drugs or revoke their approval of, or if safety, efficacy, quality, manufacturing or supply issues arise with, the drugs we choose to evaluate in combination with our drug candidate we develop, we may be unable to obtain approval of or market such combination therapy.

Our long-term prospects depend in part upon discovering, developing and commercializing additional drug candidates, which may fail in development or suffer delays that adversely affect their commercial viability.

Our future operating results are dependent on our ability to successfully discover, develop, obtain regulatory approval for and commercialize drug candidates beyond those we currently have in clinical and nonclinical development. A drug candidate can unexpectedly fail at any stage of nonclinical and clinical development. The historical failure rate for drug candidates is high due to risks relating to safety, efficacy, clinical execution, changing standards of medical care and other unpredictable variables. The results from nonclinical testing or early clinical trials of a drug candidate may not be predictive of the results that will be obtained in later stage clinical trials of the drug candidate.

The success of other future drug candidates we may develop will depend on many factors, including the following:

- generating sufficient data to support the initiation or continuation of clinical trials;
- obtaining regulatory permission to initiate clinical trials;
- contracting with the necessary parties to conduct clinical trials;
- successful enrollment of patients in, and the completion of, clinical trials on a timely basis;
- the timely manufacture of sufficient quantities of the drug candidate for use in clinical trials; and
- adverse events in the clinical trials.

Even if we successfully advance any other future drug candidates into clinical development, their success will be subject to all of the clinical, regulatory and commercial risks described elsewhere in this "Risk Factors" section. Accordingly, we cannot assure you that we will ever be able to discover, develop, obtain regulatory approval of, commercialize or generate significant revenue from our other future drug candidates.

We have conducted certain research and development operations through our Australian wholly owned subsidiary. If we lose our ability to operate in Australia, or if our subsidiary is unable to receive the research and development tax credit allowed by Australian regulations, our business and results of operations could suffer.

In July 2020, we formed a wholly owned Australian subsidiary to conduct various preclinical and clinical activities for our drug product and development candidates in Australia. Due to the geographical distance and lack of employees currently in Australia, as well as our lack of experience operating in Australia, we may not be able to efficiently or successfully monitor, develop and commercialize our drug product and development candidates in Australia, including conducting clinical trials. Furthermore, we have no assurance that the results of any clinical trials that we conduct for our drug candidates in Australia will be accepted by the FDA or foreign regulatory authorities for development and commercialization approvals.

In addition, current Australian tax regulations provide for a refundable research and development tax credit equal to 43.5% of qualified expenditures. If we lose our ability to operate our subsidiary in Australia, or if we are ineligible or unable to receive the research and development tax credit, or the Australian government significantly reduces or eliminates the tax credit, our business and results of operations may be adversely affected.

The loss of any of our key personnel could significantly harm our business, results of operations and competitive position.

In order to compete, we must attract, retain, and motivate executives and other key employees. Hiring and retaining qualified executives, scientists, technical and legal and accounting staff are critical to our business, and competition for experienced employees in our industry can be high. The loss of one or more of these key employees, or our inability to hire additional key personnel when needed, could have a material adverse effect on our business and prospects.

Risks Relating to Health Epidemics

The potential effects of health epidemics could adversely impact our business, including our nonclinical studies and clinical trials.

Our business could in the future be adversely impacted by the effects of possible health epidemics and other outbreaks which could cause disruptions that could severely impact our business, nonclinical studies and clinical trials. Such disruptions may include:

- delays or difficulties in enrolling and retaining patients in our clinical trials, particularly elderly subjects, who may be at a higher risk of severe illness or death, which can be further complicated by the presence of comorbidities that are often present in AD subjects;
- difficulties interpreting data from our clinical trials due to the possible effects of such diseases on cognition of the subjects enrolled in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures (such as endoscopies that are deemed non-essential), which may impact the integrity of subject data and clinical study endpoints;
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- interruption of, or delays in receiving, supplies of our drug candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;
- interruptions in nonclinical studies due to restricted or limited operations at our laboratory facility;
- limitations on employee resources that would otherwise be focused on the conduct of our nonclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- interruptions, difficulties or delays arising in our existing operations and company culture as a result of some or all of our employees working remotely;
- interruption or delays to our sourced discovery and clinical activities; and
- changes in clinical site procedures and requirements as well as regulatory requirements for conducting clinical trials during the pandemic.

For example, in the event of a disease outbreak or resurgence of COVID-19, we could be required to develop and implement additional clinical trial policies and procedures designed to help protect subjects from such diseases. On May 11, 2023, the federal government ended the COVID-19 public health emergency, which ended a number of temporary changes made to federally funded programs while some continue to be in effect. Since March 2020, the FDA has issued various COVID-19 related guidance documents for sponsors and manufacturers, many of which have expired or were withdrawn with the expiration of the COVID-19 public health emergency declaration, although some COVID-19 related guidance documents continue in effect. The full impact of this termination of the national emergency and the wind-down of the public health emergency on FDA and other regulatory policies and operations is unclear.

The trading prices for shares of biopharmaceutical companies have in the past been and could in the future be highly volatile as a result of health epidemics, including the COVID-19 pandemic, and the trading prices for shares of our common stock could also experience high volatility. In the event of an emergence of new disease outbreaks or a resurgence of COVID-19, we could face difficulties raising capital through sales of our common stock or such sales may be on unfavorable terms. In addition, a recession, depression or other sustained adverse market event resulting from a health epidemic, including a resurgence of COVID-19, could materially and adversely affect our business and the value of our common stock.

The ultimate impact of a possible health epidemic or other outbreak, including a resurgence of COVID-19, on our business operations is highly uncertain and subject to change and will depend on future developments, which cannot be accurately predicted. In addition, our business could be significantly adversely affected by other business disruptions to us or our third-party providers that could seriously harm our potential future revenue and financial condition and increase our costs and expenses. Our operations, and those of our CROs, commercial manufacturing organizations, or CMOs, and other contractors, consultants, and third parties could be subject to other global pandemics, earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce and process our drug candidates. Our ability to obtain clinical supplies of our drug candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

Risks Relating to Our Financial Position and Capital Needs

We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.

We have not generated any revenue from drug product sales and our drug candidates will require substantial additional investment before they may provide us with any revenue. We had net losses of $117.7 million and $95.6 million for the years ended December 31, 2023 and 2022, respectively, and an accumulated deficit of $309.2 million as of December 31, 2023.

We have devoted most of our financial resources to research and development, including our clinical and nonclinical development activities. To date, we have financed our operations primarily with proceeds from the sale and issuance of common stock, convertible preferred stock, common stock warrants, and convertible notes, and to a lesser extent from grant income and stock option exercises.

We expect to incur significant expenses and increasing operating losses for the foreseeable future as we:

- continue our research and nonclinical and clinical development of our drug candidates;
- expand the scope of our clinical studies for our current and prospective drug candidates;
- initiate additional nonclinical, clinical or other studies for our drug candidates, including any potentially pivotal trials with respect to fosgonimeton for the treatment of mild-to-moderate AD in addition to LIFT-AD, and continue the open label extension of the ACT-AD and LIFT-AD trials;
- change or add additional manufacturers or suppliers and manufacture drug supply and drug product for clinical trials and commercialization;
- seek regulatory and marketing approvals for any of our drug candidates that successfully complete clinical trials;
- attract, hire and retain additional personnel;

- operate as a public company;
- continue to expand our facilities and lab space;
- seek to identify and validate additional drug candidates;
- acquire or in-license other drug candidates and technologies or engage in other strategic transactions;
- make milestone or other payments under our in-license or other agreements;
- maintain, protect and expand our intellectual property portfolio;
- establish a sales, marketing and distribution infrastructure to commercialize any drug products for which we may obtain marketing approval;
- create additional infrastructure to support our operations and our drug product development and planned future commercialization efforts;
- incur expenses in connection with legal proceedings, and addressing potential stockholder activism; and
- experience any delays or encounter issues with any of the above.

Our expenses could increase beyond expectations for a variety of reasons, including if we are required by the FDA, the European Medicines Agency, or EMA, or other regulatory agencies, domestic or foreign, to perform clinical and other studies in addition to those that we currently anticipate. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity.

We will require substantial additional funding to finance our operations, complete the development and commercialization of fosgonimeton, and develop and commercialize other and future drug candidates. If we are unable to raise this funding when needed, we may be forced to delay, reduce, or eliminate our drug product development programs or other operations.

Since our inception, we have used substantial amounts of cash to fund our operations, and we expect our expenses to increase substantially in the foreseeable future in connection with our ongoing activities, particularly as we continue the research and development of, initiate clinical trials of, and seek marketing approval for, fosgonimeton. Developing fosgonimeton and conducting clinical trials for the treatment of AD, PDD, DLB, and any other indications that we may pursue in the future will require substantial amounts of capital. In addition, if we obtain marketing approval for fosgonimeton or any future drug candidates, we expect to incur significant commercialization expenses related to sales, marketing, manufacturing, and distribution. Furthermore, we expect to continue to incur additional costs associated with operating as a public company.

Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. As of December 31, 2023, we had cash, cash equivalents and investments of $147.4 million. Based upon our current operating plan, we estimate that our existing cash, cash equivalents and investments will be sufficient to fund our operating expenses and capital expenditure requirements through at least the next 12 months following the date of this report. However, changing circumstances may cause us to increase our spending significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We may need to raise additional funds sooner than we anticipate if we choose to expand more rapidly than we presently anticipate.

The amount and timing of our future funding requirements depends on many factors, some of which are outside of our control, including but not limited to:

- the progress, costs, clinical trial design, results of and timing of our LIFT-AD trial and other clinical trials of fosgonimeton, including for potential additional indications that we are pursuing beyond AD, such as PDD, DLB, and the continuation of the open label extension of the ACT-AD and LIFT-AD trials;
- the willingness of the FDA and EMA to accept our LIFT-AD trial, as well as data from our completed and planned clinical and nonclinical studies and other work, as the basis for review and approval of fosgonimeton for AD and the potential need for additional clinical trials (including potential confirmatory or Phase 3 registrational trials);
- the outcome, costs and timing of seeking and obtaining FDA, EMA and any other regulatory approvals;
- the number and characteristics of drug candidates that we pursue;
- our ability to manufacture sufficient quantities of our drug candidates;
- our need to expand our research and development activities;
- the costs associated with securing and establishing commercialization and manufacturing capabilities;
- the costs of acquiring, licensing or investing in businesses, drug candidates and technologies;
- the cost, timing and outcomes of any litigation involving our company, including securities class actions and government investigations which we may be or may in the future become involved in;
- our ability to maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights;
- our need and ability to retain management and hire scientific, clinical and other personnel;
- the effect of competing drugs and drug candidates and other market developments;
- our need to implement additional internal systems and infrastructure, including financial and reporting systems; and
- the economic and other terms, timing of and success of any collaboration, licensing or other arrangements into which we may enter in the future.

In January 2023, we entered into a sales agreement with Cantor Fitzgerald & Co., or Cantor Fitzgerald, and BTIG, LLC, or BTIG, to sell shares of our common stock having aggregate sales proceeds of up to $75.0 million, from time to time, through an at-the-market, or ATM, equity offering program under which Cantor Fitzgerald and BTIG are acting as sales agents. We have not sold any securities pursuant to this ATM offering. However, additional funding may not be available to us on acceptable terms or at all. Any such funding may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may affect our business. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail or abandon one or more of our research or development programs. We also could be required to seek funds through arrangements with collaborative partners or otherwise that may require us to relinquish rights to some of our technologies or drug candidates or otherwise agree to terms unfavorable to us.

We expect to finance our cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing or distribution arrangements. In addition, we may seek additional capital to take advantage of favorable market conditions

or strategic opportunities even if we believe we have sufficient funds for our current or future operating plans. Based on our research and development plans, we expect that our existing cash, cash equivalents and investments will enable us to fund our operations for at least 12 months following the date of this report. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned.

Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. For example, the current inflationary economic environment, health epidemics, and rising interest rates have resulted in a disruption of global financial markets. If the disruption persists or deepens, we could be unable to access additional capital, which could negatively affect our ability to consummate certain corporate development transactions or other important, beneficial or opportunistic investments. If additional funds are not available to us when we need them, on terms that are acceptable to us, or at all, we may be required to take steps that could adversely impact our business, including delaying, limiting, reducing or terminating nonclinical studies, clinical trials or other research and development activities or eliminating one or more of our development programs altogether, or delaying, limiting or reducing or terminating efforts to prepare for commercialization of any future approved drug products. We currently have a shelf registration statement effective and an existing ATM equity offering program, however, our ability to raise capital under this registration statement and through our ATM equity offering program may be limited by, among other things, SEC rules and regulations impacting the eligibility of smaller companies to use Form S-3 for primary offerings of securities.

Adverse events or perceptions affecting the financial services industry could adversely affect our operating results, liquidity, financial condition and prospects.

Limited liquidity, defaults, non-performance or other adverse developments affecting financial institutions or parties with which we do business, or perceptions regarding these or similar risks, have in the past and may in the future lead to market-wide liquidity problems. For example, in March 2023, Silicon Valley Bank, or SVB, was closed and placed in receivership and subsequently, additional financial institutions have been placed into receivership. We did not hold cash deposits or other accounts with SVB and did not, and as of the date of this report do not, otherwise have a direct business relationship with SVB or similarly situated financial institutions. However, companies that did have a business relationship with SVB faced:

- delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets;

- loss of access to revolving existing credit facilities or other working capital sources or the inability to refund, roll over or extend the maturity of, or enter into new credit facilities or other working capital resources;

- potential or actual breach of obligations, including U.S. federal and state wage laws and contracts that required them to maintain letters or credit or other credit support arrangements; and

- termination of cash management arrangements or delays in accessing or actual loss of funds subject to cash management arrangements.

As a result of U.S. government intervention, account holders subsequently regained access to their accounts, including the uninsured portion of deposit accounts; however, borrowers under credit agreements, letters of credit and certain other financial instruments with SVB and similarly situated financial institutions were unable to access to such sources of liquidity. There is no guarantee that the U.S. government will intervene to provide access to uninsured funds in the future in the event of the failure of other financial institutions, or that they would do so in a timely fashion. In such an event, parties with which

we have commercial agreements may be unable to satisfy their obligations to, or enter into new commercial arrangements with, us.

Concerns regarding the U.S. or international financial systems could impact the availability and cost of financing, thereby making it more difficult for us to acquire financing on acceptable terms or at all.

Any of these risks could materially impact our operating results, liquidity, financial condition and prospects.

The value of our investments is subject to significant capital markets risk related to changes in interest rates and credit spreads as well as other investment risks, which may adversely affect our operating results, liquidity, financial condition and prospects.

Our results of operations are affected by the performance of our investment portfolio. Our excess cash is invested by an external investment management service provider, under the direction of our management in accordance with our investment policy. The investment policy defines constraints and guidelines that restrict the asset classes that we may invest in by type, duration, quality and value. Our investments are subject to market-wide risks, and fluctuations, as well as to risks inherent in particular securities. The failure of any of the investment risk strategies that we employ could have a material adverse effect on our operating results, liquidity, financial condition and prospects.

The value of our investments is exposed to capital market risks, and our results of operations, liquidity, financial condition or cash flows could be adversely affected by realized losses, impairments and changes in unrealized positions as a result of: significant market volatility, changes in interest rates, changes in credit spreads and defaults, a lack of pricing transparency, a reduction in market liquidity, declines in equity prices, changes in national, state/provincial or local laws and the strengthening or weakening of foreign currencies against the U.S. dollar. Levels of write-down or impairment are impacted by our assessment of the intent to sell securities that have declined in value as well as actual losses as a result of defaults or deterioration in estimates of cash flows. If we reposition or realign portions of the investment portfolio and sell securities in an unrealized loss position, we will incur realized losses. Any such charge may have a material adverse effect on our results of operations and business.

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

As of December 31, 2023, we had federal net operating loss carryforwards, or NOLs, to offset future taxable income of approximately $9.5 million and federal tax credit carryforwards of approximately $12.4 million, which expire over a period of 8 to 14 years. Federal NOLs of $138.7 million were generated after 2017, and therefore do not expire. At December 31, 2023, we also had state NOLs of $3.3 million, which expire over a period of 18 to 20 years. A lack of future taxable income would adversely affect our ability to utilize these NOLs. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an “ownership change” is subject to limitations on its ability to utilize its NOLs to offset future taxable income. We may have already experienced one or more ownership changes. Depending on the timing of any future utilization of our NOLs and tax credit carryforwards, we may be limited as to the amount that can be utilized each year as a result of such previous ownership changes. However, we do not believe such limitations will cause our NOL and tax credit carryforwards to expire unutilized. In addition, future changes in our stock ownership as well as other changes that may be outside of our control, could result in additional ownership changes under Section 382 of the Code. Our NOLs may also be impaired under similar provisions of state law or limited pursuant to provisions of the Tax Cuts and Jobs Act amendments to the Code, as modified by the Coronavirus Aid, Relief, and Economic Security Act. We have recorded a full valuation allowance related to our NOLs and other deferred tax assets due to the uncertainty of the ultimate realization of the future benefits of those assets.

Changes in tax laws could have a material adverse effect on our business, cash flows, results of operations or financial condition.

We are subject to the tax laws, regulations, and policies of several taxing jurisdictions. Changes in tax laws, as well as other factors, could cause us to experience fluctuations in our tax obligations and effective tax rates and otherwise adversely affect our tax positions or our tax liabilities. For example, many countries and local jurisdictions and organizations such as the Organization for Economic Cooperation and Development have proposed or implemented new tax laws or changes to existing tax laws, including additional taxes on payroll or employees. Any new or changes to tax laws could adversely affect our effective tax rate, operating results, tax credits or incentives or tax payments, which could have a material adverse effect on our business, cash flows, results of operations or financial condition.

Risks Relating to Regulatory Approval and Other Legal Compliance Matters

The regulatory approval processes of the FDA and other comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our drug candidates, we will not be able to commercialize, or will be delayed in commercializing, our drug candidates, and our ability to generate revenue will be materially impaired.

Our drug candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable foreign regulatory authorities. Before we can commercialize any of our drug candidates, we must obtain marketing approval.

Obtaining approval by the FDA and other comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. 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, which may cause delays in the approval or the decision not to approve an application. Further, securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional nonclinical, clinical or other data. Even if we eventually complete clinical testing and receive approval for our drug candidates, the FDA and other comparable foreign regulatory authorities may approve our drug candidates for a more limited indication or a narrower patient population than we originally requested or may impose other prescribing limitations or warnings that limit the drug product's commercial potential. We have not submitted for, or obtained, regulatory approval for any drug candidate, and it is possible that none of our drug candidates will ever obtain regulatory approval. Further, development of our drug candidates or regulatory approval may be delayed for reasons beyond our control.

Applications for our drug candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or other comparable foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials;
- the FDA or other comparable foreign regulatory authorities may determine that our drug candidates are not safe and effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;

- the population studied in the clinical trial may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- the FDA or other comparable foreign regulatory authorities may disagree with our interpretation of data from nonclinical studies or clinical trials;
- we may be unable to demonstrate to the FDA or other comparable foreign regulatory authorities that our drug candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA or other comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications 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 other comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval or resulting in delays in our regulatory approval, including, for example, legislation or agency policies that aim to reform the accelerated approval process and FDA's increased scrutiny of post-approval confirmatory studies, which can result in withdrawal of accelerated approval if such studies fail to confirm a clinical benefit.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our drug candidates, which would significantly harm our business, results of operations and prospects. In addition, even if we obtain approval of our drug candidates, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, may impose significant limitations in the form of narrow indications, warnings, or a REMS. Regulatory authorities may not approve the price we intend to charge for drug products we may develop, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug candidate. Any of the foregoing scenarios could seriously harm our business.

Of the large number of drugs in development, only a small percentage successfully complete the FDA or comparable foreign regulatory approval processes and are commercialized. The lengthy approval processes as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our drug candidates, which would significantly harm our business, results of operations and prospects.

Our current or future drug candidates may cause significant adverse events, toxicities or other undesirable side effects when used alone or in combination with other approved products or investigational new drugs that may result in a safety profile that could inhibit regulatory approval, prevent market acceptance, limit their commercial potential or result in significant negative consequences.

As is the case with pharmaceuticals generally, it is likely that there may be side effects and adverse events associated with our drug candidates' use. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our drug 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 comparable foreign regulatory authorities. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the clinical trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

If our drug candidates are associated with undesirable side effects or have unexpected characteristics in nonclinical studies or clinical trials when used alone or in combination with other approved products or investigational new drugs we may need to interrupt, delay or abandon their development or limit 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. Treatment-related side effects could also affect patient recruitment or the ability of enrolled subjects to complete the clinical trial, or result in potential product liability claims. Any of these occurrences may prevent

us from achieving or maintaining market acceptance of the affected drug candidate and may harm our business, financial condition and prospects significantly.

Patients in our clinical trials may in the future suffer significant adverse events or other side effects not observed in our nonclinical studies or previous clinical trials. Some of our drug candidates may be used as chronic therapies or be used in populations for which safety concerns may be particularly scrutinized by regulatory agencies. In addition, if our drug candidates are used in combination with other therapies, our drug candidates may exacerbate adverse events associated with the therapy. Patients treated with our drug candidates may also be undergoing separate treatments which can cause side effects or adverse events that are unrelated to our drug candidate, but may still impact the success of our clinical trials, including, for example, by interfering with the effects of our drug candidates. A pre-specified group analysis of patients in our ACT-AD clinical trial identified a potential diminished effect of the combination of standard-of-care (AChEIs) and fosgonimeton. While more clinical studies are needed to determine the safety and efficacy of fosgonimeton, to the extent standard-of-care AChEIs impact the effects of fosgonimeton and if a significant portion of the patient population has already been treated with AChEIs, the potential target patient population or the indication we seek for fosgonimeton may be significantly smaller than we had anticipated, which could materially harm our business and prospects.

The inclusion of elderly patients in our clinical trials may result in deaths or other adverse medical events due to other therapies or medications that such patients may be using. If significant adverse events or other side effects are observed in any of our current or future clinical trials, we may have difficulty recruiting patients to the clinical trials, patients may drop out of our clinical trials, or we may be required to abandon the clinical trials or our development efforts of that drug candidate altogether. We, the FDA other comparable regulatory authorities or an IRB may suspend clinical trials of a drug candidate at any time for various reasons, including a belief that subjects in such clinical trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage clinical trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the drug candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance due to its tolerability versus other therapies. Any of these developments could materially harm our business, financial condition and prospects.

Further, if any of our drug candidates obtains marketing approval, toxicities associated with such drug candidates and not seen during clinical testing may also develop after such approval and lead to a requirement to conduct additional clinical safety trials, additional contraindications, warnings and precautions being added to the drug label, significant restrictions on the use of the drug product or the withdrawal of the drug product from the market. We cannot predict whether our drug candidates will cause toxicities in humans that would preclude or lead to the revocation of regulatory approval based on nonclinical studies or early-stage clinical trials.

Obtaining and maintaining regulatory approval of our drug candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our drug candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our drug candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction. For example, even if the FDA grants marketing approval of a drug candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion and reimbursement of the drug candidate in those countries. However, a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the United States, including additional nonclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a drug candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our drug products is also subject to approval.

We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of drug candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and establishing and maintaining compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our drug products in certain countries. If we or any future collaborator fail to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our potential drug candidates will be harmed.

Even if we receive regulatory approval of our drug candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our drug candidates.

Any regulatory approvals that we receive for our drug candidates will require surveillance to monitor the safety and efficacy of the drug candidate. The FDA may also require a REMS in order to approve our drug candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our drug candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our drug candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP regulations, GLP regulations and GCP regulations for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with our drug candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of our drug candidates, withdrawal of the drug product from the market or voluntary or mandatory product recalls;
- manufacturing delays and supply disruptions where regulatory inspections identify observations of noncompliance requiring remediation;
- revisions to the labeling, including limitation on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings;
- imposition of a REMS, which may include distribution or use restrictions;
- requirements to conduct additional post-market clinical trials to assess the safety of the drug product;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of our drug candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug 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, and we may not 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. It is difficult to predict how current and future

legislation, executive actions, and litigation, including the executive orders, will be implemented, and the extent to which they will impact our business, our clinical development, and the FDA's and other agencies' ability to exercise their regulatory authority, including FDA's pre-approval inspections and timely review of any regulatory filings or applications we submit to the FDA. To the extent any 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. In addition, if the Supreme Court reverses or curtails the Chevron doctrine, which gives deference to regulatory agencies in litigation against FDA and other agencies, more companies may bring lawsuits against FDA to challenge longstanding decisions and policies of FDA, which could undermine FDA's authority, lead to uncertainties in the industry, and disrupt FDA's normal operations, which could delay FDA's review of our marketing applications.

Moreover, the FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. 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 civil, criminal and administrative penalties. The occurrence of any event or penalty described above may inhibit our ability to commercialize our drug candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

Disruptions at the FDA, the SEC and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC, and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

To the extent the FDA's normal operations are disrupted or delayed, for example due to travel restrictions, public health or geopolitical issues, staffing shortages, or lack of funding, the FDA may not be able to complete the necessary inspections or provide feedback in a timely manner during our clinical development or review period. If any such delays or disruptions were to occur, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns or delays could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

We may attempt to secure approval from the FDA or comparable foreign regulatory authorities through the use of accelerated approval pathways. If we are unable to obtain such approval, we may be required to conduct additional nonclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous postmarketing requirements, the FDA may seek to withdraw accelerated approval.

We may seek an accelerated approval for one or more of our drug candidates. Under the accelerated approval program, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate

clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. If such post-approval studies fail to confirm the drug's clinical benefit, the FDA may withdraw its approval of the drug.

Prior to seeking accelerated approval for any of our drug candidates, we intend to seek feedback from the FDA and will otherwise evaluate our ability to seek and receive accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that after subsequent FDA feedback we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or receive an expedited regulatory designation (e.g., breakthrough therapy designation) for our drug candidates, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our drug candidate would result in a longer time period to commercialization of such drug candidate, could increase the cost of development of such drug candidate and could harm our competitive position in the marketplace.

Further, to the extent the FDA materially changes its policies or regulatory requirements with respect to the accelerated approval program or its internal review process for such program, our clinical development plans and regulatory approval under such program could be materially impacted or delayed. On December 29, 2022, the Consolidated Appropriations Act, 2023, including the FDORA, was signed into law. FDORA made several changes to the FDA's authorities and its regulatory framework, including, among other changes, reforms to the accelerated approval pathway, such as requiring the FDA to specify conditions for post-approval study requirements and setting forth procedures for the FDA to withdraw a product on an expedited basis for non-compliance with post-approval requirements. It is unclear how these proposals, future policy changes, and changes in FDA regulation will impact new drug applications in the treatment of AD and our clinical development programs.

We may face difficulties from changes to current regulations and future legislation. Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations.

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our drug candidates or any future drug candidates, restrict or regulate post-approval activities and affect our ability to profitably sell a drug product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example:

- changes to our manufacturing arrangements;
- additions or modifications to drug product labeling;

- the recall or discontinuation of our drug products; or
- additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the ACA was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry. The ACA contained provisions that may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the U.S. Department of Health and Human Services Secretary, or HHS Secretary, as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. The ACA made several changes to the Medicaid Drug Rebate Program, including increasing the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program, extending the rebate program to individuals enrolled in Medicaid managed care organizations. The ACA also established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% (increased pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D. In December 2020, the U.S. Centers for Medicare & Medicaid Services, or CMS, issued a final rule implementing significant manufacturer price reporting changes under the Medicaid Drug Rebate Program, including regulations that affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value-based purchasing arrangements. Under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business.

As discussed above, since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA. On January 28, 2021, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare. In June 2021, the United States Supreme Court held that Texas and other challengers had no legal standing to challenge the ACA, dismissing the case without specifically ruling on the constitutionality of the ACA. Further, on August 16, 2022, President Biden signed the IRA into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost through a newly established manufacturer discount program. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how additional challenges and healthcare reform measures of the Biden administration will impact the ACA. Complying with any new legislation and regulatory requirements could be time-intensive and expensive, resulting in a material adverse effect on our business.

The Bipartisan Budget Act of 2018 also amended the ACA, effective January 1, 2019, by increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. In addition, CMS has published a final rule to give states greater flexibility, starting in 2020, in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. The American Taxpayer Relief Act of 2012, or ATRA, among other things, reduced Medicare payments to

several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Other legislative changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and will remain in effect through 2032 with the exception of a temporary suspension implemented under various COVID-19 relief legislation.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, 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. For example, in July 2021, the Biden administration released an executive order, “Promoting Competition in the American Economy,” with multiple provisions aimed at increasing competition for prescription drugs. In August 2022, Congress passed the IRA, which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high-priced single source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries, among other changes. Further, the Biden administration released an additional executive order on October 14, 2022, directing the U.S. Department of Health and Human Services, or HHS, to submit a report within ninety (90) days on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. Various industry stakeholders, including pharmaceutical companies, the U.S. Chamber of Commerce, the National Infusion Center Association, the Global Colon Cancer Association, and the Pharmaceutical Research and Manufacturers of America, have initiated lawsuits against the federal government asserting that the price negotiation provisions of IRA are unconstitutional. The impact of these judicial challenges as well as other legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the government on us and the pharmaceutical industry as a whole is unclear. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drug candidates if approved.

In April 2022, CMS released a finalized national policy for coverage of aducanumab, or Aduhelm, and any future monoclonal antibodies directed against amyloid approved by the FDA with an indication for use in treating AD. According to the two-part NCD, Medicare will cover monoclonal antibodies that target amyloid (or plaque) for the treatment of AD that receive traditional approval from the FDA when furnished in accordance with the coverage criteria specified under coverage with evidence development. CMS will also provide enhanced access and coverage for Medicare patients participating in CMS-approved studies, such as data collection through routine clinical practice or registries. Additionally, for drugs that FDA has not determined to have shown a clinical benefit or that received an accelerated approval, Medicare will provide coverage in FDA or NIH approved clinical trials. In June 2023, CMS announced that Medicare will cover new Alzheimer's drugs with traditional FDA approval when a physician and clinical team participate in CMS' registry to collect evidence about how these drugs work in the real world. Current and future CMS coverage restrictions on classes of drugs that encompass our drug candidates could have a material adverse impact on our ability to commercialize our drug candidates, if approved, generate revenue and attain profitability. It is unclear how future CMS coverage decisions and policies will impact our business.

At the state level, individual states are 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. In addition, regional health care 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 health care programs. These measures could reduce the ultimate demand for our drug products, once approved, or put pressure on our drug product pricing. A number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our drug products. Further, FDA recently authorized the state of Florida to import certain prescription drugs from Canada for a period of two years to help reduce drug costs, provided that Florida's Agency for Health Care Administration meets the requirements set forth by the FDA. Other states may follow Florida. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our drug candidates or additional pricing pressures.

Our revenue prospects could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future, including repeal, replacement or significant revisions to the ACA. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare or impose price controls may adversely affect:

- the demand for our drug candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our drug products;
- our ability to obtain coverage and reimbursement approval for a drug product;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability.

We expect that other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drug candidates. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for biotechnology products. We cannot be sure to what extent the trajectory of these legislative and regulatory proposals will be implemented by the federal and state governments, whether additional legislative changes will be enacted, whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our drug candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Our relationships with healthcare professionals, clinical investigators, CROs and third party payors in connection with our current and future business activities, and our participation in the federal health care programs and acceptance of federal grant funding, such as funding from the NIH, may be subject to federal and state healthcare fraud and abuse laws, false claims laws, transparency laws, government price reporting, and health information privacy and security laws, which could expose us to, among other things, criminal sanctions, civil penalties, contractual damages, exclusion from governmental healthcare programs, reputational harm, administrative burdens and diminished profits and future earnings.

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of any drug candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, clinical investigators, CROs, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our drug products for which we obtain marketing approval. Similarly, our participation in the federal health care programs and acceptance of federal grant funding from the NIH may subject us to federal false claims laws, civil penalties and assessments, criminal prosecution, and other administrative, civil, and criminal remedies.

The laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, 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 a federal healthcare program, such as the Medicare and Medicaid programs. 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. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act, or FCA. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, but the exceptions and safe harbors are drawn narrowly and require strict compliance in order to offer protection.
- federal civil and criminal false claims laws, including the FCA, which can be enforced through civil "qui tam" or "whistleblower" actions, and civil monetary penalty laws, impose criminal and

civil penalties against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other federal health care programs that are false or fraudulent; knowingly making or causing a false statement material to a false or fraudulent claim or an obligation to pay money to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing such an obligation. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the federal civil FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs. Under the FCA, a "claim" also includes any request (including grant request) or demand for money or property made to the United States or to a contractor, recipient, if the Federal government provides or will reimburse any portion of the funds claimed. "Funds" include money that the NIH awards as part of research grants. Even if a federal grant is not awarded, the grant applicant may be subject to FCA liability if the information contained in or submitted as part of a grant application, including its certifications and assurances, is found to be false, fictitious, or fraudulent.

- HIPAA, which created new federal criminal statutes that prohibit 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 by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates and their subcontractors that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization. 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 Physician Payments Sunshine Act, created under the ACA and its implementing regulations, which require manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to payments or other transfers of value made to covered recipients, including physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician healthcare professionals (such as physician assistants and nurse practitioners, among others), and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members.
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.
- analogous state and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical

business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial 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 federal government that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; state and local laws requiring the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of available statutory exceptions and regulatory safe harbors, it is possible that some of our business activities, including our advisory board arrangements with physicians, some of whom receive stock or stock options as compensation for services provided, and any sales and marketing activities after a drug candidate has been approved for marketing in the United States, could be subject to legal challenge and enforcement actions. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to significant civil, criminal, and administrative penalties, including, without limitation, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

In addition to the risks relating to the outcome of the independent special committee's investigation noted above, we are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in misconduct or other improper activities. Misconduct by these parties could include failures to comply with FDA regulations, provide accurate information to the FDA, comply with federal and state health care fraud and abuse laws and regulations, accurately report financial information or data or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the health care 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. Misconduct by these parties could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by these 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 these laws or regulations. 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, including the imposition of significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations. We can face serious consequences for violations.

Among other matters, U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations, which are collectively referred to as Trade Laws, prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of trade laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We also expect our non-U.S. activities to increase in time. We plan to engage third parties for clinical trials or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals and we can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

Risks Relating to Our Reliance on Third Parties

We rely on third parties to conduct our nonclinical studies and clinical trials. If these third parties do not properly and successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval of or commercialize our drug candidates.

We utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs, CMOs, and strategic partners to conduct and support our nonclinical studies and clinical trials under agreements with us.

We expect to have to negotiate budgets and contracts with CROs, clinical trial sites and CMOs and we may not be able to do so on favorable terms, which may result in delays to our development timelines and increased costs. We will rely heavily on these third parties over the course of our nonclinical studies and clinical trials, and we control only certain aspects of their activities. As a result, we will have less direct

control over the conduct, timing and completion of these nonclinical studies and clinical trials and the management of data developed through nonclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with GCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for drug candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of clinical trial sponsors, principal investigators and clinical trial sites. If we or any of these third parties fail to comply with applicable GCP regulations, 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. In particular, protocol deviations or non-compliance with GCP requirements, or other data integrity reasons, can cause us or the FDA or other regulatory authorities to exclude data from non-compliant sites or investigators, which may cause the trial to be underpowered to meet the endpoints. We cannot assure you that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP regulations. In addition, our clinical trials must be conducted with pharmaceutical drug product produced under cGMP regulations and will require a large number of test patients. Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting our clinical trials are not and will not be our employees and, except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our ongoing, clinical and non-clinical drug candidates. These third parties 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 affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced 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 other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our drug candidates. As a result, our financial results and the commercial prospects for our drug candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

Switching or adding third parties to conduct our nonclinical studies and clinical trials involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines.

We contract with third parties for the manufacture of our drug candidates for nonclinical studies and our clinical trials, and expect to continue to do so for additional clinical trials and ultimately for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our drug candidates or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently have the infrastructure or internal capability to manufacture supplies of our drug candidates for use in development and commercialization. We rely, and expect to continue to rely, on third-party manufacturers for the production of our drug candidates for nonclinical studies and clinical trials under the guidance of members of our organization. We do not have long-term supply agreements. Furthermore, the raw materials for our drug candidates are sourced, in some cases, from a single-source supplier and sometimes involve long lead times from order to receipt of the materials. If we were to experience an unexpected loss of supply of any of our drug candidates or any of our future drug candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays,

disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing clinical trials. We expect to continue to rely on third-party manufacturers for the commercial supply of any of our drug candidates for which we obtain marketing approval. We may be unable to maintain or establish required agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the failure of the third party to manufacture our drug candidates according to our schedule, or at all, including if our third-party contractors give greater priority to the supply of other products over our drug candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- the reduction or termination of production or deliveries by suppliers, or the raising of prices or renegotiation of terms;
- the termination or nonrenewal of arrangements or agreements by our third-party contractors at a time that is costly or inconvenient for us;
- the breach by the third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the failure of the third party to manufacture our drug candidates according to our specifications;
- the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the misappropriation of our proprietary information, including our trade secrets and know-how.

We do not have complete control over all aspects of the manufacturing process of, and are dependent on, our contract manufacturing partners for compliance with cGMP regulations for manufacturing both active drug substances and finished drug products. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure or maintain marketing approval for their manufacturing facilities. In addition, we do not have control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our drug candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our drug candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of drug candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our drug candidates or drugs and harm our business and results of operations. Our current and anticipated future dependence upon others for the manufacture of our drug candidates or drugs may adversely affect our future profit margins and our ability to commercialize any drug candidates that receive marketing approval on a timely and competitive basis.

Our manufacturing process needs to comply with FDA regulations relating to the quality and reliability of such processes. Any failure to comply with relevant regulations could result in delays

in or termination of our clinical programs and suspension or withdrawal of any regulatory approvals.

In order to commercially produce our drug products either at our own facility or at a third party's facility, we will need to comply with the FDA's cGMP regulations and guidelines. We may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. We are subject to inspections by the FDA and comparable foreign regulatory authorities to confirm compliance with applicable regulatory requirements. Any failure to follow cGMP or other regulatory requirements or delay, interruption or other issues that arise in the manufacture, fill-finish, packaging, or storage of our precision medicines as a result of a failure of our facilities or the facilities or operations of third parties to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our drug candidates, including leading to significant delays in the availability of our precision medicines for our clinical trials or the termination of or suspension of a clinical trial, or the delay or prevention of a filing or approval of marketing applications for our drug candidates. Significant non-compliance could also result in the imposition of sanctions, including warning or untitled letters, fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our drug candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage our reputation and our business.

If our third-party manufacturers use hazardous materials in a manner that causes injury or violates applicable law, we may be liable for damages.

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical materials, by our third-party manufacturers. Our manufacturers are subject to federal, state and local laws and regulations in the United States governing the use, manufacture, storage, handling and disposal of medical and hazardous materials. Although we believe that our manufacturers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury resulting from medical or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. We do not have any insurance for liabilities arising from medical or hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations.

We may use strategic collaborations, licensing arrangements or partnerships to accelerate the development and maximize the commercial potential of our programs, and we may not realize the benefits of such collaborations, arrangements or partnerships.

We own worldwide rights to fosgonimeton as well as our pipeline of small molecule candidates. Where appropriate, we may use strategic collaborations, licensing arrangements or partnerships to accelerate the development and maximize the commercial potential of our programs. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business.

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 a strategic partnership or other alternative arrangements for our drug candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our drug candidates as having the requisite potential to demonstrate safety and efficacy and obtain marketing approval. In addition, the effects to our business and reputation discussed in "*—An independent special committee of our board of directors engaged in a review of papers co-authored by our former chief executive officer in connection with her doctoral research at WSU. The special committee's findings included that (1)*

our former chief executive officer altered images in her 2011 doctoral dissertation and at least four research papers that she co-authored while a graduate student at WSU, and published from 2011 to 2014, (2) that we cited challenged research papers in certain communications and applications, and (3) that WSU's dihexa patent, exclusively licensed to us, incorporated certain of these altered images. WSU has undertaken a review of claims of potential research misconduct involving our former chief executive officer's doctoral research at WSU. We cannot predict when WSU's investigation will be completed or what conclusions WSU will reach," may discourage potential counterparties from entering into relationships with us.

If and when we seek to enter into collaborations, we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of a drug 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 increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our drug candidates or bring them to market and generate product revenue.

Even if we are successful in entering into collaborations involving our drug candidates, these relationships are subject to numerous risks, which may include the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration;
- collaborators may not pursue development and commercialization of our drug candidates or may elect not to continue or renew development or commercialization of our drug candidates based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial, abandon a drug candidate, repeat or conduct new clinical trials or require a new formulation of a drug candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our drug candidates;
- a collaborator with marketing and distribution rights to one or more drug products may not commit sufficient resources to their marketing and distribution;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our drug candidates, or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable drug candidates; and
- collaborators may own or co-own intellectual property covering our drug products that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property.

As a result, if we enter into additional strategic collaborations, licensing arrangements or partnerships, 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, which could delay our timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic collaboration, licensing arrangement or partnership, we will achieve the revenue or specific net income that justifies such transaction. Any delays in entering into new strategic collaborations, licensing arrangements or partnerships related to our drug candidates could delay the development and commercialization of our drug candidates in certain geographies for certain indications, which would harm our business prospects, financial condition and results of operations.

If we engage in future acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

From time to time, we evaluate various acquisition opportunities and strategic transactions and partnerships, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent liabilities;
- the issuance of our equity securities;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and marketing approvals; and
- our inability to generate revenue from acquired technology or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we undertake acquisitions or pursue partnerships in the future, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense.

Risks Relating to Our Ability to Commercialize our Drug Product

Even if approved, our drug candidates may not achieve adequate market acceptance among physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

Even if our drug candidates receive regulatory approval, they may not gain adequate market acceptance among physicians, patients, healthcare payors and others in the medical community. The degree of market acceptance or reimbursement of any of our approved drug candidates will depend on a number of factors, including:

- the efficacy and safety profile as demonstrated in clinical trials compared to alternative treatments;
- the timing of market introduction of the drug candidate as well as competitive products;

- the clinical indications for which the drug candidate is approved;
- the extent of physician acceptance of FDA-approved therapies for AD or other target indications;
- restrictions on the use of our drug candidates, such as boxed warnings or contraindications in labeling, or a REMS, if any, which may not be required of alternative treatments and competitor products;
- the potential and perceived advantages of our drug candidates over alternative treatments;
- the cost of treatment in relation to alternative treatments;
- pricing and the availability of coverage and adequate reimbursement by third-party payors, including government authorities;
- the availability of the approved drug candidate for use as a combination therapy;
- relative convenience and ease of administration;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the effectiveness of sales and marketing efforts;
- unfavorable publicity relating to our drug products or drug candidates or similar approved products or product candidates in development by third parties; and
- the approval of other new therapies for the same indications.

If any of our drug candidates are approved but do not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors and patients, we may not generate or derive sufficient revenue from such drug candidates and our financial results could be negatively impacted.

We have never commercialized a drug candidate before and may lack the necessary expertise, personnel and resources to successfully commercialize any drug products on our own or together with suitable collaborators.

We have never commercialized a drug candidate. We may license certain rights with respect to our drug candidates to collaborators, and, if so, we will rely on the assistance and guidance of those collaborators. For drug candidates for which we retain commercialization rights and marketing approval, we will have to develop our own sales, marketing and supply organization or outsource these activities to a third party.

Factors that may affect our ability to commercialize our drug candidates, if approved, on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, developing adequate educational and marketing programs to increase public acceptance of our approved drug candidates, ensuring regulatory compliance of our company, employees and third parties under applicable healthcare laws, and other unforeseen costs associated with creating an independent sales and marketing organization. Developing a sales and marketing organization will be expensive and time-consuming and could delay the launch of our drug candidates upon approval. We may not be able to build an effective sales and marketing organization. If we are unable to build our own distribution and marketing capabilities or to find suitable partners for the commercialization of our drug candidates, we may not generate revenues from them or be able to reach or sustain profitability.

If the market opportunity for any drug candidate that we develop is smaller than we believe, our revenue may be adversely affected and our business may suffer.

We intend to initially focus our drug candidate development on treatments for various CNS and PNS disorder indications. The addressable patient populations that may benefit from treatment with our drug candidates, if approved, are based on our estimates. These estimates, which have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations and market research, may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these

CNS and PNS disorders. Any regulatory approval of our drug candidates would be limited to the therapeutic indications examined in our clinical trials and as determined by the FDA, which would not permit us to market our drug products for any other therapeutic indications not expressly approved by the FDA. Additionally, the potentially addressable patient population for our drug candidates may not ultimately be amenable to treatment with our drug candidates. For example, pre-specified subgroup analysis based on topline data from our ACT-AD clinical trial identified a potential diminished effect of the combination of standard-of-care (AChEIs) and fosgonimeton. If such hypothesis is supported by additional research, patients receiving AChEIs could be excluded from the addressable patient population for fosgonimeton. Even if we receive regulatory approval for any of our drug candidates, such approval could be conditioned upon label restrictions that materially limit the addressable patient population. Our market opportunity may also be limited by future competitor treatments that enter the market. If any of our estimates prove to be inaccurate, the market opportunity for any drug candidate that we or our strategic partners develop could be significantly diminished and have an adverse material impact on our business.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our drug candidates.

We face an inherent risk of product liability as a result of the planned clinical testing of our drug candidates and will face an even greater risk if we commercialize any drug products. For example, we may be sued if our drug candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical 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, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our drug candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our drug candidates or drug products that we may develop;
- injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- diversion of management's time and our resources;
- substantial monetary awards to clinical trial participants or patients;
- drug product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any drug candidate; and
- a decline in our share price.

Failure to obtain or retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of drug products we develop, alone or with corporate collaborators. Although we have clinical trial insurance, our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle

us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

The insurance coverage and reimbursement status of newly-approved products is uncertain. Our drug candidates may become subject to unfavorable pricing regulations, third-party coverage and reimbursement practices, or healthcare reform initiatives, which would harm our business. Failure to obtain or maintain adequate coverage and reimbursement for new or current drug products could limit our ability to market those drug products and decrease our ability to generate revenue.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs vary widely from country to country. In the United States, recently enacted legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a drug product in a particular country, but then be subject to price regulations that delay our commercial launch of the drug product, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the drug product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if any drug candidates we may develop obtain marketing approval.

In the United States and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our drug candidates will depend in part on the extent to which coverage and adequate reimbursement for these drug products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments such as gene therapy products. Sales of these or other future drug candidates that we may identify will depend substantially, both domestically and abroad, on the extent to which the costs of our drug candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our drug candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. Reimbursement by a third-party payor may depend upon a number of factors, including, but not limited to, the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. In many countries, the prices of medical products are subject to

varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines, 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 drug candidates. Accordingly, in markets outside the United States, the reimbursement for products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

There is also significant uncertainty related to the insurance coverage and reimbursement of newly approved products and coverage may be more limited than the purposes for which the medicine is approved by the FDA or comparable foreign regulatory authorities. In the United States, the principal decisions about reimbursement for new medicines are typically made by CMS, an agency within HHS. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. No uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement levels 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 may require us to provide scientific and clinical support for the use of our drug products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. It is difficult to predict what CMS will decide with respect to reimbursement for fundamentally novel products such as ours. Reimbursement agencies in Europe may be more conservative than CMS. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved drug products we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize drug candidates, and our overall financial condition.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable reimbursement rates third-party payors for any approved drug products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize drug products and our overall financial condition.

Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any drug candidate that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any drug candidate for which we obtain marketing approval. In order to obtain reimbursement, physicians may need to show that patients have superior treatment outcomes with our drug products compared to standard of care drugs, including lower-priced generic versions of standard of care drugs. We expect to experience pricing pressures in connection with the sale of any of our drug candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

A variety of risks associated with marketing our drug candidates internationally may materially adversely affect our business.

We plan to eventually seek regulatory approval of our drug candidates outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- differing regulatory requirements in foreign countries, such as the lack of pathways for accelerated drug approval, may result in foreign regulatory approvals taking longer and being more costly than obtaining approval in the United States;
- foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials or our interpretation of data from nonclinical studies or clinical trials;
- approval policies or regulations of foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval;
- impact of health epidemics, including COVID-19, on our ability to produce our drug candidates and conduct clinical trials in foreign countries;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with legal requirements applicable to privacy, data protection, information security and other matters;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes and government payors in foreign countries;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the Foreign Corrupt Practices Act of 1977 or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with international operations may materially adversely affect our ability to attain or maintain profitable operations.

Risks Relating to Our Intellectual Property

Our success depends on our ability to protect our intellectual property and our proprietary technologies.

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our drug candidates, proprietary technologies and their uses as well as our ability to operate without infringing upon the proprietary rights of others. We generally seek to protect our proprietary position by filing patent applications in the United States and abroad related to our drug candidates, proprietary technologies and their uses that are important to our business. We may also seek to protect our proprietary position by acquiring or in-licensing relevant issued patents or pending applications from third parties.

Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology. There can be no assurance that our patent applications or the patent applications of any current or future licensors will result in additional patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around, found unenforceable or invalidated by third parties.

Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties or the patent owner before various patent offices or in courts. Thus, the degree of future protection for our and any current or future licensors' proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. These uncertainties or limitations in our ability to properly protect the intellectual property rights relating to our drug candidates could have a material adverse effect on our financial condition and results of operations.

We cannot be certain that the claims in our pending patent applications or those of any current or future licensors will be considered patentable by the USPTO courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our owned or in-licensed patents will not be found invalid or unenforceable if challenged.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our potential future collaborators will be successful in protecting our drug candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- patent applications may not result in any patents being issued;
- patents and patent applications may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- changes to patent laws in the United States or in other countries may limit the ability to obtain, defend or enforce patents, or may apply retroactively to affect the terms or scope of patents;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use and sell our potential drug candidates;

- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope or term of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

The patent prosecution process is also expensive and time-consuming, and we and any current or future licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. It is also possible that we or any current or future licensors will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

In addition, although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed. Certain of these parties may also be subject to public information disclosure statutes and could determine to disclose patentable aspects of our research and development output pursuant to a request thereunder, notwithstanding the existence of a non-disclosure and confidentiality agreement. Any of these actions could jeopardize our ability to seek patent protection.

Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates or their use might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical product candidates would be adversely affected.

The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications and those of any current or future licensors may not result in patents being issued which protect our drug candidates or their use or which effectively prevent others from commercializing competitive product candidates.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we own or in-license currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we own or in-license may be challenged or circumvented by third parties or may be narrowed, invalidated or rendered unenforceable as a result of challenges by third parties. Consequently, we do not know whether our drug candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents or the patents of any current or future licensors 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.

The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our patents or the patents of any current or future licensors may be challenged in the courts or patent offices in the United States and abroad. We may be subject to a third-party pre-issuance submission of prior art to the USPTO, or become involved in opposition, derivation, revocation, reexamination, post-grant review, or

PGR, and *inter partes* review, or IPR, or other similar proceedings challenging our patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our patent rights, allow third parties to commercialize our drug candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

Moreover, our patents or the patents of any current or future licensors may become subject to post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our claim of priority of invention, scope, validity or patentability with respect to our patents and patent applications and those of any current or future licensors.

For example, in view of the lawsuits disclosed elsewhere in this report including in this "Risk Factors" section under the heading "—*We and certain of our directors and executive officers have been, and may in the future be, named as defendants in lawsuits that could result in substantial costs and divert management's attention*," and in "Part I, Item 3—Legal Proceedings," third parties may challenge the validity or enforceability of our in-licensed patents and patent applications. The outcome following legal assertions of invalidity and unenforceability is unpredictable. Such challenges may result in loss of patent rights, loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar technology and drug products such as other modifications to dihexa not covered by our issued patents. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. In addition, if the breadth or strength of protection provided by our in-licensed patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop, or commercialize current or future drug candidates. Further, these proceedings could have a material adverse effect on our business, results of operations and financial condition.

Even though we own patents and patent applications covering fosgonimeton and its use, our patents and any future patents we obtain may not effectively prevent others from developing or commercializing products similar to our drug candidates. While the fosgonimeton patent family is distinct from, and not part of the same patent family as, the dihexa patent licensed from WSU, and therefore is not implicated in the allegations that Dr. Kawas altered images in connection with her doctoral studies, third parties may use these allegations to cast doubt on the validity and enforceability of our owned patents or patent applications. Such events may result in substantial cost and require significant time from our scientists and management, and could dissuade companies from collaborating with us to license, develop, or commercialize current or future drug candidates, even if the eventual outcome is favorable to us.

We or WSU may in the future file one or more requests for supplemental examination of certain patents for the USPTO to reconsider the enforceability and validity of the patents (including any patents relating to dihexa) in view of the allegations that Dr. Kawas altered images in connection with her doctoral studies. The outcome of any supplemental examination procedure is unpredictable. If a substantial new question of patentability is found, the USPTO Director will order ex parte reexamination of the patent. An adverse determination in such a proceeding could reduce the scope of, or invalidate or render unenforceable, the affected patent rights. While supplemental examination proceedings that result in our favor would bolster the presumption of validity and enforceability of the examined patents, third parties may still challenge the patents and patent applications in litigation or other legal proceedings.

Intellectual property rights do not necessarily 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. For example:

- others may be able to develop products that are similar to our drug candidates but that are not covered by the claims of the patents that we own or license;
- we or any current or future licensors or collaborators might not have been the first to make the inventions covered by the issued patents or patent application that we own or license;
- we or any current or future licensors or collaborators might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that the pending patent applications we own or license will not lead to issued patents;
- issued patents that we own or license 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 and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may have an adverse effect on our business; and
- we may choose not to file a patent application in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent application covering such intellectual property.

Should any of these events occur, it could significantly harm our business, results of operations and prospects.

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.

Our commercial success depends in part on avoiding infringement of the patents and proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our drug candidates and drug products that may be approved in the future, or impair our competitive position. There is a substantial amount of litigation and other legal actions, both within and outside the United States, involving patent and other intellectual property rights in the biopharmaceutical industry, including patent infringement lawsuits, reexaminations, IPR proceedings and PGR proceedings and oppositions before the USPTO and/or corresponding foreign patent offices. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing drug candidates. There may be third-party patents or patent applications with claims to compositions, materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our drug candidates.

As the biopharmaceutical industry expands and more patents are issued, the risk increases that our drug candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained as confidential for a certain period of time, until the relevant application is published, we may be unaware of third-party patents or patent applications that may be infringed by commercialization of any of our drug candidates, and we cannot be certain that we were the first to file a patent application related to a drug candidate, its use, or our technology. Moreover, because patent applications can take many years to issue, there may be currently-pending patent applications that may later result in issued patents that our drug candidates or their use may infringe. In addition, identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. There is also no assurance that there is not prior art of which we are aware, but which we do not believe is relevant to our business, which may, nonetheless, ultimately be found to limit our ability to make, use, sell, offer for sale or import our drug candidates that may be approved in the future, or impair our competitive position. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Any defense to claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation that may cause negative publicity;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing any of our drug candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis;
- subject us to significant liability to third parties; or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all, or which might be non-exclusive, which could result in our competitors gaining access to the same technology.

Although no third party has asserted a claim of patent infringement against us as of the date of this report, others may hold proprietary rights that could prevent our drug candidates from being marketed. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our drug candidates, treatment indications, or processes could subject us to significant liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or market our drug candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion for management and other personnel. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Moreover, even if we or a future strategic partner were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. In addition, we cannot be certain that we could redesign our drug candidates, our treatment indications, or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing our drug candidates, which could harm our business, financial condition and operating results. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our drug candidates and technology.

Parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have

material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

We may not be successful in obtaining or maintaining necessary rights to our drug candidates through acquisitions and in-licenses.

Because our development programs may in the future require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license, or use these third-party proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for our drug candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property, or if we are unable to maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or drug candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We may be involved in lawsuits to protect or enforce our patents or any current or future licensors' patents, which could be expensive, time consuming and unsuccessful. Further, our issued patents or any current or future licensors' patents could be found invalid or unenforceable if challenged in court.

Competitors may infringe our intellectual property rights. To prevent infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in a patent infringement proceeding, a court may decide that a patent we own or in-license is not valid, is unenforceable, or is not infringed. If we or any of our potential future collaborators were to initiate legal proceedings against a third party to enforce a patent directed at one of our drug candidates or their method of use, the defendant could counterclaim that our patent or the patent of any current or future licensors is invalid or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including allegations of a lack of novelty, obviousness, lack of sufficient written description, non-enablement, or obviousness-type double patenting. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent application misrepresented or fraudulently withheld relevant information from the USPTO or made a misleading statement during prosecution.

Third parties may also raise similar invalidity claims before the USPTO or patent offices abroad, even outside the context of litigation. Such mechanisms include re-examination, PGR, IPR, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in the revocation of, cancellation of, or amendment to our patents or any current or future licensors' patents in such a way that they no longer cover our technology or platform, or any drug candidates that we may develop. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to a validity claim, 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 third party 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 technology or platform, or any drug candidates that we may develop. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations and prospects.

The outcome following legal assertions of invalidity or unenforceability is unpredictable, and prior art could render our patents or any current or future licensors' patents invalid. There is no assurance that all potentially relevant prior art relating to our patents and patents applications or the patents and patent applications of any current or future licensors has been found. There is also no assurance that there is not prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim in our patents and patent applications or the patents and patent applications of any current or future licensors, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. Additionally, a finding that issued claims lack sufficient written description or are not enabled could render our patent or any current or future licensors' patent invalid.

If a third party were to prevail on a legal assertion of invalidity or unenforceability, we may lose at least part, and perhaps all, of the patent protection on such drug candidate. In addition, if the breadth or strength of protection provided by our patents and patent applications or the patents and patent applications of any current or future licensors is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future drug candidates. Such a loss of patent protection would have a material adverse impact on our business.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our management and other 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 perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other legal proceedings relating to our intellectual property rights, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

In addition, the issuance of a patent does not give us the right to practice the patented invention. Third parties may have blocking patents that could prevent us from marketing our own patented drug product and practicing our own patented technology.

Intellectual property litigation or legal proceedings may lead to unfavorable publicity that harms our reputation and causes the market price of our common stock to decline.

During the course of any intellectual property litigation or legal proceeding, there could be public announcements of the initiation of the litigation or legal proceeding as well as results of hearings, rulings on motions, and other interim proceedings. If securities analysts or investors regard these announcements as negative, the perceived value of our existing drug candidates, programs or intellectual property could be diminished. Accordingly, the market price of shares of our common stock may decline. Such announcements could also harm our reputation or the market for our future drug products, which could have a material adverse effect on our business.

Derivation proceedings may be necessary to determine priority of inventions, and an unfavorable outcome may require us to cease using the related technology or to attempt to license rights from the prevailing party.

Derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of any current or future licensors or of third parties. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other personnel. In addition, the uncertainties associated with such proceedings could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our drug candidates to market.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications or those of any current or future licensors and the enforcement or defense of our issued patents or those of any current or future licensors.

On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a “first inventor to file” system in which, assuming that other requirements of patentability are met, the first inventor to file a patent application will be entitled to the patent regardless of whether a third party was first to invent the claimed invention. A third party that filed a patent application in the USPTO after March 2013 but before us could therefore be awarded a patent covering an invention of ours or our current or future licensors even if we or our current or future licensors had made the invention before it was made by such third party. This requires us to be cognizant going forward of the time from invention to filing of a patent application. Furthermore, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our technology and the prior art allow our technology to be patentable over the prior art. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we may not be certain that we or any current or future licensors are the first to either (1) file any patent application related to our drug candidates, their use, or our technology or (2) invent any of the inventions claimed in the patents or patent applications.

The Leahy-Smith Act also included a number of significant changes that affect the way patent applications are prosecuted and also may affect patent litigation. These include allowing third-party submission of printed publications to the USPTO during patent prosecution and additional procedures to attack the validity or enforceability of a patent by USPTO-administered post-grant proceedings, including PGR, IPR, and derivation proceedings. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position.

Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States 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 or those of our current or future licensors that would not have been invalidated if first challenged by the third party in a district court action. Thus, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications or those of any current or future licensors and the enforcement or defense of our issued patents or those of any current or future licensors, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Changes in U.S. patent law, or laws in other countries, could diminish the value of patents in general, thereby impairing our ability to protect our drug candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. Changes in either the patent laws or in the interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property and may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. We cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. In addition, Congress or other foreign legislative bodies may pass patent reform legislation that is unfavorable to us.

For example, 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 the U.S. Congress, the U.S. federal courts, the USPTO, or similar authorities in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patent and the patents we might obtain or license in the future. As an example, European patent applications now provide the option, upon grant of a patent, of becoming a Unitary Patent, which is subject to the jurisdiction of the Unitary Patent Court, or UPC. The option of a Unitary Patent is a significant change in European patent practice. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation in the UPC.

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

We may also be subject to claims that former employees or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distraction to management and other employees.

Patent terms may be inadequate to protect our competitive position on our drug candidates for an adequate amount of time.

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 drug candidates or their use are obtained, once the patent life has expired, we may be open to competition from competitive products, including generic versions of our drug products. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing drug products similar or identical to ours.

If we do not obtain patent term extension for our drug candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our drug candidates, one or more of our U.S. patents or those of any current or future licensors may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, or Hatch-

Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. A maximum of one patent may be extended per FDA approved product as compensation for the patent term lost during clinical trials and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension may also be available in certain foreign countries upon regulatory approval of our drug candidates, although the requirements and terms of such extensions vary country-by-country. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products or launch generic versions of our drug products following our patent expiration, and our revenue could be reduced, possibly materially. Further, if this occurs, our competitors may take advantage of our investment in development and clinical trials by referencing our clinical and nonclinical data and launch their drug product earlier than might otherwise be the case.

We will not be able to protect our intellectual property rights throughout the world.

We own and in-license patents and pending patent applications in the United States and in jurisdictions outside of the United States. However, filing, prosecuting and defending patents in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States may be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we will not be able to prevent third parties from practicing our inventions in all countries outside the United States or from selling or importing drug products made using our inventions in and into the United States or other jurisdictions. Competitors may use our inventions in jurisdictions where we have not obtained patent protection to develop their own drug products and, further, may export otherwise infringing drug products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These drug products may compete with our drug candidates, and our patents, the patents of any current or future licensors, or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of many foreign countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or any current or future licensors' patents or marketing of competing drug products in violation of our proprietary rights. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents or the patents of any current or future licensors at risk of being invalidated or interpreted narrowly and our patent applications or the patent applications of any current or future licensors 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.

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 patents. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Geopolitical actions could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the United States and foreign government actions related to Russia's invasion of Ukraine may limit or prevent filing, prosecution and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees that have citizenship or nationality in, are registered in, or have a predominately primary place of business or profit-making activities in the United States and other countries that Russia has deemed unfriendly without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

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

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents or applications will be due to the USPTO and various foreign patent offices at various points over the lifetime of our patents or applications and those of any current or future licensors. We have systems in place to remind us to pay these fees, and we rely on our outside patent annuity service to pay these fees when due. Additionally, the USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, it could have a material adverse effect on our business.

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

We intend to use registered or unregistered trademarks or trade names to brand and market ourselves and our drug products. Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest, and it may be difficult and costly to register, maintain or protect our rights to these trademarks and trade names in jurisdictions in and outside of the United States. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to 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, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition, we rely on the protection of our trade secrets, including unpatented know-how, technology and other proprietary information to maintain our competitive position. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with our employees, consultants and advisors, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party improperly disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets.

Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced, and our competitive position would be harmed. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

We may be subject to claims that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of third parties.

We have entered into and may enter in the future into non-disclosure and confidentiality agreements to protect the proprietary positions of third parties, such as outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors, potential partners, lessees of shared multi-company property and other third parties. We may become subject to litigation where a third party asserts that we or our employees inadvertently or otherwise breached the agreements and used or disclosed their trade secrets or other information proprietary to the third parties. Defense of such matters, regardless of their merit, could involve substantial litigation expense and be a substantial diversion of employee resources from our business. We cannot predict whether we would prevail in any such actions. Moreover, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our drug candidates. Failure to defend against any such claim could subject us to significant liability for monetary damages or prevent or delay our developmental and commercialization efforts, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees.

Parties making claims against us may be able to sustain the costs of complex intellectual property litigation more effectively than we can because they have substantially greater resources. 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. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, operating results, financial condition and prospects.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is common in the biopharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our drug candidates. Many of these consultants, and many

of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other biopharmaceutical companies including our competitors or potential competitors. We may become subject to claims that we, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees.

Our rights to develop and commercialize our drug candidates may be subject, in part, to the terms and conditions of licenses granted to us by others.

We have entered into license agreements with third parties and we may enter into additional license agreements in the future with others to advance our research and development or allow commercialization of drug candidates. These and other licenses may not provide exclusive rights to use such intellectual property and other rights in all relevant fields of use and in all territories in which we may wish to develop or commercialize our drug candidates in the future. Further, these and other licenses may also include certain restrictions or obligations that limit our ability to engage with third parties, including potential restrictions on sublicensing or outsourcing certain activities.

In addition, subject to the terms of any such license agreements, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering our drug candidates that we license from third parties. In such an event, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If any of our current or future licensors fail to prosecute, maintain, enforce, and defend such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our drug candidates that are subject of such licensed rights could be adversely affected.

Our licensors and any future licensors may have relied on third party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents we in-license. If it is later determined that third parties own the rights to our in-licensed patents, or if other third parties have ownership rights to our in-licensed patents, such third parties may be able to license such patents to our competitors, and our competitors could market drug products similar or identical to our drug candidates. This could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects.

It is possible that we may be unable to obtain additional licenses at a reasonable cost or on reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same rights licensed to us. In that event, we may be required to expend significant time and resources to redesign our drug candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected drug candidates, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third party patents do not exist which might be enforced against our current manufacturing methods, drug candidates, methods of use, or future methods or drug candidates resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties or other forms of compensation to third parties, which could be significant.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights or other rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

Disputes may arise between us and our current or future licensors regarding intellectual property and other rights subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our drug candidates infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense to third parties;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- our right to transfer or assign the license;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we license intellectual property or other rights from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or other rights, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property or other rights that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected drug candidates, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In spite of our best efforts, our licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize drug candidates covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, drug products identical to ours. This could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects.

The patent protection and patent prosecution for some of our drug candidates may be dependent on third parties.

While we normally seek to obtain the right to control prosecution, maintenance and enforcement of the patent applications and patents relating to our drug candidates and their use, there may be times when the filing and prosecution activities for patent applications and patents relating to our drug candidates are controlled by licensors or collaboration partners. If a licensor or collaboration partner fails to prosecute, maintain and enforce such patents and patent applications in a manner consistent with the best interests of our business, including by payment of all applicable fees for patent applications and patents covering our drug candidates, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, our ability to develop and commercialize those drug candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling drug products similar or identical to our drug candidates. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed to and from third parties, we may still be adversely

affected or prejudiced by actions or inactions of our licensees, our licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution.

Intellectual property discovered or developed through government funded programs may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a manufacturing preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights and limit our ability to contract with non-U.S. manufacturers, which could adversely affect our ability to successfully develop and commercialize our drug products.

We entered an exclusive license agreement with WSU for certain licensed patents that include intellectual property that was generated through the use of U.S. government funding, and we received a grant from the NIA of the NIH to support our ACT-AD clinical trial. Pursuant to the Bayh-Dole Act, the U.S. government may have certain rights in any invention developed or reduced to practice with government funding. In addition, in the future we may discover, develop, acquire, or license new intellectual property that has been generated through the use of U.S. government funding or grants in which the U.S. government may have certain rights pursuant to the Bayh-Dole Act. These U.S. government rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right, under certain limited circumstances, to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (1) adequate steps have not been taken to commercialize the invention; (2) government action is necessary to meet public health or safety needs; or (3) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). Such "march-in" rights would apply to new subject matter arising from the use of such government funding or grants and would not extend to pre-existing subject matter or subject matter arising from funds unrelated to the government funding or grants. If the U.S. government exercises its march-in rights in our intellectual property rights that are generated through the use of U.S. government funding or grants, we could be required to license or sublicense intellectual property discovered or developed by us or that we license on terms unfavorable to us, and there can be no assurance that we would receive compensation from the U.S. government for the exercise of such rights. The U.S. government also has the right to take title to these inventions if the grant recipient fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. Reporting of a subject invention and compliance with the Bayh-Dole Act requirements were delayed for the patent family directed to methods of treating AD with fosgonimeton. As such, this patent family may be subject to U.S. government action which may include loss of rights in the subject invention, suspending or terminating the grant or future awards, or withholding further awards. Should any of these events occur, it could significantly harm our business, results of operations and prospects. In addition, the Bayh-Dole Act requires that, in certain circumstances, any products embodying intellectual property generated with the use of U.S. government funds or produced through the use of any such intellectual property be manufactured substantially in the United States. This preference for U.S. industry may be waived by the federal agency that provided the funding if the owner or assignee of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. industry may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property, which could adversely affect our ability to successfully develop and commercialize our drug products and have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks Relating to Cybersecurity

We are dependent on networks, infrastructure and data, which exposes us to data security risks, including security failures or breaches of our systems or those used by our CROs or other contractors or consultants. We are dependent upon our own or third-party information technology

systems, infrastructure and data, including mobile technologies, to operate our business. The multitude and complexity of our computer systems may fail or suffer security breaches.

As discussed in this report in "Part I, Item I.C—Cybersecurity," we have implemented various processes and policies for identifying, assessing, and managing material risks from cybersecurity threats. However, despite the implementation of such safeguards and security measures, our internal computer systems and those of our CROs and other contractors and consultants may nevertheless be vulnerable to damage from computer viruses and unauthorized access. Likewise, data privacy or security incidents or breaches by employees or others may pose a risk that sensitive data, including our intellectual property, trade secrets or personal information of our employees, patients, customers or other business partners may be exposed to unauthorized persons or to the public or may otherwise be misused. Cyberattacks, malicious internet-based activity, online and offline fraud, and other similar activities threaten the confidentiality, integrity, and availability of our personal, sensitive, confidential or proprietary information and information technology systems, and those of the third parties upon which we rely. For example, in April 2023, CRO Evotec SE faced a cybersecurity attack that temporarily disrupted its systems and operations. Such threats are prevalent and continue to rise, are increasingly difficult to detect, and come from a variety of sources, including traditional computer "hackers," threat actors, "hacktivists," organized criminal threat actors, personnel (such as through theft or misuse), sophisticated nation states, and nation-state-supported actors. Some actors now engage and are expected to continue to engage in cyber-attacks, including without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we, the third parties upon which we rely, may be vulnerable to a heightened risk of these attacks, including retaliatory cyber-attacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our goods and services.

We and the third parties upon which we rely may be subject to a variety of evolving threats, including but not limited to social-engineering attacks (including through phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial-of-service attacks (such as credential stuffing), credential harvesting, personnel misconduct or error, ransomware attacks, supply-chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, earthquakes, fires, floods, and other similar threats. Increases in remote work impacting how our employees work and access our systems could lead to additional opportunities for bad actors to launch cyberattacks or for employees to cause inadvertent security risks or incidents and may amplify the impacts of any security breach or incident. Future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies.

We may rely on third-party service providers and technologies to operate critical business systems to process sensitive information and other company data in a variety of contexts. We may also rely on third-party service providers to provide certain products or services, or otherwise to operate our business. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. Security incidents or other interruptions suffered by our third-party service providers could cause us to experience adverse consequences. While we may be entitled to damages if our third-party service providers fail to satisfy their privacy- or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. In addition, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third-party partners' supply chains have not been compromised.

Our business partners face similar risks, and any security breach of, or security incident impacting, their systems or that they otherwise suffer could adversely affect our security posture. A security breach or incident or privacy violation that leads to loss of or unauthorized use, disclosure or modification of, or access to trade secrets, company resources, personal, sensitive, confidential or proprietary information, including protected health information or other patient information, or that prevents access to patient information, as

well as the perception that any of the foregoing has occurred, could harm our reputation, compel us to comply with federal or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, cause us to provide other notification or take other steps in response to such breach or violation, require us to verify the correctness of database contents and otherwise subject us to litigation, claims, investigations, penalties or other liability under laws and regulations, any of which could disrupt our business or result in increased costs or loss of revenue or company resources. Moreover, the prevalent use of mobile devices that access confidential information, increase the risk of security breaches and incidents.

Despite efforts to create security barriers to the above-described threats, it is impossible for us to entirely mitigate these risks. To date, we have not experienced any material impact to our business, financial position or results of operations resulting from cyberattacks or other information security incidents such as phishing, social engineering, ransomware or malware attacks; however, because of the frequently changing attack techniques, along with the increased volume and sophistication of such attacks, our business, financial position or results of operations could be adversely impacted in the future. We may be unable to anticipate or prevent techniques used to obtain unauthorized access or to compromise our systems because they change frequently and are generally not detected until after an incident has occurred. If a compromise or other security breach or incident were to occur and cause the loss or corruption of data or interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss, unavailability, or corruption of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Any disruption or security breach or incident resulting in loss or unavailability of, or damage to, our data or systems, or inappropriate use, disclosure or modification of personal, sensitive, confidential or proprietary information, could result in us incurring liability and in delays to further development and commercialization of our drug candidates could be delayed. While we have invested, and continue to invest, in the protection of our data and information technology infrastructure, there can be no assurance that our efforts will prevent service interruptions, or prevent or identify vulnerabilities or security breaches or incidents, that could adversely affect our business and operations or result in the loss, unavailability, or corruption of, or inappropriate access to or use of, critical or sensitive information or company resources. Any such interruptions, breaches or incidents, or the perception any have occurred, could result in financial, legal, business or reputational harm to us. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyberattacks and other privacy and security breaches or incidents.

Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.

Data collection is governed by restrictive regulations governing the use, processing and cross-border transfer of personal information.

As we conduct our clinical trials and continue to enroll patients in our current and future clinical trials, we may be subject to additional restrictions relating to privacy, data protection and data security. The collection, use, storage, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals in the European Economic Area, or EEA, is subject to the EU General Data Protection Regulation, or GDPR. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA, including the United States, and permits data protection authorities to impose

large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers. Certain aspects of cross-border data transfers under the GDPR are subject to uncertainty, including as the result of legal proceedings in the EU. For example, in 2020, the Court of Justice for the EU invalidated the EU-U.S. Privacy Shield and imposed additional obligations in connection with the use of standard contractual clauses approved by the EU Commission. These and other developments with respect to cross-border data transfers may increase the complexity of transferring personal data across borders and may require us to review and amend our mechanisms relating to cross-border data transfer.

Further, the exit of the United Kingdom, or UK, from the EU has created uncertainty regarding data protection regulation in the UK. The UK has implemented legislation similar to the GDPR, referred to as the UK GDPR, which provides for fines of up to the greater of up to the greater of £17.5 million or 4% of global turnover. The GDPR and UK GDPR increased our responsibility and liability in relation to personal data that we process where subject to these regimes, and we may be required to put in place or modify policies and measures to ensure compliance with the GDPR, including as implemented by individual countries, and the UK GDPR, each of which may require us to modify our policies and procedures and engage in additional contractual negotiations, and which may cause us to incur liabilities, expenses, costs, and operational losses. Compliance with the GDPR and UK GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite our efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our activities in the EEA and the UK.

In addition, in the United States, federal, state, and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal data privacy laws, consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), and other similar laws (e.g., wiretapping laws). California has enacted the California Consumer Privacy Act, or CCPA, which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA requires covered companies to provide new disclosure to consumers about such companies' data collection, use and sharing practices, provide such consumers new ways to opt-out of certain sales or transfers of personal information, and provide consumers with additional causes of action. The California Privacy Rights Act of 2020 (CPRA), which became operative January 1, 2023, expands the CCPA's requirements, including applying to personal information of business representatives and employees and establishing a new regulatory agency to implement and enforce the law. Although the CCPA exempts some data processed in the context of clinical trials, the CCPA and CPRA may increase compliance costs and potential liability with respect to other personal data we maintain about California residents. Additionally, numerous other states have proposed or enacted laws addressing privacy and security, including Washington's My Health, My Data Act, and several laws imposing obligations similar to those of the CCPA. The CCPA, CPRA, and other evolving legislation relating to privacy, data protection, and information security may impact our business activities and exemplify the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information.

We may also be bound by contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. For example, certain privacy laws, such as the GDPR and the CCPA/CPRA, require us to impose specific contractual restrictions on our service providers, and we may also be subject to use and disclosure limitations in our contracts with providers who share information with us for clinical trials. Additionally, we may publish privacy policies, marketing materials and other statements, such as compliance with certain certifications or self-regulatory principles, regarding data privacy and security. If these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators or other adverse consequences.

Obligations related to data privacy and security are quickly changing, becoming increasingly stringent, and creating regulatory uncertainty. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent or conflict among jurisdictions. Preparing for and complying with these obligations requires us to devote significant resources. These obligations may necessitate changes to our business model, information technologies, systems, and practices and to those of any third parties that process personal data on our behalf. We may at times fail (or be perceived to have failed) in our efforts to comply with our data privacy and security obligations. Moreover, despite our efforts, our personnel or third parties on whom we rely may fail to comply with such obligations, which could negatively impact our business operations.

Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Any actual or alleged failure to comply with U.S. or international laws and regulations relating to privacy, data protection, and information security could result in governmental investigations, proceedings and enforcement actions (which could result in civil or criminal penalties), private litigation or adverse publicity, harm to our reputation, and could negatively affect our operating results and business. Moreover, clinical trial subjects about whom we or our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information or impose other obligations or restrictions in connection with our use, retention and other processing of information, and we may otherwise face contractual restrictions applicable to our use, retention, and other processing of information. Claims that we have violated individuals' privacy rights, failed to comply with laws relating to privacy, data protection, or information security, or breached our contractual obligations, even if we are not found liable, could be expensive and time consuming to defend and could result in adverse publicity that could harm our business.

Risks Relating to Ownership of Our Common Stock

We and certain of our directors and executive officers have been, and may in the future be, named as defendants in lawsuits that could result in substantial costs and divert management's attention.

As described elsewhere in this report in "Part I, Item 3—Legal Proceedings," we and certain of our executive officers and directors have been named as defendants in a class action lawsuit that generally alleges that we and certain of our officers and directors violated Sections 10(b) and 20(a) of the Exchange Act and Rule 10b-5 promulgated thereunder and Sections 11, 12, and 15 of the Securities Act by making allegedly false or misleading statements and omitting material adverse facts regarding our business. Certain of our executive officers and directors have also been named as defendants in derivative actions, which are based on similar allegations, and generally allege that defendants breached their fiduciary duties to us, among other things. We are named as a nominal defendant in these derivative proceedings. These complaints seek unspecified compensatory and punitive damages, and reasonable costs and expenses, including attorneys' fees, and other relief. As of the date of this report, we are unable to predict the outcome of these matters. Although we have insurance, it provides for a substantial retention of liability and is subject to limitations and may not cover a significant portion, or any, of the expenses or liabilities we may incur or be subject to in connection with class action lawsuit or other litigation to which we are party. Moreover, any conclusion of these matters in a manner adverse to us and for which we incur substantial costs or damages not covered by our directors' and officers' liability insurance would have a material adverse effect on our financial condition and business. In addition, the litigation has caused and will continue to cause our management and board of directors to divert time and attention to the litigation and could adversely impact our reputation and further divert management and our board of directors' attention and resources from other priorities, including the execution of our business plan and strategies that are important to our ability to grow our business and advance our drug candidates, any of which could have a material adverse effect on our business. In addition, additional lawsuits may be filed, the conclusion of which in a manner adverse to us and for which we incur substantial costs or damages not covered by our directors' and officers' liability insurance would have a material adverse effect on our financial condition and business.

Actions by activist stockholders have in the past been, and may in the future be, disruptive and could cause uncertainty about the strategic direction of our business.

Our business could be negatively affected as a result of stockholder activism, which could be disruptive and cause uncertainty about the strategic direction of our business. For example, in February 2022, an activist stockholder announced his intention to nominate himself and one other candidate for election to our board of directors at our 2022 annual meeting of stockholders. While this proxy contest was unsuccessful, stockholder activism could recur and have an adverse effect on our business, results of operations, and financial condition. For example, at times our market capitalization has been less than the aggregate value of our cash, cash equivalents and investments. Other biotechnology companies in this situation have received proposals from shareholder activists to liquidate and return capital to investors.

We strive to maintain constructive communications with our stockholders and welcome their views and opinions with the goal of enhancing value for all stockholders. However, a proxy contest or other activist behaviors could have an adverse effect on us because:

- responding to actions by activist stockholders can disrupt our operations, is costly and time-consuming, and diverts the attention of our board of directors and senior management team from the pursuit of business strategies, each of which could adversely affect our results of operations and financial condition;
- perceived uncertainties as to our future direction as a result of changes to the composition of our board of directors may lead to the perception of a change in the direction of our business, as well as instability or lack of continuity, all of which may be exploited by our competitors, may result in the loss of potential business opportunities, may cause concern for those enrolling in our clinical trials, and make it more difficult to attract and retain qualified personnel and business partners;
- actions by activist stockholders may interfere with any efforts that we undertake in the future to raise capital;
- actions by activist stockholders could cause significant fluctuations in our stock price based on temporary or speculative market perceptions or other factors that do not necessarily reflect the underlying fundamentals and prospects of our business; and
- if individuals are elected to our board of directors with a specific agenda as a result of a proxy contest, it may adversely affect our ability to effectively implement our business strategy and to create additional value for our stockholders.

Even if a proxy contest or other activist efforts are not successful, the increased costs that we would bear and the distraction of our board of directors and senior management could negatively impact our business, although we cannot predict with certainty the extent of such negative impacts.

We do not know whether an active market for our common stock will be sustained, and, as a result, it may be difficult for you to sell your shares of our common stock.

If an active market for our common stock is not sustained, it may be difficult for you to sell your shares of common stock at an attractive price or at all. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations and progression of our drug product pipeline may not meet the expectations of public market analysts and investors, and, as a result of these and other factors, the price of our common stock may fall.

The market price of our common stock has been and may continue to be volatile, which could result in substantial losses for investors.

The market price of our common stock may be volatile. As a result, you may not be able to sell your common stock at or above the price that you paid for such shares. Some of the factors that may cause the market price of our common stock to fluctuate include:

- results of nonclinical studies and clinical trials;

- the potential impact of health epidemics, including COVID-19, on our business;
- the success of existing or new competitive products or technologies;
- the timing and results of clinical trials for our current drug candidates and any future drug candidates that we may develop;
- commencement or termination of collaborations for our drug candidates;
- failure or discontinuation of any of our drug candidates;
- results of nonclinical studies, clinical trials or regulatory approvals of drug candidates of our competitors, or announcements about new research programs or drug candidates of our competitors;
- investor reactions to other companies' drug development results, including product failures or negative responses from regulatory authorities;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- negative press coverage;
- the status of ongoing litigation and government investigations and potential commencement of additional litigation or investigations;
- the results of the investigation by the independent special committee of the board of directors and the separate ongoing investigation by WSU;
- the level of expenses related to any of our research programs, drug candidates that we may develop;
- the results of our efforts to develop additional drug candidates or drug products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- announcement or expectation of additional financing efforts, including, but not limited to, under our ATM offering;
- sales of our common stock by us, our insiders, or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- volatility with the banking system;
- direct or indirect impacts on our business, our suppliers and other third parties and our clinical sites as a result of geopolitical events, including the Russia-Ukraine war;
- general economic, industry, and market conditions; and
- the other factors described in this "Part I, Item 1A—Risk Factors" section.

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is

experiencing those price and volume fluctuations. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. Following periods of such volatility in the market price of a company's securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management's attention and resources from our business.

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

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. In addition, shares issued upon the exercise of stock options outstanding under our equity incentive plans or pursuant to future awards granted under those plans will become available-for-sale in the public market to the extent permitted by the provisions of applicable vesting schedules, any applicable market standoff and lock-up agreements, and Rule 144 and Rule 701 under the Securities Act.

Moreover, as of December 31, 2023, the holders of approximately 5.7 million shares of our common stock are eligible to exercise certain rights, subject to various conditions and limitations, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also register shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

Our directors, executive officers and significant stockholders own a substantial percentage of our common stock, which could limit your ability to affect the outcome of key transactions, including a change of control.

Our directors, executive officers, significant holders of our outstanding common stock and their respective affiliates beneficially own a substantial amount of our outstanding common stock as of December 31, 2023. As a result, these stockholders, if they act together, will be able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company and might affect the market price of our common stock.

We are an "emerging growth company," and the reduced disclosure 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 of 2012, or the JOBS Act. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, Section 404, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. As a result, the information we provide stockholders will be different than the information that is available with respect to other public companies. We cannot predict whether investors

will find our common stock less attractive if we 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 stock price may be more volatile.

Failure to build and maintain our finance infrastructure and improve our accounting systems and controls could impair our ability to comply with the financial reporting and internal controls requirements for publicly traded companies.

As a public company, we operate in an increasingly demanding regulatory environment, which requires us to comply with the Sarbanes-Oxley Act, the regulations of The Nasdaq Global Select Market, the rules and regulations of the SEC, expanded disclosure requirements, accelerated reporting requirements and more complex accounting rules. Company responsibilities required by the Sarbanes-Oxley Act include establishing corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud. We must perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act. We may experience difficulty in meeting these reporting requirements in the future.

The process of building and maintaining our accounting and financial functions and infrastructure has required and will continue to require significant additional professional fees, internal costs and management efforts. Any disruptions or difficulties in implementing or using such a system could adversely affect our controls and harm our business. Moreover, such disruption or difficulties could result in unanticipated costs and diversion of management attention. In addition, we may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed, investors could lose confidence in our reported financial information and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities.

Anti-takeover provisions in our charter documents and under Delaware or Washington law could make an acquisition of us difficult, limit attempts by our stockholders to replace or remove our current management and limit our stock price.

Provisions of our amended and restated certificate of incorporation and amended and restated bylaws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares, or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our common stock. Among other things, the amended and restated certificate of incorporation and amended and restated bylaws:

- permit the board of directors to issue up to 100,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate;
- provide that the authorized number of directors may be changed only by resolution of the board of directors;

- provide that all vacancies, including newly-created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- divide the board of directors into three classes;
- provide that a director may only be removed from the board of directors by the stockholders for cause;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and may not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner, and meet specific requirements as to the form and content of a stockholder's notice;
- prevent cumulative voting rights (therefore allowing the holders of a plurality of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose);
- provide that special meetings of our stockholders may be called only by the chairman of the board, our chief executive officer or by the board of directors; and
- provide that stockholders are permitted to amend the bylaws only upon receiving at least two-thirds of the total votes entitled to be cast by holders of all outstanding shares then entitled to vote generally in the election of directors, voting together as a single class.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with any "interested" stockholder for a period of three years following the date on which the stockholder became an "interested" stockholder. Likewise, because our principal executive offices are located in Washington, the anti-takeover provisions of the Washington Business Corporation Act may apply to us under certain circumstances now or in the future. These provisions prohibit a "target corporation" from engaging in any of a broad range of business combinations with any stockholder constituting an "acquiring person" for a period of five years following the date on which the stockholder became an "acquiring person."

Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware and the federal district courts of the United States are the exclusive forums for substantially all disputes between us and 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 amended and restated bylaws provide that the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, another state court in Delaware or the federal district court for the District of Delaware) will be the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising under the Delaware General Corporation Law, our certificate of incorporation or our amended and restated bylaws; any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or our amended and restated bylaws; and any action asserting a claim against us that is governed by the internal affairs doctrine. This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act or any other claim for which the U.S. federal courts have exclusive jurisdiction.

Our amended and restated bylaws further provide that the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. The enforceability of similar exclusive federal forum provisions in other companies' organizational documents has been challenged in legal proceedings, and while the Delaware Supreme Court has ruled that this type of exclusive federal forum provision is facially valid under Delaware law, there

is uncertainty as to whether other courts would enforce such provisions and that investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder.

These exclusive forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find either exclusive forum provision in our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving such action in other jurisdictions, all of which could have a material adverse effect on our business, financial condition, and results of operations.

General Risk Factors

Our advisors and consultants are classified as independent contractors, and we can face consequences if it is determined that they are misclassified as such.

There is often uncertainty in the application of worker classification laws, and consequently there is risk to us that our independent contractors could be deemed to be misclassified under applicable law. The tests governing whether a service provider is an independent contractor or an employee are typically highly fact sensitive and can vary by governing law. Laws and regulations that govern the status and misclassification of independent contractors are also subject to divergent interpretations by various authorities, which can create uncertainty and unpredictability. A misclassification determination or allegation creates potential exposure for us, including but not limited to monetary exposure arising from or relating to failure to withhold and remit taxes, unpaid wages, and wage and hour laws and requirements (such as those pertaining to minimum wage and overtime); claims for employee benefits, social security, workers' compensation and unemployment; claims of discrimination, harassment, and retaliation under civil rights laws; claims under laws pertaining to unionizing, collective bargaining, and other concerted activity; and other claims, charges, or other proceedings under laws and regulations applicable to employers and employees, including risks relating to allegations of joint employer liability. Such claims could result in monetary damages (including but not limited to wage-based damages or restitution, compensatory damages, liquidated damages, and punitive damages), interest, fines, penalties, costs, fees (including but not limited to attorneys' fees), criminal and other liability, assessment, or settlement. Such an allegation, claim, adverse determination, including but not limited to with respect to advisors and consultants that provide services to us could also harm our brand and reputation, which could adversely impact our business.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. If no or few analysts commence coverage of us, the trading price of our stock could decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

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

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting, and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Select Market, and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We have hired, and we expect that

we will continue to need to hire, additional accounting, finance, and other personnel in connection with our efforts to comply with the requirements of being a public company, and our management and other personnel will need to devote a substantial amount of time towards maintaining compliance with these requirements. These requirements will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that the rules and regulations applicable to us as a public company may make it more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We continue to evaluate and monitor these rules and regulations and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, 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.

If we are unable to maintain effective internal controls, our business, financial position and results of operations could be adversely affected.

As a public company, we are subject to reporting and other obligations under the Exchange Act, including the requirements of Sarbanes-Oxley Act Section 404, which require annual management assessments of the effectiveness of our internal control over financial reporting.

The rules governing the standards that must be met for management to determine that our internal control over financial reporting is effective are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes-Oxley Act. These reporting and other obligations place significant demands on our management and administrative and operational resources, including accounting resources.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. 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 accounting principles generally accepted in the United States. Any failure to maintain effective internal controls could have an adverse effect on our business, financial position and results of operations.

Attention to ESG (environmental, social and governance) matters may cause us to incur additional costs or expose us to additional risks.

A variety of stakeholder groups, including investors, governmental and nongovernmental organizations are focused on corporate environmental, social and governance, or ESG, practices. Our ESG practices may not meet the standards of our investors or other stakeholders, and they as well as advocacy groups may campaign for us to change our business, operations or practices to better address ESG-related concerns. A failure, or perceived failure, of us to respond to any such campaigns could harm our business and reputation and have a negative impact on the market price of our common stock. Moreover, if ESG best practices, reporting standards and disclosure requirements continue to develop, we may incur increasing costs related to ESG monitoring and reporting.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

Cybersecurity Risk Management Strategy

We have implemented various processes and policies for identifying, assessing, and managing material risks from cybersecurity threats. Our cybersecurity risk management strategy is designed following the Cybersecurity Framework set by the National Institute of Standard and Technology, or NIST.

We assess our information technology, or IT, environment against the NIST Cybersecurity Framework, as well as various cyber-attack vectors, working to identify and remediate risks. We implement reasonable administrative, technical and procedural safeguards to manage cybersecurity risks, for example, by enforcing single sign-on or multi-factor authentication where supported, and the use of mobile device management to secure company resources on employee personal devices. Additionally, we engage third-party cybersecurity experts to assess the security of our network and perform continuous system monitoring, and we engage a third party to perform internal audits of our IT General Controls, or ITGCs. We have implemented certain processes to oversee and identify risks from cybersecurity threats associated with our use of third-party service providers, for example, by evaluating such service providers' own cybersecurity processes and reviewing available certification and audit reports, including International Organization for Standardization, or ISO, certifications for information security management systems, and System and Organization Controls, or SOC, reports.

At this time, we have not experienced cybersecurity incidents, or are aware of any risks from cybersecurity threats, that have materially affected or are reasonably likely to materially affect us, including our business strategy, results of operations, or financial condition.

Cybersecurity Governance

Board of Directors

Our board of directors is responsible for general oversight and regular review of information regarding our risks, including cybersecurity risks. Members of management communicate an overview of our current cybersecurity environment to our board of directors at least annually and provide updates to our board of directors regarding cybersecurity matters periodically throughout the year. Additionally, our third-party auditors inform the audit committee of our board of directors of our ITGC framework and control testing results, which include controls related to cybersecurity risks. Further, management has established cybersecurity incident response processes for escalating the communication of cybersecurity incidents up to the board of directors, as appropriate.

Management

Material risks from cybersecurity threats are assessed and managed by a dedicated team comprised of internal and external IT professionals experienced in cybersecurity threat risk management, who ultimately report to our chief operating officer. Our chief operating officer has extensive strategic and operational experience at several life sciences companies, leading a wide range of business functions, including IT. Our technology team leader has over 20 years of experience with IT and cybersecurity risk management, having served in senior executive-level IT positions at multiple Fortune 500 companies and companies within the life sciences industry.

The technology team leader oversees our internal team of IT professionals, which continuously monitors our IT environment for cybersecurity threats and incidents. Our IT professionals routinely report on cybersecurity incident prevention, detection, mitigation, and remediation efforts to our technology team leader and chief operating officer. Additionally, we have established policies addressing processes for responding to potential cybersecurity incidents, including assessment, communication, and remediation

protocols. Our incident response processes further provide for the escalation of cybersecurity incidents to our executive management team and board of directors, as appropriate.

Item 2. Properties.

Our corporate headquarters is located in Bothell, Washington, where we currently lease approximately 19,326 square feet of laboratory and office space, which leases expire in August 2027. We believe these facilities will be adequate for the foreseeable future and that suitable additional or substitute space will be available as and when needed.

Item 3. Legal Proceedings.

From time to time, we are subject to various legal proceedings or claims that arise in the ordinary course of business. The following is a brief description of the more significant legal proceedings in which we are involved.

Securities Class Actions

On June 25, 2021, plaintiffs Fan Wang and Hang Gao filed a putative securities class action lawsuit in the U.S. District Court for the Western District of Washington against us and our former chief executive officer, Dr. Leen Kawas, captioned *Wang v. Athira Pharma, Inc., et al.*, No. 2:21-cv-00861. Plaintiffs Wang and Gao assert claims under Sections 10(b) and 20(a) of the Exchange Act, and SEC Rule 10b-5, alleging that the defendants made materially false and misleading statements and omitted material adverse facts regarding our business. Specifically, the *Wang* plaintiffs allege that we failed to disclose to investors that certain research conducted by Dr. Kawas was allegedly tainted by scientific misconduct during her doctoral work at WSU including the manipulation of data, and that as a result, the defendants' positive statements about our business, operations, and prospects were materially misleading. The *Wang* plaintiffs seek unspecified compensatory and punitive damages, and reasonable costs and expenses, including attorneys' fees.

That same day, on June 25, 2021, plaintiff Harshdeep Jawandha filed a putative securities class action lawsuit in the U.S. District Court for the Western District of Washington against us, Dr. Kawas, our then chief financial officer, certain members of our board of directors at the time of our IPO, as well as the IPO underwriters, captioned *Jawandha v. Athira Pharma, Inc., et al.*, No. 2:21-cv-00862. The *Jawandha* complaint asserts violations of Sections 11 and 15 of the Securities Act, alleging that that our IPO registration statement was materially false and misleading because it omitted to state that certain of Dr. Kawas's published doctoral research papers at WSU contained allegedly improperly altered images, that the research was allegedly foundational to Athira's efforts to develop treatments for Alzheimer's, that, as a result, and that the defendants' positive statements about our business, operations, and prospects were materially misleading. The *Jawandha* plaintiff seeks unspecified compensatory damages, and reasonable costs and expenses, including attorneys' fees.

Also on June 25, 2021, plaintiffs Timothy Slyne and Tai Slyne filed a putative securities class action lawsuit in the U.S. District Court for the Western District of Washington against us, Dr. Kawas, our then chief financial officer, and the same members of our board of directors and underwriters as in the *Jawandha* complaint, captioned *Slyne v. Athira Pharma, Inc. et al.*, No. 2:21-cv-00864. The *Slyne* complaint asserts violations of Sections 11 and 15 of the Securities Act, alleging that purported issues with Dr. Kawas's doctoral research at WSU should have been disclosed in our IPO registration statement. The *Slyne* plaintiffs seek unspecified compensatory damages, reasonable costs and expenses, including attorneys' fees, and injunctive and other equitable relief.

On August 9, 2021, the court issued an order consolidating the three cases. On October 5, 2021, the district court issued an order appointing lead plaintiffs and approved their selection of lead and liaison counsel.

On January 7, 2022, lead plaintiffs filed a consolidated amended complaint, which asserts violations of Sections 10(b) and 20(a) of the Exchange Act and SEC Rule 10b-5 and Sections 11, 12, and 15 of the Securities Act. The consolidated amended complaint is brought against us, Dr. Kawas, our then chief financial officer, certain members of our board of directors at the time of our IPO and secondary public offering, or SPO, and the IPO and SPO underwriters. As with the previous complaints, it is based on allegations that the IPO and SPO registration statements and/or other public statements were materially false and misleading because they omitted to state that certain of Dr. Kawas's published doctoral research papers at WSU contained allegedly improperly altered images. Lead plaintiffs seek unspecified compensatory damages, as well as equitable and injunctive relief on behalf of themselves and the purported class. On March 8, 2022, the defendants filed a motion to dismiss lead plaintiffs' consolidated amended complaint for failure to state a claim under the federal securities laws. On July 29, 2022, the court issued an order granting in part and denying in part the motion to dismiss. The order dismissed the Section 10(b) and Section 20(a) claims arising under the Exchange Act, dismissed the Section 11 claim arising under the Securities Act as to all defendants other than the Company and Dr. Kawas, dismissed the Section 12(a)(2) claim arising under the Securities Act as to the lead plaintiffs, and dismissed the Section 15 claim arising under the Securities Act against all defendants other than Dr. Kawas. The order permitted lead plaintiffs until August 19, 2022 to file a second consolidated amended complaint. Lead plaintiffs did not file a second consolidated amended complaint.

On August 12, 2022, defendant Dr. Kawas filed a motion for partial reconsideration of the court's July 29, 2022 order. On October 4, 2022, the court denied the motion. On October 24, 2022, the parties filed a (1) joint status report and discovery plan and (2) stipulation and case scheduling order, wherein the parties proposed deadlines for material case events, including the completion of fact discovery, expert discovery, and dispositive motion practice. On November 2, 2022, the court entered an order setting certain case deadlines. On November 4, 2022, we and Dr. Kawas filed our individual answers to the consolidated amended complaint. In mid-November 2022, the parties began conducting fact discovery.

On March 10, 2023, following a mediation and the parties' agreement in principle to settle the securities class action for $10.0 million, the court entered a stipulated order setting a deadline of April 28, 2023 for the parties to file a stipulation of settlement and for lead plaintiffs to file a motion for preliminary approval of the settlement, which the parties filed on that date. The settlement is subject to preliminary and final approval by the U.S. District Court for the Western District of Washington. On May 31, 2023, the court issued a minute order requiring the parties to file a joint status report on or before June 30, 2023 addressing several aspects of the proposed settlement, including revision of certain notices to putative class members regarding the settlement, which the parties filed on that date. On September 27, 2023, the court issued an order denying plaintiffs' motion for preliminary approval without prejudice, citing the motion's failure to satisfy the court's questions and concerns regarding traceability of certain Securities Act claims. The court permitted plaintiffs to file a renewed motion for preliminary approval, which plaintiffs filed on December 15, 2023.

On February 15, 2024, the court issued an order granting in part and deferring in part plaintiffs' renewed motion for preliminary approval and ordered the parties to submit a joint status report by March 15, 2024 proposing a date on which the court may schedule the final approval hearing, among other things. In its order, the court preliminarily approved the proposed settlement and certified a class and two subclasses. The court deferred ruling in part as to the proposed notices and claim form relating to the settlement.

As a result of the foregoing, we recorded a legal settlement expense of $10.0 million in operating expenses in the fourth quarter of 2022 and an accrued liability of $10.0 million on the accompanying consolidated balance sheets. Additionally, we recorded an insurance recovery of $1.6 million in operating expenses in the fourth quarter of 2023 and an insurance recovery receivable of $1.6 million on the accompanying consolidated balance sheets. This insurance recovery represents the amount of the settlement to be covered by our insurers.

Shareholder Derivative Actions

On April 14, 2022, a shareholder derivative action was filed by plaintiff Stephen Bushansky in the U.S. District Court for the Western District of Washington against certain current and former members of our board of directors, captioned *Bushansky v. Kawas et al.*, No. 2:22-cv-497. Plaintiff purports to bring the action derivatively on our behalf, and we are a nominal defendant to the action. The derivative complaint alleges that our board of directors breached its fiduciary duties by failing to prevent alleged misstatements in our public filings, failing to discover altered images in certain research papers, and failing to take appropriate action. The derivative complaint asserts claims for violations of Section 14(a) of the Exchange Act as well as claims for breach of fiduciary duty, contribution and indemnification, aiding and abetting, and waste of corporate assets. The derivative complaint seeks unspecified damages, disgorgement of profits, benefits, and other compensation received by the individual defendants, restitution, declaratory relief, and an award of costs and expenses to the derivative plaintiff, including attorneys' fees.

On May 6, 2022, a second shareholder derivative action was filed by plaintiff Thomas Houlihan in the U.S. District Court for the Western District of Washington against certain of our current and former directors and officers, captioned *Houlihan v. Kawas et al*., No. 2:22-cv-620. Plaintiff purports to bring the action derivatively on our behalf, and we are a nominal defendant to the action. The derivative complaint alleges that certain of our current and former directors and officers breached their fiduciary duties by failing to prevent alleged misstatements in our public filings and failing to take appropriate action regarding altered images in certain research papers. The derivative complaint asserts claims for violations of Section 14(a) of the Exchange Act as well as claims for breach of fiduciary duties, contribution, and indemnification. The derivative complaint seeks unspecified damages, unspecified corporate governance reforms, restitution, and an award of costs and expenses to the derivative plaintiff, including attorneys' fees.

On May 26, 2022, the court issued an order consolidating the cases and staying them until further order of the court. We believe we have adequate reserves related to this matter as of the balance sheet date.

Government Investigations

In November 2022, we received a Civil Investigative Demand from the Civil Division of the Department of Justice, or the Demand. The Demand seeks documents and information relating to our relationship with WSU, certain of our grant applications in 2016 and 2019 with the NIH and our receipt of a NIH grant in 2020. We are cooperating with the Department of Justice with respect to the Demand.

In February 2023, the SEC sent us a subpoena seeking documents and information relating to, among other things, our former chief executive officer's alterations of images in certain research papers. We are cooperating with the SEC with respect to the subpoena.

We cannot predict the outcome of these lawsuits or government investigations. Failure by us to obtain a favorable resolution of these actions could have a material adverse effect on our business, results of operations and 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 for Common Stock

Our common stock began trading on The Nasdaq Global Select Market under the symbol "ATHA" on September 18, 2020. Prior to that date, there was no public trading market for our common stock.

Holders of Record

As of February 16, 2024, there were approximately 42 holders of record of our common stock. Because many of our shares are held by brokers and other institutions on behalf of shareholders, we are unable to estimate the total number of shareholders represented by these record holders.

Dividend Policy

We currently intend to retain all available funds and future earnings to fund the development and growth of our business and we do not anticipate paying any cash dividends in the foreseeable future.

Recent Sales of Unregistered Securities

None.

Stock Performance Graph

As a smaller reporting company, we are not required to provide the information requested by this item pursuant to Item 201(e) of Regulation S-K.

Issuer Repurchases of Equity Securities

None.

Item 6. [Reserved].

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

You should read the following management's discussion and analysis of financial condition and results of operations in conjunction with our consolidated financial statements and notes thereto included in Part II, Item 8 of this Annual Report on Form 10-K. This discussion and analysis and other parts of this report contain forward-looking statements based upon current beliefs, plans and expectations related to future events and our future financial performance that involve risks, uncertainties and assumptions, such as statements regarding our intentions, plans, objectives, expectations, forecasts and projections. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under the section of this Annual Report on Form 10-K titled "Risk Factors" and elsewhere in this report. You should carefully read the "Risk Factors" to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section of this report titled "Special Note Regarding Forward-Looking Statements."

Overview

We are a late clinical-stage biopharmaceutical company focused on developing small molecules engineered to restore neuronal health and slow neurodegeneration. Our approach is designed to modulate the neurotrophic HGF system, that is critical to normal brain function and may play a key role in maintaining the health and functioning of neuronal networks. We believe that by acting on the neurotrophic HGF system and its multiple downstream signaling pathways, we may be able to enhance the body's natural ability to protect and repair neuronal networks by reducing inflammation, promoting regeneration, and reducing disease-specific protein pathologies, thereby positively impacting the course of disease. We aim to achieve these goals by advancing our pipeline of novel small molecule compounds which are designed to and have exhibited properties in enhancing the neurotrophic HGF system in either the CNS, by crossing the BBB, or the PNS.

Our lead drug candidate, fosgonimeton, is a potentially first-in-class, small molecule drug candidate designed to positively modulate the neurotrophic HGF system for potential treatment of CNS disorders. The effects of fosgonimeton in its primary target indication, AD, are currently being evaluated in multiple clinical trials:

- ACT-AD* was a randomized, double-blind, placebo-controlled, parallel-group 26-week exploratory Phase 2 clinical trial in mild-to-moderate AD, with ERP P300 latency as the primary endpoint. Initiated in November 2020, the trial was designed to better characterize the overall effects of fosgonimeton on working memory processing speed and cognitive measures and inform the Phase 2/3 LIFT-AD trial. Topline results for this exploratory Phase 2 ACT-AD trial were announced in June 2022, and the primary and all secondary endpoints were not met by protocoled analysis. However, a post hoc analysis of results from ACT-AD in a pre-specified subgroup suggested positive effects on measures of cognition, function and neurodegeneration in participants taking fosgonimeton alone without background AChEIs. Additionally, data from post hoc analysis of plasma biomarkers from participants on fosgonimeton without background AChEIs showed descriptive improvements (non-statistically significant) in markers of neuroinflammation and AD-specific protein pathologies when compared to placebo. Fosgonimeton was generally well tolerated in the ACT-AD study, with a favorable safety profile, and there were no treatment related serious adverse events or deaths observed.

- LIFT-AD is a randomized, double-blind, placebo-controlled, parallel-group 26-week Phase 2/3 clinical trial with fosgonimeton for the treatment of mild-to-moderate AD. In September 2020, we began site initiation and patient screening for LIFT-AD. The primary endpoint for the Phase 2/3 LIFT-AD trial will be measured by the GST, which is a composite score that combines the scores from cognition (ADAS-Cog11), and function (ADCS-ADL23). Guided by the results from the completed exploratory ACT-AD Phase 2 trial, in September 2022, we proactively amended LIFT-AD to focus on participants not on background AChEIs. In October 2022, we announced that following an unblinded interim efficacy and futility analysis, an independent DMC recommended

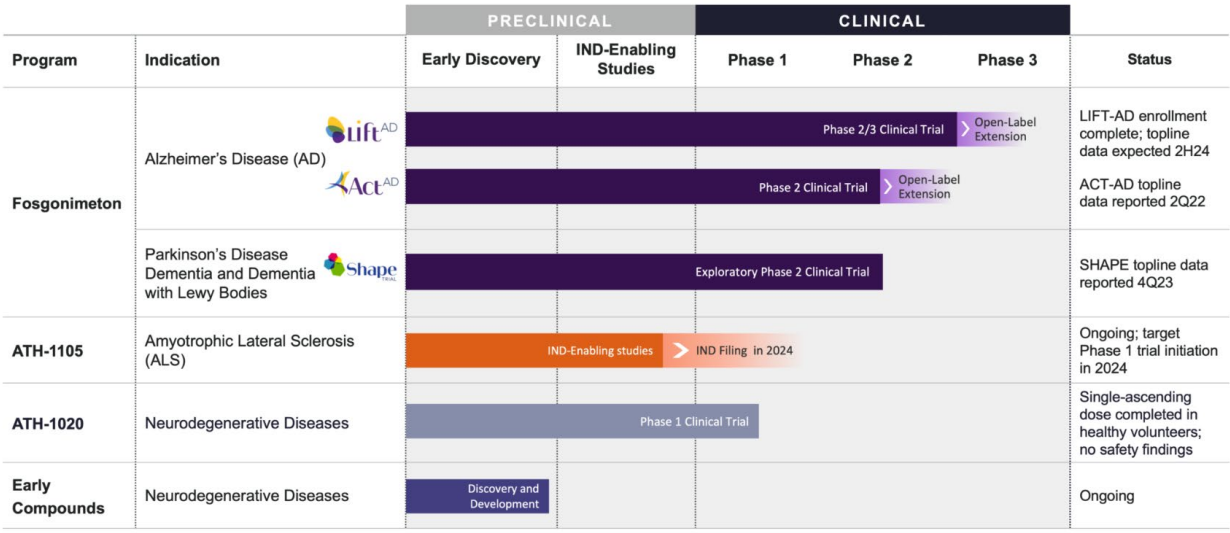
continuation of the LIFT-AD trial. The committee also determined that, with the additional enrollment of fewer than 150 participants for a total enrollment of less than 300 participants without background AChEIs, the amended trial will be well powered for the primary endpoint given the preliminary effect size observed. In May 2023, we further amended LIFT-AD to focus on 40 mg dosing, which we have selected for further development and as the potential dose for regulatory approval of fosgonimeton in this indication. This selection was based on a review of the totality of the preclinical and clinical data, biomarker results, observations from the open label extension study and in consultation with independent regulatory and biostatistical consultants based on patients treated with 40 mg fosgonimeton without concomitant AChEIs. In January 2024 we announced the completion of enrollment with a total of 318 patients randomized. We expect to report topline LIFT-AD results in the second half of 2024. In July 2023, we completed an end of Phase 2 meeting with the FDA to gain alignment on our plans for the continued clinical development of fosgonimeton as a treatment for mild-to-moderate AD. During this meeting we provided an update and discussed with the FDA the ongoing LIFT-AD trial, including use of the 40 mg dose, concomitant AChEIs use, biomarker analyses including NfL, and the SAP. The FDA noted the importance of showing effects on both cognition (ADAS-Cog11) and function (ADCS-ADL23) in the trial population. The FDA is open to ongoing dialogue with us regarding the LIFT-AD trial once completed as well as other aspects of our program to develop fosgonimeton as a potential treatment for mild-to-moderate AD.

- In July 2021, we announced that we are enrolling participants into a 26-week OLEX trial* for our LIFT-AD and ACT-AD clinical trials, allowing us to collect up to a total of one year of safety data with fosgonimeton. In May 2022, we announced that we extended the 26-week OLEX for our LIFT-AD and ACT-AD clinical trials for an additional 12 months, enabling eligible participants who have completed either trial and elect to participate in the ongoing OLEX to receive up to 18 months of open-label treatment with fosgonimeton. In May 2023, we amended the OLEX to further extend the trial by an additional 12 months. Eligible participants who have completed the LIFT-AD or ACT-AD trials and elect to participate in the ongoing OLEX may now receive up to 30 months of open-label treatment, which allows us to collect up to 36 months total of long-term exposure data.

  **The ACT-AD trial and the related OLEX for ACT-AD participants have been supported by a grant from the National Institute on Aging of the National Institutes of Health under Award Number R01AG06268. The information presented is solely the responsibility of Athira and does not necessarily represent the official views of the National Institutes of Health.*

The following figure illustrates the current development stage of our proprietary drug candidates and early discovery and development programs. Our pipeline consists of both BBB permeable and peripherally restricted drug candidates for CNS, PNS and other indications. In addition, we are exploring the use of our ATH compounds in additional indications in the CNS and PNS as we aim to improve neuronal health in

multiple neurodegenerative diseases. Our drug discovery efforts are focused on designing and testing new early compounds to enhance the HGF/MET system for a variety of clinical applications.



We constantly strive to grow and optimize our portfolio through in-house discovery and plan on additional external business development activities enabled by our innovative internal research and development capabilities.

We were incorporated in March 2011 and since our inception, we have devoted substantially all of our resources to our research and development efforts such as small molecule compound discovery, nonclinical studies and clinical trials, as well as manufacturing activities, establishing and maintaining our intellectual property portfolio, hiring personnel, raising capital, and providing general and administrative support for these operations. We do not have any drug products approved for commercial sale, and we have not generated any revenues related to our drug products since inception. Our ability to generate drug product revenue sufficient to achieve profitability, if ever, will depend on the successful development of one or more of our drug candidates which we expect will take a number of years.

We are focused on the development of small molecule therapeutics which enables us to use well-established and widely available manufacturing processes and infrastructure, formulation compositions and drug administration technologies or devices. We do not currently operate our own facilities for manufacturing, storing, or distributing our drug candidates. We utilize third-party CMOs to manufacture and supply our preclinical and clinical materials during the development of our drug candidates. We believe the synthesis of fosgonimeton is reliable and reproducible and the synthetic methods can be further optimized to enable large-scale production that continues to avoid use of toxic materials or specialized equipment or handling during the manufacturing process. We plan to continue to optimize the manufacturing process to support future large-scale and commercial supply. Our goal is to identify and develop small molecule drug candidates that are cost-effective to manufacture and easily transferable to third party CMOs. We expect to use similar contract resources for commercialization of our drug products, at least until our resources and operations are at a scale that justifies investment in internal manufacturing capabilities.

Given our stage of development, we have not yet established a commercial organization or distribution capabilities. We intend to build a commercial infrastructure to support sales of our drug candidates. We expect to manage sales, marketing and distribution through internal resources and third-party relationships. While we may commit significant financial and management resources to commercial activities, we will also consider collaborating with one or more pharmaceutical companies to enhance our commercial capabilities.

To date, we have funded our operations primarily through proceeds from the sale of equity securities, including proceeds from the sale and issuance of common stock in our IPO and in a subsequent follow-on

public offering, the sale and issuance of convertible preferred stock, common stock warrants, and convertible notes, and to a lesser extent from grant income and stock option exercises. From inception to December 31, 2023, we have raised aggregate net cash proceeds of approximately $407.4 million primarily from the issuance of our common stock (excluding option exercises), convertible preferred stock, common stock warrants, and convertible notes. We have incurred significant operating losses to date. Our net losses were $117.7 million and $95.6 million for the years ended December 30, 2023 and 2022, respectively. As of December 31, 2023, we had an accumulated deficit of $309.2 million and cash, cash equivalents and investments of $147.4 million.

We expect to continue to incur increasing operating losses for the foreseeable future as we:

- continue to advance fosgonimeton and our other drug candidates through preclinical studies and clinical trials, and continue the open label extension of the ACT-AD and LIFT-AD trials;
- expand our pipeline of drug candidates;
- continue to grow our discovery organization and invest in the ATH platform;
- ramp up manufacturing activities;
- attract, hire and retain additional personnel;
- obtain, maintain, expand and protect our intellectual property portfolio;
- operate as a public company;
- expand our laboratory and office facilities;
- implement and maintain operational, financial and management information systems;
- seek regulatory approval for any drug candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize any drug candidate for which we may obtain marketing approval; and
- incur legal expenses associated with ongoing litigation, as further described in “Part I, Item 3—Legal Proceedings,” and elsewhere in this report.

Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials and our expenditures on other research and development activities.

We will require substantial additional funding to support our continuing operations and further the development of our drug candidates. Until such time as we can generate significant revenue from drug product sales, if ever, we expect to finance our operations through the sale of equity, debt financings, or other capital sources, which could include income from collaboration, licensing or similar arrangements, for the foreseeable future. Adequate funding may not be available when needed or on terms acceptable to us, or at all. If we are unable to raise additional capital as needed, we may have to significantly delay, scale back or discontinue development of our drug candidates. Our ability to raise additional funds may be adversely impacted by potential worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide. If we fail to obtain necessary capital when needed on acceptable terms, or at all, it could force us to delay, limit, reduce or terminate our drug product development programs, commercialization efforts or other operations. Insufficient liquidity may also require us to relinquish rights to drug candidates at an earlier stage of development or on less favorable terms than we would otherwise choose. We cannot assure you that we will ever be profitable or generate positive cash flow from operating activities. Based upon our current operating plan, we estimate that our existing cash, cash equivalents and investments will be sufficient to fund our operating expenses and capital expenditure requirements through at least the next 12 months following the date of this report.

Our Collaboration and Grant Agreements

Amended and Restated WSU License Agreement

We are party to an amended and restated exclusive license agreement with sublicensing terms with WSU that we entered into in 2015. Under this agreement, we have an exclusive license to make, use, sell, and offer for sale products covered by certain licensed patents, including dihexa, the chemical compound into which fosgonimeton metabolizes following administration. The term of the license continues until the earlier of the date in which no valid claim remains enforceable and the payment of royalties ceases for more than four consecutive quarters after such royalty payments begin.

The initiation of our first Phase 2 clinical trial in September 2020 triggered a $50,000 liability to WSU, which was paid in full as of December 31, 2020.

We are obligated to pay to WSU the following if the related milestones are reached:

- $300,000 – At initiation of the first Phase 3 clinical trial in the United States, European Union or Japan for the first licensed product.
- $600,000 – Marketing approval in the United States, European Union or Japan for the first licensed product.

We are obligated to pay WSU a royalty in the mid-single digits of net sales.

Additionally, under the agreement we have the right to sublicense the licensed rights, subject to additional payments to WSU for sublicense consideration received. Such amounts are dependent on the terms of the underlying sublicense, and range from the mid-single digits to mid tens of any non-sales based payments received, and low twenties of net sales-based sublicense royalties.

National Institutes of Health Grant

In December 2020, we accepted a grant from the NIH to support our ACT-AD Phase 2 clinical trial for fosgonimeton. Under the terms of the agreement and approval received from the NIH, we were awarded an aggregate of $15.2 million, all of which had been received as of December 31, 2023. For additional information regarding this grant, see the section of this report titled “Business—Our Collaboration and Grant Agreements.” We recognized $0.2 million and $5.2 million of income related to our NIH grant during the years ended December 31, 2023 and 2022, respectively. During the years ended December 31, 2023 and 2022, we received cash of $1.4 million and $6.3 million, respectively, in connection with the NIH grant. As of December 31, 2022, we had incurred qualifying expenses in excess of cash received of approximately $1.2 million, which is included in unbilled grant receivable on the consolidated balance sheets. As of December 31, 2023, we had recognized aggregate grant income of $15.2 million in connection with the NIH grant, equal to the total grant amount approved. We will not recognize any additional grant income in connection with the NIH grant in the future.

Components of Operating Results

Operating Expenses

Research and Development

Research and development expenses consist primarily of direct and indirect costs incurred for our research activities, including development of the ATH platform, our drug discovery efforts and the development of our drug candidates. Direct costs include laboratory materials and supplies, contracted research and manufacturing, clinical trial costs, consulting fees, and other expenses incurred to sustain our research and development program. Indirect costs include personnel-related expenses, consisting of employee salaries, related benefits, and stock-based compensation expense for employees engaged in research and development activities, and facilities and other expenses consisting of direct and allocated expenses for rent and depreciation, and lab consumables.

We expense research and development costs as incurred. Non-refundable advance payments for goods and services that will be used over time for research and development are capitalized and recognized as goods are delivered or as the related services are performed. In-licensing fees and other costs to acquire technologies used in research and development that have not yet received regulatory approval and that are not expected to have an alternative future use are expensed when incurred. We track direct costs by stage of program, clinical or preclinical. However, we do not track indirect costs on a program specific basis because these costs are deployed across multiple programs and, as such, are not separately classified.

As of the date of this report, we cannot reasonably determine the nature, timing, and estimated costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, any of our drug candidates. Drug candidates in later stages of development generally have higher development costs than those in earlier stages. We expect that our research and development expenses will increase for the foreseeable future as we continue to invest in research and development activities related to developing our drug candidates, as our drug candidates advance into later stages of development, as we conduct larger clinical trials, as we seek regulatory approvals for any drug candidates that successfully complete clinical trials, as we expand our drug product pipeline, as we maintain, expand, protect and enforce our intellectual property portfolio, and as we incur expenses associated with hiring additional personnel to support our research and development efforts. In particular, we have seen, and expect to continue to see, our research and development expenses increase as we conduct our clinical trials for fosgonimeton, including open-label extensions for those trials. Additionally, we may experience an overall increase in research and development expenses as a result of inflation.

The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and the successful development of our drug candidates is highly uncertain. Our research and development expenses may vary significantly based on factors such as:

- the number and scope of preclinical and IND-enabling studies;
- the phases of development of our drug candidates;
- the progress and results of our research and development activities;
- per subject trial costs;
- the number of trials required for regulatory approval, in particular with respect to fosgonimeton for the treatment of mild-to-moderate AD (including any potential confirmatory or Phase 3 registrational trials);
- the continuation of the open label extension of the ACT-AD and LIFT-AD trials;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible subjects and initiate clinical trials;
- the number of subjects that participate in the trials;
- the drop-out and discontinuation rate of subjects;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of subject participation in the trials and follow-up;
- the cost and timing of manufacturing of our drug candidates;
- the receipt of regulatory approvals from applicable regulatory authorities;
- the timing, receipt and terms of any marketing approvals from applicable regulatory authorities;
- the hiring and retention of research and development personnel;
- the degree to which we obtain, maintain, defend and enforce our intellectual property rights;

- the impact of health epidemics, including COVID-19, on timelines and clinical operations, which may lead to increased costs; and
- the extent to which we establish collaboration, licensing or similar arrangements and the performance of any related third parties.

A change in the outcome of any of these variables with respect to the development of any of our drug candidates could significantly change the costs and timing associated with the development of that drug candidate.

General and Administrative

General and administrative expenses consist primarily of personnel-related costs, consisting of employee salaries, related benefits, and stock-based compensation expense for our employees in the executive, legal, finance and accounting, human resources, and other administrative functions. General and administrative expenses also include third-party costs such as legal costs, insurance costs, accounting, auditing and tax related fees, business development fees, consulting fees and facilities and other expenses not otherwise included as research and development expenses. We expense general and administrative costs as incurred.

We expect that our general and administrative expenses will increase for the foreseeable future as we increase our headcount to support our continued research activities and development of our programs. We also anticipate that we will continue to incur expenses as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the SEC, and those of any national securities exchange on which our securities are traded, legal, auditing, additional insurance expenses, investor relations activities, and other administrative and professional services. We expect continued legal expenses related to our ongoing legal proceedings and proposed settlement to resolve such claims. We also expect to continue to increase the size of our administrative function to support the growth of our business. Additionally, we may experience an overall increase in general and administrative expenses as a result of inflation.

Legal Settlement and Insurance Recovery Related to Legal Settlement

Legal settlement expense and insurance recovery related to legal settlement consist of the proposed settlement of the securities class action litigation and the amount to be covered by our insurers. For more information see Part I, Item 3 “Legal Proceedings—Securities Class Actions".

Grant Income

Grant income consists of income related to the NIH grant and is recognized as qualifying expenses under the grant agreement are incurred. As of December 31, 2023, we had recognized aggregate grant income of $15.2 million in connection with the NIH grant, equal to the total grant amount approved. We will not recognize additional grant income in connection with the NIH grant in the future.

Other Income, Net

Other income, net consists primarily of interest earned on our cash, cash equivalents and investments and the amortization of premiums and accretion of discounts on our available-for-sale securities. Absent further fundraising, we expect interest earned on our cash, cash equivalents and investments to decrease as we continue to expend our cash balances to fund our ongoing operations.

Results of Operations

Comparison of the Years Ended December 31, 2023 and 2022

The following table summarizes our results of operations for the periods presented:

	Year Ended December 31,			
	2023	2022	Dollar Change	% Change
	(in thousands)			
Operating expenses:				
Research and development	$ 93,790	$ 61,464	$ 32,326	53%
General and administrative	33,304	32,552	752	2
Legal settlement	—	10,000	(10,000)	(100)
Insurance recovery related to legal settlement	(1,628)	—	(1,628)	(100)
Total operating expenses	125,466	104,016	21,450	21
Loss from operations	(125,466)	(104,016)	(21,450)	21
Grant income	157	5,161	(5,004)	(97)
Other income, net	7,637	3,216	4,421	137
Net loss	$(117,672)	$ (95,639)	$(22,033)	23

Research and Development Expenses

The following table shows the primary components of our research and development expenses for the periods presented:

	Year Ended December 31,			
	2023	2022	Dollar Change	% Change
	(in thousands)			
Direct costs:				
Fosgonimeton (ATH-1017)	$ 66,524	$ 39,416	$ 27,108	69%
ATH-1020	704	1,874	(1,170)	(62)
Preclinical programs and other direct costs	6,619	5,978	641	11
Total direct costs	73,847	47,268	26,579	56
Indirect costs:				
Personnel-related costs, including stock-based compensation	17,955	12,620	5,335	42
Facilities and other costs	1,988	1,576	412	26
Total research and development expenses	$ 93,790	$ 61,464	$ 32,326	53

Research and development expenses increased by $32.3 million, from $61.5 million for the year ended December 31, 2022 to $93.8 million for the year ended December 31, 2023. The increase was driven primarily by an increase in expenses for fosgonimeton of $27.1 million related to continued patient enrollment and clinical site visit activity for our Phase 2/3 clinical trial and the corresponding open-label extension for our Phase 2 and Phase 2/3 clinical trials, as well as higher costs relating to manufacturing process development and increases in manufacturing batch size capabilities, an increase in personnel-related costs of $5.3 million due to changes in headcount and an increase in stock-based compensation expense in connection with current period equity grants to new hires and existing employees, an increase in preclinical research and development expenses of $0.6 million, and an increase of $0.4 million related to facilities and other indirect costs, partially offset by a decrease in ATH-1020 program expenses of $1.2 million.

General and Administrative Expenses

General and administrative expenses increased by $0.7 million, from $32.6 million for the year ended December 31, 2022 to $33.3 million for the year ended December 31, 2023. The increase was primarily due to an increase in personnel-related expenses of $1.0 million driven by changes in headcount, an

increase in consulting and professional services expenses of $0.7 million, an increase in business development expenses of $0.4 million, and an increase in facilities expenses of $0.3 million, partially offset by a decrease in general corporate expenses of $0.9 million and a decrease in legal costs of $0.8 million.

Legal Settlement Expense and Insurance Recovery Related to Legal Settlement

In connection with the proposed settlement of the securities class action litigation, we recorded a legal settlement expense of $10.0 million for the year ended December 31, 2022. Additionally, we recorded an insurance recovery of $1.6 million for the year ended December 31, 2023, representing the amount of the settlement to be covered by our insurers. For more information see the section of this report titled “Legal Proceedings—Securities Class Actions".

Grant Income

Grant income decreased by $5.0 million, from $5.2 million for the year ended December 31, 2022 to $0.2 million for the year ended December 31, 2023. Grant income recognized during the year ended December 31, 2023 of $0.2 million represented the remaining balance of the total $15.2 million approved grant amount available at the beginning of the year, all of which was recognized during the three months ended March 31, 2023.

Other Income, Net

Other income, net, increased by $4.4 million, from $3.2 million for the year ended December 31, 2022 to $7.6 million for the year ended December 31, 2023 due to higher income from accretion of discounts on debt securities purchased below par value and held to maturity, in addition to higher interest income earned on our available-for-sale securities resulting from rising interest rates on debt securities.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have funded our operations primarily with proceeds from the sale and issuance of common stock, convertible preferred stock, common stock warrants, and convertible notes, and to a lesser extent from grant income and stock option exercises. From our inception through December 31, 2023, we have raised aggregate net cash proceeds of $407.4 million primarily from the issuance of our common stock (excluding option exercises), convertible preferred stock, common stock warrants, and convertible notes.

As of December 31, 2023, we had $147.4 million in cash, cash equivalents and investments and have not generated positive cash flows from operations. Since our inception, we have devoted substantially all of our resources to our research and development efforts such as small molecule compound discovery, nonclinical studies and clinical trials, as well as manufacturing activities, establishing and maintaining our intellectual property portfolio, hiring personnel, raising capital, and providing general and administrative support for these operations.

Material Cash and Future Funding Requirements

Our material cash requirements include our operating leases for laboratory and office facilities. As of December 31, 2023, we had lease payment obligations of $1.8 million, with $0.5 million payable within 12 months. For additional information regarding our lease commitments, see Note 7 to our consolidated financial statements included elsewhere in this report. We are contingently committed to $0.9 million of potential future milestone payments, in addition to sales-based payments and royalties, under our license agreement with WSU. Payments generally are due and payable only upon achievement of certain developmental, regulatory, and sales milestones for which the specific timing cannot be predicted. Refer to Note 6 to our consolidated financial statements for additional information regarding the WSU license agreement. Additionally, we have purchase obligations and open purchase orders that support normal

operations and are primarily due in the next 12 months. These purchase obligations and open purchase orders are generally cancellable in full or in part through the contractual provisions. We also anticipate that our research and development expenses and our general and administrative expenses will increase over at least the near-term as we advance our clinical development and our drug candidates through clinical trials, increase our headcount to support our operations, and incur legal and other professional expenses related to our ongoing legal proceedings. We cannot predict with certainty the amount and timing of these increased expenses.

Based upon our current operating plan, we estimate that our $147.4 million of cash, cash equivalents and investments at December 31, 2023 will be sufficient to fund our operating expenses and capital expenditure requirements through at least the next 12 months following the date of this report. We will need to raise substantial additional capital to fund the development of our drug candidates. Until such time as we can generate significant revenue from drug product sales, we expect to finance our operations through the sale of equity securities, debt financings, or other capital, which could include income from collaboration, licensing or similar arrangements with third parties, or receiving research contributions, or grants. For example, in January 2023, we entered into a sales agreement with Cantor Fitzgerald and BTIG to sell shares of our common stock having aggregate sales proceeds of up to $75.0 million, from time to time, through an ATM equity offering program under which Cantor Fitzgerald and BTIG are acting as sales agents. As of the date of this report, we have not sold any securities pursuant to this ATM offering. 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 or could 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. If we raise funds through collaborations, licenses and other similar arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or drug candidates or grant licenses on terms that may not be favorable to us or may reduce the value of our common stock. Adequate funding may not be available when needed or on terms acceptable to us, or at all. Our ability to raise additional funds may be adversely impacted by potential worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide. If we fail to obtain necessary capital when needed on acceptable terms, or at all, it could force us to delay, limit, reduce or terminate our drug product development programs, commercialization efforts or other operations. Insufficient liquidity may also require us to relinquish rights to drug candidates at an earlier stage of development or on less favorable terms than we would otherwise choose. We cannot assure you that we will ever be profitable or generate positive cash flows from operating activities.

We have based our projections of operating capital requirements on assumptions that may prove to be incorrect and we may use all our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with research, development and commercialization of biotechnology products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the scope, timing, progress and results of our ongoing preclinical studies and clinical trials of our drug candidates;
- the number of trials required for regulatory approval, in particular with respect to fosgonimeton for the treatment of mild-to-moderate AD;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials of other drug candidates that we may pursue;
- our ability to establish and maintain collaboration, licensing or other similar arrangements, and the financial terms of any such arrangements, including the timing and amount of any future milestone, royalty or other payments due thereunder;

- the costs, timing and outcome of regulatory review of our drug candidates;
- the costs and timing of future commercialization activities, including drug product manufacturing, marketing, sales and distribution, for any of our drug candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our drug candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the costs related to ongoing legal proceedings;
- any expenses needed to attract, hire and retain skilled personnel;
- the costs of operating as a public company;
- the costs associated with expanding our laboratory and office facilities; and
- the extent to which we acquire or in-license other companies' product candidates and technologies or engage in other strategic transactions.

A change in the outcome of any of these or other factors with respect to the development of any of our drug candidates could significantly change the costs and timing associated with the development of that drug candidate. Furthermore, our operating plan may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such operating plan.

Cash Flows

The following table summarizes our cash flows for the periods indicated:

	Year Ended December 31,	
	2023	2022
	(in thousands)	
Net cash (used in) provided by:		
Operating activities	$ (100,753)	$ (72,469)
Investing activities	95,089	57,664
Financing activities	493	654
Net decrease in cash, cash equivalents and restricted cash	$ (5,171)	$ (14,151)

Operating Activities

During the year ended December 31, 2023, net cash used in operating activities was $100.8 million. This consisted primarily of a net loss of $117.7 million, partially offset by non-cash charges of $10.4 million and a decrease in our net operating assets of $6.5 million. The non-cash charges primarily consisted of stock-based compensation expense, depreciation expense, and amortization of premiums and accretion of discounts on our available-for-sale securities. The decrease in our net operating assets was primarily due to a decrease in unbilled grant receivable and an increase in accounts payable and accrued expenses, partially offset by the recognition of an insurance recovery receivable related to the securities class action litigation.

During the year ended December 31, 2022, net cash used in operating activities was $72.5 million. This consisted primarily of a net loss of $95.6 million, partially offset by non-cash charges of $11.2 million and a decrease in our net operating assets of $11.9 million. The non-cash charges primarily consisted of stock-based compensation expense, depreciation expense, and amortization of premiums and accretion of discounts on our available-for-sale securities. The decrease in our net operating assets was primarily due to a decrease in unbilled grant receivable, an increase in accounts payable and accrued expenses, and an

accrual for legal settlement expenses related to the securities class action litigation, partially offset by an increase in prepaid expenses and other current assets.

Investing Activities

During the year ended December 31, 2023, net cash provided by investing was $95.1 million. This consisted of maturities of available-for-sale securities of $123.1 million, partially offset by purchases of available-for-sale securities of $27.7 million and property and equipment of $0.3 million.

During the year ended December 31, 2022, net cash provided by investing was $57.7 million. This consisted of maturities of available-for-sale securities of $154.1 million, partially offset by purchases of available-for-sale securities of $95.3 million and property and equipment of $1.1 million.

Financing Activities

During the year ended December 31, 2023, net cash provided by financing activities was $0.5 million, consisting of proceeds received from exercises of stock options.

During the year ended December 31, 2022, net cash provided by financing activities was $0.7 million, consisting of proceeds received from exercises of stock options.

Critical Accounting Policies, Significant Judgments and Use of Estimates

Our financial statements have been prepared in accordance with U.S. generally accepted accounting principles, or GAAP. The preparation of these financial statements requires us to make estimates and assumptions 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 revenue and expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Grant Income

In December 2020, we accepted a grant from the NIH to support our ACT-AD Phase 2 clinical trial for fosgonimeton. As of December 31, 2023, we have recognized aggregate grant income of $15.2 million in connection with the NIH grant, equal to the total grant amount approved and we will not recognize any additional grant income in connection with the NIH grant. We recognized income related to the NIH grant within the consolidated statement of operations and comprehensive loss as qualifying expenses under the grant agreement are incurred. We recorded qualifying expenses incurred in excess of cash received in unbilled grant receivable on the consolidated balance sheets.

Research and Development Costs

Research and development costs, including costs associated with our clinical trials, are expensed as incurred. In-licensing fees and other costs to acquire technologies used in research and development that have not yet received regulatory approval and that are not expected to have an alternative future use are expensed when incurred. Non-refundable advance payments for goods and services that will be used over time for research and development are capitalized and recognized as goods are delivered or as the related services are performed. We estimate the period over which such services will be performed and the level of effort to be expended in each period. If actual timing of performance or the level of effort varies from the

estimate, we will adjust the amounts recorded accordingly. We have not experienced any material differences between accrued or prepaid costs and actual costs since inception.

Stock-based Compensation

We maintain a stock-based compensation plan as a long-term incentive for employees, non-employee directors and consultants. The plan allows for the issuance of incentive stock options, non-qualified stock options, restricted stock units, and other forms of equity awards.

We recognize stock-based compensation expense for stock options on a straight-line basis over the requisite service period and account for forfeitures as they occur. Our stock-based compensation costs for stock options are based upon the grant date fair value of options estimated using the Black-Scholes option pricing model. To the extent any stock option grants are made subject to the achievement of a performance-based milestone, management evaluates when the achievement of any such performance-based milestone is probable based on the relative satisfaction of the performance conditions as of the reporting date.

The Black-Scholes option pricing model utilizes inputs which are highly subjective assumptions and generally require significant judgment. These assumptions include:

- *Fair Value of Common Stock*. The fair value of each share of common stock is based on the closing price of the Company's common stock on the date of grant, or other relevant determination date, as reported on The Nasdaq Global Select Market.
- *Risk-Free Interest Rate*. The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of the option.
- *Expected Volatility*. Because we were privately held prior to September 2020 and do not yet have sufficient trading history for our common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded life sciences companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on the similar size, stage in life cycle or area of specialty. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.
- *Expected Term*. The expected term represents the period that the stock-based awards are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term), as we do not have sufficient historical data to use any other method to estimate expected term.
- *Expected Dividend Yield*. We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

See Note 9 to our consolidated financial statements included elsewhere in this report for more information concerning certain of the specific assumptions we used in applying the Black-Scholes option pricing model to determine the estimated fair value of our stock options. Certain of such assumptions involve inherent uncertainties and the application of significant judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our stock-based compensation could be materially different.

We recorded stock-based compensation expense of $10.6 million and $10.6 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, there was $16.0 million of total unrecognized stock-based compensation expense related to non-vested stock options which we expect to recognize over a remaining weighted-average period of 1.99 years. We expect to continue to grant stock options and other equity-based awards in the future, and to the extent that we do, our stock-based compensation expense recognized in future periods will likely increase.

Income Taxes

We recognize deferred income taxes for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carry forwards. In evaluating our valuation allowance, we consider all available positive and negative evidence, including scheduled reversals of deferred tax liabilities, projected future taxable income, tax planning strategies, and recent financial performance. Due to our lack of earnings history and uncertainties surrounding our ability to generate future taxable income, the net deferred tax assets have been fully offset by a valuation allowance.

As of December 31, 2023, we had $9.5 million of federal NOL carryforwards and $12.4 million of tax credit carryforwards which expire over a period of 8 to 14 years. As of December 31, 2023, we had $138.7 million of such NOLs that do not expire. As of December 31, 2023, we also had state net operating loss carryforwards of $3.3 million, which expire over a period of 18 to 20 years.

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, substantial changes in our ownership may limit the amount of NOL and research and development credit carryforwards that could be used annually in the future to offset taxable income. The tax benefits related to future utilization of federal and state NOL carryforwards, credit carryforwards, and other deferred tax assets may be limited or lost if cumulative changes in ownership exceeds 50% within any three-year period. We have not completed a Section 382/383 analysis under the Code regarding the limitation of NOL and credit carryforwards. If a change in ownership were to have occurred, the annual limitation may result in the expiration of NOL carryforwards and credits before utilization.

We record unrecognized tax benefits as liabilities or reduce the underlying tax attribute, as applicable, and adjust them when our judgment changes as a result of the evaluation of new information not previously available. Because of the complexity of some of these uncertainties, the ultimate resolution may result in a payment that is materially different from our current estimate of the unrecognized tax benefit liabilities. These differences will be reflected as increases or decreases to income tax expense in the period in which new information is available.

Recent Accounting Pronouncements

See Note 2 to our consolidated financial statements included elsewhere in this report for additional information.

Emerging Growth Company Status

We are an emerging growth company, as defined in the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that we (1) are no longer an emerging growth company and (2) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

We will remain an emerging growth company until the earliest to occur of: (1) the last day of the fiscal year in which we have at least $1.235 billion in annual revenue; (2) the last day of the fiscal year in which we are deemed to be a “large accelerated filer,” as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our common stock held by non-affiliates exceeded $700.0 million as of the last business day of the second fiscal quarter of such year; (3) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period; and (4) the last day of the fiscal year in which the fifth anniversary of our initial public offering occurred.

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

As a smaller reporting company, we are not required to provide the information requested by this item pursuant to Item 305 of Regulation S-K.

Item 8. Financial Statements and Supplementary Data.

Athira Pharma, Inc.

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Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Athira Pharma, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Athira Pharma, Inc. (the Company) as of December 31, 2023 and 2022, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the two years in the period ended December 31, 2023, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2023, in conformity with U.S. generally accepted accounting principles.

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 2018.

Seattle, Washington
February 22, 2024

Athira Pharma, Inc.
Consolidated Balance Sheets
(in thousands, except share and per share amounts)

	December 31,	
	2023	2022
Assets		
Current assets:		
Cash and cash equivalents	$ 90,584	$ 95,966
Short-term investments	56,835	104,378
Unbilled grant receivable	—	1,227
Prepaid expenses and other current assets	5,682	5,962
Insurance recovery receivable related to legal settlement (Note 7)	1,628	—
Total current assets	154,729	207,533
Restricted cash	631	420
Property and equipment, net	3,388	4,053
Operating lease right-of-use asset	1,049	1,263
Long-term investments	—	44,829
Other long-term assets	448	55
Total assets	$ 160,245	$ 258,153
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 129	$ 2,501
Accrued liabilities	18,343	8,604
Accrued legal settlement (Note 7)	10,000	10,000
Current operating lease liability	368	326
Total current liabilities	28,840	21,431
Operating lease liability, less current portion	1,217	1,585
Total liabilities	30,057	23,016
Stockholders' equity:		
Common stock, $0.0001 par value; 900,000,000 shares authorized at December 31, 2023 and December 31, 2022, respectively; 38,172,603 and 37,877,387 shares issued and outstanding at December 31, 2023 and December 31, 2022, respectively	4	4
Additional paid-in capital	439,739	428,623
Accumulated other comprehensive loss	(349)	(1,956)
Accumulated deficit	(309,206)	(191,534)
Total stockholders' equity	130,188	235,137
Total liabilities and stockholders' equity	$ 160,245	$ 258,153

The accompanying notes are an integral part of these consolidated financial statements.

Athira Pharma, Inc.
Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share amounts)

	Year Ended December 31,	
	2023	2022
Operating expenses:		
Research and development	$ 93,790	$ 61,464
General and administrative	33,304	32,552
Legal settlement	—	10,000
Insurance recovery related to legal settlement	(1,628)	—
Total operating expenses	125,466	104,016
Loss from operations	(125,466)	(104,016)
Grant income	157	5,161
Other income, net	7,637	3,216
Net loss	$ (117,672)	$ (95,639)
Unrealized gain (loss) on available-for-sale securities	1,607	(1,568)
Comprehensive loss attributable to common stockholders	$ (116,065)	$ (97,207)
Net loss per share attributable to common stockholders, basic and diluted	$ (3.09)	$ (2.53)
Weighted-average shares used in computing net loss per share attributable to common stockholders, basic and diluted	38,020,182	37,733,240

The accompanying notes are an integral part of these consolidated financial statements.

Athira Pharma, Inc.
Consolidated Statements of Stockholders' Equity
(in thousands, except share amounts)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance as of January 1, 2022	37,379,077	$ 4	$ 417,363	$ (388)	$ (95,895)	$ 321,084
Issuance of common stock upon exercise of common stock options and vesting of restricted stock units	419,949	—	309	—	—	309
Issuance of common stock under employee stock purchase plan	78,361	—	345	—	—	345
Stock-based compensation	—	—	10,606	—	—	10,606
Unrealized loss on available-for-sale securities	—	—	—	(1,568)	—	(1,568)
Net loss	—	—	—	—	(95,639)	(95,639)
Balance as of December 31, 2022	37,877,387	$ 4	$ 428,623	$ (1,956)	$ (191,534)	$ 235,137
Issuance of common stock upon exercise of common stock options	128,534	—	167	—	—	167
Issuance of common stock under employee stock purchase plan	166,682	—	326	—	—	326
Stock-based compensation	—	—	10,623	—	—	10,623
Unrealized gain on available-for-sale securities	—	—	—	1,607	—	1,607
Net loss	—	—	—	—	(117,672)	(117,672)
Balance as of December 31, 2023	38,172,603	$ 4	$ 439,739	$ (349)	$ (309,206)	$ 130,188

The accompanying notes are an integral part of these consolidated financial statements.

Athira Pharma, Inc.
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,	
	2023	2022
Operating activities		
Net loss	$ (117,672)	$ (95,639)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	10,623	10,606
Depreciation expense	969	845
Non-cash lease expense	214	203
Amortization of premiums and accretion of discounts on available-for-sale securities, net	(1,414)	(422)
Changes in operating assets and liabilities:		
Unbilled grant receivable	1,227	1,109
Prepaid expenses and other current and long-term assets, net	(113)	(1,257)
Insurance recovery receivable related to legal settlement	(1,628)	—
Accounts payable and accrued liabilities	7,367	2,101
Accrued legal settlement	—	10,000
Operating lease liability	(326)	(15)
Net cash used in operating activities	(100,753)	(72,469)
Investing activities		
Purchases of available-for-sale securities	(27,671)	(95,288)
Maturities of available-for-sale securities	123,064	154,093
Purchases of property and equipment	(304)	(1,141)
Net cash provided by investing activities	95,089	57,664
Financing activities		
Proceeds from exercise of common stock options and issuance of common stock under employee stock purchase plan	493	654
Net cash provided by financing activities	493	654
Net decrease in cash, cash equivalents and restricted cash	(5,171)	(14,151)
Cash, cash equivalents and restricted cash, beginning of period	96,386	110,537
Cash, cash equivalents and restricted cash, end of period	$ 91,215	$ 96,386

The accompanying notes are an integral part of these consolidated financial statements.

1. Description of Business

Organization

Athira Pharma, Inc. (the "Company") was incorporated as M3 Biotechnology, Inc. in the state of Washington on March 31, 2011 and reincorporated in the state of Delaware on October 27, 2015. In April 2019, the Company changed its name to Athira Pharma, Inc. The Company currently has office and laboratory space in Bothell, Washington. The Company is a late clinical-stage biopharmaceutical company focused on developing small molecules to restore neuronal health and slow neurodegeneration.

Liquidity and Capital Resources

Since the Company's inception, it has funded its operations primarily with proceeds from the sale and issuance of common stock, convertible preferred stock, common stock warrants, and convertible notes, and to a lesser extent from grant income and stock option exercises. From the Company's inception through December 31, 2023, it has raised aggregate net cash proceeds of $407.4 million primarily from the issuance of its common stock (excluding option exercises), convertible preferred stock, common stock warrants, and convertible notes. As of December 31, 2023, the Company had $147.4 million in cash, cash equivalents, and investments and had not generated positive cash flows from operations. Since the Company's inception, it has devoted substantially all of its resources to its research and development efforts such as small molecule compound discovery, nonclinical studies and clinical trials, as well as manufacturing activities, establishing and maintaining the Company's intellectual property portfolio, hiring personnel, raising capital, and providing general and administrative support for these operations.

Based upon the Company's current operating plan, it estimates that its $147.4 million of cash, cash equivalents, and investments at December 31, 2023 will be sufficient to fund its operating expenses and capital expenditure requirements through at least the next 12 months following the date of the Company's Annual Report on Form 10-K.

At The Market Common Stock Offering

In January 2023, the Company entered into a sales agreement with Cantor Fitzgerald and BTIG to sell shares of our common stock having aggregate sales proceeds of up to $75.0 million, from time to time, through an "at the market" ("ATM") equity offering program under which Cantor and BTIG are acting as sales agents. The Company has not sold any securities pursuant to this ATM offering.

2. Significant Accounting Policies

Basis of Presentation

The consolidated financial statements have been prepared in conformity with U.S. generally accepted accounting principles ("U.S. GAAP"). The consolidated financial statements include the operations of Athira Pharma, Inc., and its wholly owned Australian subsidiary. All intercompany balances and transactions have been eliminated upon consolidation.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Estimates include those used for fair value of assets and liabilities, accrued liabilities, valuation allowance for deferred tax assets, and stock-based compensation. Management evaluates related assumptions on an ongoing basis using historical experience and other

factors and adjusts those estimates and assumptions when facts and circumstances dictate. Actual results could differ from those estimates.

Cash and Cash Equivalents

The Company considers highly liquid investments with original maturities of three months or less to be cash equivalents.

Restricted Cash

Restricted cash consists primarily of collateral pledged in connection with the Company's corporate credit cards. The table below reconciles the balances of cash and cash equivalents and restricted cash reported on the consolidated balance sheets to the balances of cash, cash equivalents and restricted cash reported on the consolidated statements of cash flows.

	December 31,	
	2023	2022
Cash and cash equivalents	$ 90,584	$ 95,966
Restricted cash	631	420
Cash, cash equivalents and restricted cash	$ 91,215	$ 96,386

Short-term and Long-term Investments

The Company generally invests its excess cash in investment grade short- to intermediate-term fixed income securities. Such investments are included in cash and cash equivalents, short-term investments, and long-term investments on the consolidated balance sheets, classified as available-for-sale, and reported at fair value with unrealized gains and losses included in accumulated other comprehensive loss. Amortization and accretion are included in other income, net. Realized gains and losses on the sale of these securities are recognized in other income, net.

The Company periodically evaluates whether declines in fair values of its investments below their book value are due to expected credit losses, as well as the Company's ability and intent to hold the investment until a forecasted recovery occurs. Expected credit losses are recorded as an allowance through other income, net.

Concentration of Credit Risk

The Company is exposed to credit risk from its deposits of cash in excess of amounts insured by the Federal Deposit Insurance Corporation. The Company has not experienced any losses on its deposits of cash since inception.

Property and Equipment

Property and equipment consist of computer equipment, computer software, laboratory equipment, leasehold improvements and furniture and office equipment. Property and equipment, excluding leasehold improvements, are recorded at cost and depreciation is recognized using the straight-line method based on estimated useful life, generally three to five years. Leasehold improvements are amortized over the shorter of their useful life or the remaining lease term. Maintenance and repairs are charged to expense as incurred, and costs of improvements are capitalized.

The Company reviews long-lived assets for impairment whenever events or circumstances indicate the carrying amount of an asset group may not be recoverable. Should an impairment exist, the impairment loss would be measured based on the excess of the asset's carrying amount over its fair value. Gains and losses from asset disposals and impairment losses are classified within the consolidated statements of operations and comprehensive loss in accordance with the use of the asset. There were no impairment

losses in the years ended December 31, 2023 and 2022 as there have been no events warranting an impairment analysis.

Fair Value Measurements

The carrying amounts of certain financial instruments, including cash, cash equivalents, restricted cash, investments, accounts payable and accrued expenses approximate their fair values due to the short-term nature of those amounts.

Grant Income

In December 2020, the Company accepted a grant from the National Institute on Aging ("NIA") of the National Institutes of Health ("NIH") to support its ACT-AD Phase 2 clinical trial for fosgonimeton (then-named ATH-1017), the Company's lead therapeutic candidate being developed for the treatment of individuals with mild-to-moderate Alzheimer's disease. The Company recognizes income related to the NIH grant in the accompanying consolidated statements of operations and comprehensive loss as qualifying expenses under the grant agreement are incurred. As of December 31, 2023, the Company has recognized aggregate grant income of $15.2 million in connection with the NIH grant, equal to the total grant amount approved. The Company will not recognize any additional grant income in connection with the NIH grant in the future.

During the years ended December 31, 2023 and 2022, the Company recognized grant income of $0.2 million and $5.2 million, respectively, in connection with the NIH grant. As of December 31, 2022, the Company incurred qualifying expenses in excess of cash received of $1.2 million, which is included in unbilled grant receivable on the consolidated balance sheets. The Company received cash of $1.4 million related to the NIH grant during the year ended December 31, 2023, compared to $6.3 million during the year ended December 31, 2022.

Research and Development Expenses

Research and development expenses consist primarily of direct and indirect costs incurred for research activities, including development of the pipeline from the Company's proprietary drug discovery platform ("ATH platform"), the Company's drug discovery efforts and the development of its drug candidates. Direct costs include laboratory materials and supplies, contracted research and manufacturing, clinical trial costs, consulting fees, and other expenses incurred to sustain the Company's research and development program. Indirect costs include personnel-related expenses, consisting of employee salaries, related benefits, and stock-based compensation expense for employees engaged in research and development activities, and facilities and other expenses consisting of direct and allocated expenses for rent and depreciation and lab consumables.

Research and development costs are expensed as incurred. In-licensing fees and other costs to acquire technologies used in research and development that have not yet received regulatory approval and that are not expected to have an alternative future use are expensed when incurred. Non-refundable advance payments for goods and services that will be used over time for research and development are capitalized and recognized as goods are delivered or as the related services are performed. The Company estimates the period over which such services will be performed and the level of effort to be expended in each period. If actual timing of performance or the level of effort varies from the estimate, the Company adjusts the amounts recorded accordingly. The Company has not experienced any material differences between accrued or prepaid costs and actual costs since inception.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel-related costs, consisting of employee salaries, related benefits, and stock-based compensation expense for employees in the executive, legal, finance and accounting, human resources, and other administrative functions. General

and administrative expenses also include third-party costs such as legal costs, insurance costs, accounting, auditing and tax related fees, consulting fees and facilities and other expenses not otherwise included as research and development expenses. General and administrative costs are expensed as incurred.

Leases

The Company adopted Accounting Standards Codification ("ASC") *Topic 842 - Leases* effective January 1, 2020. The Company determines if an arrangement contains a lease at inception. The Company performed an evaluation of contracts in accordance with ASC 842 and has determined it has an operating lease agreement for the laboratory and office facilities that the Company occupies. Operating lease right-of-use ("ROU") assets and operating lease liabilities are recognized at the date the underlying asset becomes available for the Company's use. Operating lease liabilities are based on the present value of the future minimum lease payments over the lease term. ROU assets are measured at the amount of the lease liability, adjusted for any initial direct costs incurred and any lease payments made at or before the lease commencement date, less lease incentives received. As the Company's leases generally do not provide an implicit interest rate, the present value of the future minimum lease payments is determined using the Company's incremental borrowing rate. This rate is an estimate of the collateralized borrowing rate the Company would incur on its future lease payments over a similar term and is based on the information available to the Company at the lease commencement date.

The Company's leases contain options to extend the leases; lease terms are adjusted for these options only when it is reasonably certain the Company will exercise these options. The Company's lease agreements do not contain residual value guarantees or covenants.

The Company has made a policy election regarding its real estate leases not to separate non-lease components from lease components, to the extent they are fixed. Non-lease components that are not fixed are expensed as incurred as variable lease expense. The Company's lease includes variable non-lease components, such as common-area maintenance costs. The Company has elected not to record on the balance sheet a lease that has a lease term of 12 months or less and does not contain a purchase option that the Company is reasonably certain to exercise. The Company accounts for leases with initial terms of 12 months or less as operating expenses on a straight-line basis over the lease term.

Lease expense is recognized within operating expenses on a straight-line basis over the terms of the lease. Incentives granted under the Company's facilities lease, including rent holidays, are recognized as adjustments to lease expense on a straight-line basis over the term of the lease.

Stock-based Compensation

The Company measures compensation expense for all stock-based payments to employees, officers and directors based on the estimated fair value of the award at the grant date. For stock options, the Company estimates the grant date fair value of each option award using the Black-Scholes option-pricing model. The grant date fair value of restricted stock units is based upon the fair market value of the Company's common stock based on its closing price as reported on the date of grant on the Nasdaq Global Select Market. Compensation expense is recognized over the requisite service period on a straight-line basis. Forfeitures are recognized as they occur.

The Company records compensation expense for stock option and restricted stock unit grants subject to performance-based milestone vesting over the remaining implicit service period when management determines that achievement of the milestone is probable. Management evaluates when the achievement of a performance-based milestone is probable based on the relative satisfaction of the performance conditions as of the reporting date.

Income Taxes

Income taxes are accounted for under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carry forwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

In assessing the Company's ability to realize deferred tax assets, management considers whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which those temporary differences are deductible. Management considers the scheduled reversal of deferred tax liabilities, projected future income, tax planning strategies in making this assessment.

The Company recognizes the effect of income tax positions only if those positions are more likely than not of being sustained. Recognized income tax positions are measured at the largest amount that is greater than 50% likely of being realized. Changes in recognition or measurement are reflected in the period in which the change in judgment occurs. The Company accrues interest and penalties related to unrecognized tax benefits in its provision for incomes taxes.

Comprehensive Loss Attributable to Common Stockholders

Comprehensive loss attributable to common stockholders consists of net loss and other gains and losses affecting stockholders' equity that, under U.S. GAAP, are excluded from net loss. The Company's comprehensive loss attributable to common stockholders is comprised of net loss and unrealized gains and losses on available-for-sale securities.

Net Loss Per Share Attributable to Common Stockholders

Basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding for the period, without consideration of potentially dilutive securities. Diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders since the effect of potentially dilutive securities is anti-dilutive given the net loss of the Company.

Foreign Currency Transaction Remeasurement Adjustments

Monetary assets and liabilities denominated in foreign currencies were translated into U.S. dollars, the reporting currency, at the exchange rate prevailing at the balance sheet date. Income and expenses denominated in foreign currencies were translated into U.S. dollars at the average exchange rate for the period and the transaction remeasurement adjustments are reported within other income, net in the consolidated statement of operations and comprehensive loss. The functional currency of the Company's Australian subsidiary is the U.S. dollar.

Segments

The Company has determined that it operates and manages one operating segment, which is the business of developing and commercializing therapeutics. The Company's chief operating decision maker, its chief executive officer, reviews financial information on an aggregate basis for the purpose of allocating resources.

Emerging Growth Company Status

The Company is an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 ("JOBS Act"). Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. The Company has elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that it is (1) no longer an emerging growth company and (2) affirmatively and irrevocably opts out of the extended transition period provided in the JOBS Act, unless early adoption is permitted. As a result, these financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

Recently Adopted Accounting Pronouncements

In June 2016, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) 2016-13, Financial Instruments: Credit Losses (Topic 326) as clarified in ASU 2019-04, ASU 2019-05, and ASU 2020-02. The objective of the standard is to provide information about expected credit losses on financial instruments at each reporting date and to change how other-than-temporary impairments on investment securities are recorded. The Company adopted ASU 2016-13 effective January 1, 2023 and it did not have a material impact on its financial condition, results of operations or cash flows.

3. Fair Value

The Company has certain assets and liabilities that are measured at fair value on a recurring basis according to a fair value hierarchy that prioritizes the inputs, assumptions and valuation techniques used to measure fair value. The three levels of the fair value hierarchy are:

Level 1—Unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities.

Level 2—Quoted prices in markets that are not active or financial instruments for which all significant inputs are observable, either directly or indirectly.

Level 3—Inputs are generally unobservable and reflect management's estimates of assumptions that market participants would use in pricing the asset or liability. The fair values are determined using model-based techniques, including probability-based simulation methodologies.

The determination of a financial instrument's level within the fair value hierarchy is based on an assessment of the lowest level of any input that is significant to the fair value measurement. The Company considers observable data to be market data, which is readily available, regularly distributed or updated, reliable and verifiable, not proprietary, and provided by independent sources that are actively involved in the relevant market.

The following tables reflect the Company's financial asset balances measured at fair value on a recurring basis (in thousands):

	December 31, 2023				
	Level	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash equivalents:					
Money market fund	1	$ 63	$ —	$ —	$ 63
Commercial paper	2	59,227	—	(30)	59,197
Total cash equivalents		$ 59,290	$ —	$ (30)	$ 59,260
Short-term investments:					
Commercial paper	2	6,431	—	(4)	6,427
U.S. government debt and agency securities	2	50,723	—	(315)	50,408
Total short-term investments		$ 57,154	$ —	$ (319)	$ 56,835

	December 31, 2022				
	Level	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash equivalents:					
Money market fund	1	$ 7	$ —	$ —	$ 7
Commercial paper	2	78,028	—	(26)	78,002
Total cash equivalents		$ 78,035	$ —	$ (26)	$ 78,009
Short-term investments:					
Commercial paper	2	36,933	—	(168)	36,765
U.S. government debt and agency securities	2	65,157	—	(784)	64,373
Corporate bonds	2	3,302	—	(62)	3,240
Total short-term investments		$105,392	$ —	$ (1,014)	$104,378
Long-term investments:					
U.S. government debt and agency securities	2	45,745	—	(916)	44,829
Total long-term investments		$ 45,745	$ —	$ (916)	$ 44,829

All the commercial paper, U.S. government debt, and agency securities, U.S. treasury bills, and corporate bonds designated as short-term investments have an effective maturity date that is equal to or less than one year from the respective balance sheet date. Those that are designated as long-term investments have an effective maturity date that is more than one year, but less than two years, from the respective balance sheet date.

As of December 31, 2023, the Company does not intend to sell any securities in unrealized loss positions, and it is not more-likely-than-not that the Company will be required to sell such securities prior to the recovery of the amortized cost basis. Based on the Company's assessment, the Company concluded all impairments as of December 31, 2023 to be due to factors other than credit loss, such as changes in interest rates. A credit loss allowance was not recognized and the unrealized gains (losses) for available-for-sale securities were recorded in other comprehensive loss.

4. Property and Equipment, Net

Property and equipment consisted of the following (in thousands):

	December 31,	
	2023	2022
Lab equipment	$ 688	$ 433
Office furniture, fixtures, and computer equipment	712	692
Leasehold improvement	4,322	4,296
Property and equipment, at cost	5,722	5,421
Less: accumulated depreciation	(2,334)	(1,368)
Property and equipment, net	$ 3,388	$ 4,053

Depreciation expense was $969,000 and $845,000 for the years ended December 31, 2023 and 2022, respectively.

5. Accrued Liabilities

Accrued liabilities consisted of the following (in thousands):

	December 31,	
	2023	2022
Research and development expenses	$ 11,916	$ 3,843
Employee compensation and benefits	4,545	3,415
Professional services and other	1,882	1,346
Total accrued liabilities	$ 18,343	$ 8,604

6. Significant Agreements

WSU License Agreement

The Company is party to an amended and restated exclusive license agreement with sublicensing terms with WSU that the Company entered into in 2015. Under this agreement, the Company has an exclusive license to make, use, sell, and offer for sale products covered by certain licensed patents, including dihexa, the chemical compound into which fosgonimeton metabolizes following administration.

To keep in good standing, the agreement requires the Company to meet certain development milestones and pay annual maintenance fees. All contractual requirements have been met as of December 31, 2023.

During the year ended December 31, 2020, the Phase 2 clinical trial milestone had been reached and a payment of $50,000 to WSU was recorded.

The Company may also be obligated to pay the following if the related milestones are reached:

- $300,000 – At initiation of the first Phase 3 clinical trial in the United States, European Union or Japan for the first licensed product; and
- $600,000 – Upon receipt of marketing approval in the United States, European Union or Japan for the first licensed product.

Under the terms of the agreement, the Company will pay a royalty in the mid-single digits of net sales, with the first $100,000 of net sales being exempt from royalty payment, and annual minimum royalty payments of $25,000 beginning after the first commercial sale of a licensed product. As of December 31, 2023, no sales of any licensed products had occurred and the Company had not incurred a royalty obligation under this agreement.

Additionally, the agreement allows the Company to sublicense the rights conveyed by the agreement, subject to additional payments to WSU based upon the sublicense consideration received in such event. Such amounts are dependent on the terms of the underlying sublicense and range from the mid-single digits to mid-teens of any non-sales based payments received, and low twenties of net sales based sublicense royalties. As of December 31, 2023, the Company has not entered into or incurred any liability from a sublicense agreement.

7. Commitments and Contingencies

Legal Proceedings

From time to time, the Company is subject to various legal proceedings or claims that arise in the ordinary course of business. The Company accrues a liability when the Company's management believes that it is both probable that a liability has been incurred and the amount of loss can be reasonably estimated. The following is a brief description of the more significant legal proceedings.

Securities Class Actions

On June 25, 2021, plaintiffs Fan Wang and Hang Gao filed a putative securities class action lawsuit in the U.S. District Court for the Western District of Washington against the Company and the Company's former chief executive officer Dr. Leen Kawas, captioned *Wang v. Athira Pharma, Inc., et al.*, No. 2:21-cv-00861. Plaintiffs Wang and Gao assert claims under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 ("Exchange Act") and SEC Rule 10b-5, alleging that the defendants made materially false and misleading statements and omitted material adverse facts regarding the Company's business. Specifically, the *Wang* plaintiffs allege that the Company failed to disclose to investors that certain research conducted by Dr. Kawas was allegedly tainted by scientific misconduct during her doctoral work at WSU, including the manipulation of data, and that as a result, the defendants' positive statements about the Company's business, operations, and prospects were materially misleading. The *Wang* plaintiffs seek unspecified compensatory and punitive damages, and reasonable costs and expenses, including attorneys' fees.

That same day, on June 25, 2021, plaintiff Harshdeep Jawandha filed a putative securities class action lawsuit in the U.S. District Court for the Western District of Washington against the Company, Dr. Kawas, the Company's then chief financial officer, certain members of the Company's board of directors at the time of the Company's initial public offering ("IPO"), as well as the IPO underwriters, captioned *Jawandha v. Athira Pharma, Inc., et al.*, No. 2:21-cv-00862. The *Jawandha* complaint asserts violations of Sections 11 and 15 of the Securities Act of 1933 ("Securities Act"), alleging that that the Company's IPO registration statement was materially false and misleading because it omitted to state that certain of Dr. Kawas's published doctoral research papers at WSU contained allegedly improperly altered images, that the research was allegedly foundational to the Company's efforts to develop treatments for Alzheimer's disease, and that the defendants' positive statements about the Company's business, operations, and prospects were materially misleading. The *Jawandha* plaintiff seeks unspecified compensatory damages, and reasonable costs and expenses, including attorneys' fees.

Also on June 25, 2021, plaintiffs Timothy Slyne and Tai Slyne filed a putative securities class action lawsuit in the U.S. District Court for the Western District of Washington against the Company, Dr. Kawas, the Company's then chief financial officer, and the same members of the Company's board of directors and underwriters as in the *Jawandha* complaint, captioned *Slyne v. Athira Pharma, Inc. et al.*, No. 2:21-cv-00864. The *Slyne* complaint asserts violations of Sections 11 and 15 of the Securities Act, alleging that purported issues with Dr. Kawas's doctoral research at WSU should have been disclosed in the Company's IPO registration statement. The *Slyne* plaintiffs seek unspecified compensatory damages, reasonable costs and expenses, including attorneys' fees, and injunctive and other equitable relief.

On August 9, 2021, the court issued an order consolidating the three cases. On October 5, 2021, the district court issued an order appointing lead plaintiffs and approved their selection of lead and liaison counsel.

On January 7, 2022, lead plaintiffs filed a consolidated amended complaint, which asserts violations of Sections 10(b) and 20(a) of the Exchange Act and SEC Rule 10b-5 and Sections 11, 12, and 15 of the Securities Act. The consolidated amended complaint is brought against the Company, Dr. Kawas, the Company's then chief financial officer, certain members of the Company's board of directors at the time of the Company's IPO and secondary public offering ("SPO"), and the IPO and SPO underwriters. As with the previous complaints, it is based on allegations that the IPO and SPO registration statements and/or other public statements were materially false and misleading because they omitted to state that certain of Dr. Kawas's published doctoral research papers at WSU contained allegedly improperly altered images. Lead plaintiffs seek unspecified compensatory damages, as well as equitable and injunctive relief on behalf of themselves and the purported class. On March 8, 2022, the defendants filed a motion to dismiss lead plaintiffs' consolidated amended complaint for failure to state a claim under the federal securities laws. On July 29, 2022, the court issued an order granting in part and denying in part the motion to dismiss. The order dismissed the Section 10(b) and Section 20(a) claims arising under the Exchange Act, dismissed the Section 11 claim arising under the Securities Act as to all defendants other than the Company and Dr. Kawas, dismissed the Section 12(a)(2) claim arising under the Securities Act as to the lead plaintiffs, and dismissed the Section 15 claim arising under the Securities Act against all defendants other than Dr. Kawas. The order permitted lead plaintiffs until August 19, 2022 to file a second consolidated amended complaint. Lead plaintiffs did not file a second consolidated amended complaint.

On August 12, 2022, defendant Dr. Kawas filed a motion for partial reconsideration of the court's July 29, 2022 order. On October 24, 2022, the parties filed a (1) joint status report and discovery plan and (2) stipulation and case scheduling order, wherein the parties proposed deadlines for material case events, including the completion of fact discovery, expert discovery, and dispositive motion practice. On November 2, 2022, the court entered an order setting certain case deadlines. On November 4, 2022, the Company and Dr. Kawas filed their individual answers to the consolidated amended complaint. In mid-November 2022, the parties began conducting fact discovery.

On March 10, 2023, following a mediation and the parties' agreement in principle to settle the securities class action, the court entered a stipulated order setting a deadline of April 28, 2023 for the parties to file a stipulation of settlement and for lead plaintiffs to file a motion for preliminary approval of the settlement, which the parties filed on that date. The settlement is subject to preliminary and final approval by the U.S. District Court for the Western District of Washington. On May 31, 2023, the court issued a minute order requiring the parties to file a joint status report on or before June 30, 2023 addressing several aspects of the proposed settlement, including revision of certain notices to putative class members regarding the settlement, which the parties filed on that date. On September 27, 2023, the court issued an order denying plaintiffs' motion for preliminary approval without prejudice, citing the motion's failure to satisfy the court's questions and concerns regarding traceability of certain Securities Act claims. The court permitted plaintiffs to file a renewed motion for preliminary approval, which plaintiffs filed on December 15, 2023.

On February 15, 2024, the court issued an order granting in part and deferring in part plaintiffs' renewed motion for preliminary approval and ordered the parties to submit a joint status report by March 15, 2024 proposing a date on which the court may schedule the final approval hearing, among other things. In its order, the court preliminarily approved the proposed settlement and certified a class and two subclasses. The court deferred ruling in part as to the proposed notices and claim form relating to the settlement.

As a result of the foregoing, the Company recorded a legal settlement expense of $10.0 million in operating expenses in the fourth quarter of 2022 and an accrued liability of $10.0 million on the accompanying consolidated balance sheets. Additionally, the Company recorded an insurance recovery of $1.6 million in operating expenses in the fourth quarter of 2023 and an insurance recovery receivable of $1.6 million on the accompanying consolidated balance sheets. This insurance recovery represents the amount of the settlement to be covered by the Company's insurers.

Shareholder Derivative Actions

On April 14, 2022, a shareholder derivative action was filed by plaintiff Stephen Bushansky in the U.S. District Court for the Western District of Washington against certain current and former members of the Company's board of directors, captioned *Bushansky v. Kawas et al.*, No. 2:22-cv-497. Plaintiff purports to bring the action derivatively on behalf of the Company, which is a nominal defendant to the action. The derivative complaint alleges that the Company's board of directors breached its fiduciary duties by failing to prevent alleged misstatements in the Company's public filings, failing to discover altered images in certain research papers, and failing to take appropriate action. The derivative complaint asserts claims for violations of Section 14(a) of the Exchange Act as well as claims for breach of fiduciary duty, contribution and indemnification, aiding and abetting, and waste of corporate assets. The derivative complaint seeks unspecified damages, disgorgement of profits, benefits, and other compensation received by the individual defendants, restitution, declaratory relief, and an award of costs and expenses to the derivative plaintiff, including attorneys' fees.

On May 6, 2022, a second shareholder derivative action was filed by plaintiff Thomas Houlihan in the U.S. District Court for the Western District of Washington against certain current and former directors and officers of the Company, captioned *Houlihan v. Kawas et al*., No. 2:22-cv-620. Plaintiff purports to bring the action derivatively on behalf of the Company, which is a nominal defendant to the action. The derivative complaint alleges that certain of the Company's current and former directors and officers breached their fiduciary duties by failing to prevent alleged misstatements in the Company's public filings and failing to take appropriate action regarding altered images in certain research papers. The derivative complaint asserts claims for violations of Section 14(a) of the Exchange Act as well as claims for breach of fiduciary duties, contribution, and indemnification. The derivative complaint seeks unspecified damages, unspecified corporate governance reforms, restitution, and an award of costs and expenses to the derivative plaintiff, including attorneys' fees.

On May 26, 2022, the court issued an order consolidating the cases and staying them until further order of the court. The Company believes it has adequate reserves related to this matter as of the latest balance sheet date.

Government Investigations

In November 2022, the Company received a Civil Investigative Demand from the Civil Division of the Department of Justice (the "Demand"). The Demand seeks documents and information relating to our relationship with WSU, certain of our grant applications in 2016 and 2019 with the NIH, and our receipt of a NIH grant in 2020. The Company is cooperating with the Department of Justice with respect to the Demand.

In February 2023, the Securities and Exchange Commission ("SEC"), sent the Company a subpoena seeking documents and information relating to, among other things, the Company's former chief executive officer's alterations of images in certain research papers. The Company is cooperating with the SEC with respect to the subpoena.

The Company cannot predict the outcome of these lawsuits or government investigations. Failure by the Company to obtain a favorable resolution of these actions could have a material adverse effect on our business, results of operations and financial condition.

Indemnifications

In the ordinary course of business, the Company enters into agreements that may include indemnification provisions. Pursuant to such agreements, the Company may indemnify, hold harmless and defend an indemnified party for losses suffered or incurred by the indemnified party. Some of the provisions will limit losses to those arising from third party actions. In some cases, the indemnification will continue after the termination of the agreement. The maximum potential amount of future payments the Company could be required to make under these provisions is not determinable. To date the Company has not

incurred material costs to defend lawsuits or settle claims related to these indemnification provisions. The Company enters into indemnification agreements with its directors and officers that may require the Company to indemnify its directors and officers against liabilities that may arise by reason of their status or service as directors or officers to the fullest extent permitted by Delaware corporate law. The Company currently has directors' and officers' insurance coverage that reduces its exposure and enables the Company to recover a portion of any future amounts paid.

Operating Leases

The Company has operating leases for laboratory and office facilities in Bothell, Washington that expire in August 2027. The initial terms of the leases range from 6.3 to 7 years and the Company has options to extend the leases for an additional five years that it is not reasonably certain to exercise. As of December 31, 2023, the Company was not party to any finance leases.

The following table reconciles the Company's undiscounted operating lease cash flows to its operating lease liability (in thousands):

	December 31, 2023
2024	480
2025	494
2026	509
Thereafter	346
Total undiscounted lease payments	1,829
Present value adjustment for minimum lease commitments	(244)
Net lease liability	$ 1,585

The weighted average remaining lease term and the weighted average discount rate used to determine the operating lease liability were as follows:

	December 31, 2023
Weighted average remaining lease term (years)	3.7
Weighted average discount rate	8.1%

Operating lease expense was $353,000 and $368,000 for the years ended December 31, 2023 and 2022, respectively. Separately, variable lease expense was $186,000 and $167,000 for operating leases during the years ended December 31, 2023 and 2022, respectively.

8. Common Stock

Each share of common stock has the right to one vote. The holders of common stock are also entitled to receive dividends whenever funds are legally available and if declared by the Company's board of directors, subject to the prior rights of holders of all classes of stock outstanding having priority rights as to dividends. No cash dividends have been declared by the board of directors from inception.

The Company has reserved the following shares of common stock for future issuance, on an as-converted basis, as follows:

	December 31,	
	2023	2022
Shares issuable upon the exercise of outstanding common stock options and the vesting of outstanding common restricted stock units granted	7,130,956	4,269,861
Shares available for future grant under the 2020 Equity Incentive Plan	3,158,094	4,253,854
Shares available for future grant under the Employee Stock Purchase Plan	1,128,732	916,640
Total	11,417,782	9,440,355

The Company's 2020 Equity Incentive Plan ("2020 Plan") provides for annual increases in the number of shares that may be issued under the 2020 Plan on January 1, 2021 and each subsequent January 1, thereafter, by a number of shares equal to the least of (1) 3,230,000 shares, (2) 5% of the number of shares of common stock issued and outstanding on the immediately preceding December 31, and (3) an amount determined by the Company's board of directors.

The Company's 2020 Employee Stock Purchase Plan ("ESPP") provides for annual increases in the number of shares that may be issued under the ESPP on January 1, 2021 and each subsequent January 1, thereafter, by a number of shares equal to the least of (1) 646,000 shares, (2) 1% of the number of shares of common stock issued and outstanding on the immediately preceding December 31, and (3) an amount determined by the Company's board of directors.

Effective January 1, 2023, the Company's 2020 Plan and ESPP reserves increased by 1,893,869 shares and 378,774 shares, respectively.

Effective January 1, 2024, the Company's 2020 Plan and ESPP reserves increased by 1,908,630 shares and 381,726 shares, respectively.

9. Stock-based Compensation

Stock-based compensation expense recognized was as follows (in thousands):

	Year Ended December 31,	
	2023	2022
Research and development	$ 4,003	$ 3,217
General and administrative	6,620	7,389
Total stock-based compensation expense	$ 10,623	$ 10,606

Valuation Assumptions

The fair value of stock options was determined using the Black-Scholes option-pricing model and the assumptions below. Each of these inputs is subjective and generally required significant judgment.

- *Fair Value of Common Stock*—The fair value of each share of common stock is based on the closing price of the Company's common stock on the date of grant, or other relevant determination date, as reported on The Nasdaq Global Select Market.

- *Risk-Free Interest Rate*—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of the option.
- *Expected Volatility*—Because the Company was previously privately held and did not have any trading history for its common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded life sciences companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on the similar size, stage in life cycle or area of specialty. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.
- *Expected Term*—The expected term represents the period that the stock-based awards are expected to be outstanding and is determined using the simplified method (based on the midpoint between the vesting date and the end of the contractual term) as the Company has limited history of relevant stock option exercise activity.
- *Expected Dividend Yield*—The Company has never paid dividends on its common stock and has no plans to pay dividends going forward. Therefore, it used an expected dividend yield of zero.

The fair value of each stock option was estimated using the Black-Scholes option-pricing model with the following weighted-average assumptions:

	Year Ended December 31,	
	2023	2022
Risk-free interest rate	3.54%	2.15%
Expected volatility	99.18%	92.95%
Expected term (in years)	5.84	6.02
Expected dividend yield	—	—

The grant date fair value of restricted stock units is based upon the fair market value of the Company's common stock based on its closing price as reported on the date of grant on the Nasdaq Global Select Market.

The fair value of options granted during the years ended December 31, 2023 and 2022 were $9.8 million and $16.3 million, respectively. The fair value of restricted stock units granted during the year ended December 31, 2023 and 2022 was $0.5 million and $0.1 million, respectively.

Stock Option Activity

Changes in shares available for grant under the 2020 Plan during the year ended December 31, 2023 were as follows:

	Shares Available for Grant
Shares available for grant at December 31, 2022	4,253,854
2020 Plan reserve increase on January 1, 2023	1,893,869
Options and restricted stock units granted	(3,834,783)
Options and restricted stock units forfeited, cancelled, or expired	845,154
Shares available for grant at December 31, 2023	3,158,094

A summary of option activity for the year ended December 31, 2023 was as follows:

	Shares	Weighted-Average Exercise price per Share	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Balance at December 31, 2022	4,033,522	$ 11.75	8.40	$ 827
Granted	3,696,783	3.34		
Exercised	(128,534)	1.29		
Forfeited/expired	(780,902)	6.72		
Balance at December 31, 2023	6,820,869	$ 7.97	8.24	$ 387
Expected to vest	4,000,554	$ 6.41	8.72	$ —
Options exercisable	2,820,315	$ 10.18	7.56	$ 387

The total fair value of options granted that vested during the years ended December 31, 2023 and 2022 was $9.8 million and $6.8 million, respectively.

The aggregate intrinsic value in the table above is calculated as the difference between the exercise price of the underlying options and the estimated fair value of the Company's common stock underlying all options that were in-the-money at December 31, 2023. The aggregate intrinsic value of options exercised was $0.2 million and $3.0 million during the year ended December 31, 2023 and 2022, respectively, determined as of the date of option exercise. As of December 31, 2023, there was $16.0 million of total unrecognized compensation cost related to non-vested stock options. The Company expects to recognize this cost over a remaining weighted-average period of 1.99 years. The Company utilizes newly issued shares to satisfy option exercises.

Stock options outstanding and exercisable consisted of the following at December 31, 2023:

Exercise Price ($)	Shares Outstanding	Shares Exercisable
0.16 to 4.22	3,709,593	1,005,785
8.93 to 19.94	2,759,028	1,615,758
20.55 to 29.41	352,248	198,772
Total	6,820,869	2,820,315

Restricted Stock Unit Activity

A summary of RSU activity for the year ended December 31, 2023 is as follows:

	Share Equivalent	Weighted-Average Grant Date Fair Value
Non-vested at December 31, 2022	236,339	$ 15.16
Granted	138,000	3.28
Cancelled	(64,252)	7.63
Vested	—	—
Non-vested at December 31, 2023	310,087	$ 11.44

Employee Stock Purchase Plan

Under the ESPP, eligible employees can authorize payroll deductions for amounts up to the lesser of 15% of their qualifying wages or the statutory limit under the U.S. Internal Revenue Code. The ESPP provides for offering periods of six months in duration with one purchase period per offering period beginning May 18 and November 18 of each year. Participants in an offering period will be granted the right to purchase shares of our common stock at a price per share that is 85% of the lesser of the fair market value of the shares at (1) the first day of the offering period or (2) the end of each purchase period within the offering period. A maximum of 10,000 shares of common stock may be purchased by each participant at the purchase date during the offering period. The fair market value of the ESPP options granted is determined using the Black-Scholes model and is amortized on a straight-line basis. Stock-based compensation expense recognized during the years ended December 31, 2023 and 2022 associated with the ESPP was $0.1 million and $0.2 million, respectively. During the year ended December 31, 2023, the Company issued 166,682 shares of common stock to employees under the ESPP.

10. Income Taxes

Components of Income and Income Tax

The Company did not record a provision (benefit) for income taxes for the years ended December 31, 2023 and 2022. Net loss is attributable to the following tax jurisdictions (in thousands):

	Year Ended December 31,	
	2023	2022
United States	$(117,440)	$ (95,778)
Foreign	(232)	139
Net Loss	$(117,672)	$ (95,639)

The provision for income taxes differs from the amount expected by applying the federal statutory rates to the net loss before taxes as follows:

	Year Ended December 31,	
	2023	2022
Federal statutory income tax rate	21.0%	21.0%
State taxes	—	(0.4)
Stock-based compensation	(1.1)	(1.3)
Non-deductible expenses and others	(0.1)	(0.1)
Tax credits	4.2	2.2
Change in valuation allowance	(24.0)	(21.4)
Effective income tax rate	—%	—%

Deferred Tax Assets and Liabilities

The components of the Company's deferred tax assets and liabilities were as follows (in thousands):

	Year Ended December 31,	
	2023	2022
Deferred tax assets:		
Net operating loss carryforwards	$ 31,342	$ 24,092
Research and development tax credit carryforwards	9,327	4,218
Accrued liabilities	2,828	2,781
Stock-based compensation	2,564	1,676
Operating lease liability	333	404
Other	180	121
Capitalized research and development	25,182	10,729
Total deferred tax assets	71,756	44,021
Deferred tax liabilities:		
Right of use asset	(221)	(267)
Prepaid expenses and other	(75)	(475)
Investments	(214)	(294)
Total deferred tax liabilities	(510)	(1,036)
Less valuation allowance	(71,246)	(42,985)
Net deferred tax assets	$ —	$ —

Deferred income taxes reflect temporary differences between the carrying amounts of assets and liabilities for financial reporting and income tax purposes, and operating losses and tax credit carryforwards. The Company considers a number of factors concerning the realizability of its net deferred tax assets, including its history of operating losses, the nature of the deferred tax assets, and the timing, likelihood and amount, if any, of future taxable income during the periods in which those temporary differences and carryforwards become deductible, all of which require significant judgment. As of December 31, 2023, the Company has recorded a full valuation allowance on its net deferred tax assets as the Company has concluded that it is not more likely than not that such losses or credits will be utilized. The valuation allowance increased by $28.3 million and $20.4 million during 2023 and 2022, respectively.

At December 31, 2023, the Company has federal net operating loss and tax credit carryforwards of $9.5 million and $12.4 million, respectively, which expire over a period of 8 to 14 years. Net operating loss carryforwards of $138.7 million were generated after 2017, and therefore do not expire. As of December 31, 2023, the Company also had state net operating loss carryforwards of $3.3 million, which expire over a period of 18 to 20 years.

The Tax Cuts and Jobs Act contained a provision which requires the capitalization of Section 174 costs incurred in years beginning on or after January 1, 2022. Section 174 costs are expenditures which represent research and development costs that are incident to the development or improvement of a product, process, formula, invention, computer software, or technique. This provision changes the treatment of Section 174 costs such that the expenditures are no longer allowed as an immediate deduction but rather must be capitalized and amortized. We have included the impact of this provision, which results in a deferred tax asset of approximately $25.2 million as of December 31, 2023.

Uncertain Tax Positions

The Company files federal income tax returns. With few exceptions, the Company is no longer subject to income tax examinations by tax authorities for years prior to 2016. However, to the extent allowed by law, the tax authorities may have the right to examine prior periods where net operating losses or tax credits

were generated and carried forward and may make adjustments to the amount of the net operating loss or credit carryforward amount. The Company is not currently under examination in any jurisdiction.

A reconciliation of the beginning and ending amount of unrecognized tax benefits for uncertain tax positions were as follows (in thousands):

	Year Ended December 31,	
	2023	2022
Beginning balance	$ 1,406	$ 722
Additions for tax positions taken in prior years	182	-
Additions for tax positions taken in the current year	1,521	684
Ending balance	$ 3,109	$ 1,406

If the unrecognized tax benefits for uncertain tax positions as of December 31, 2023 are recognized, there will be no impact to the effective tax rate due to the valuation allowance. The Company recognizes interest and penalties related to unrecognized tax benefits within the income tax expense line in the accompanying consolidated financial statements. At December 31, 2023, there were no material interest and penalties on uncertain tax benefits. The Company does not anticipate any significant changes to its unrecognized tax benefits in the next 12 months.

11. Employee Benefit Plans

The Company has a 401(k) Plan for all of its employees. The 401(k) Plan allows eligible employees to defer, at the employee's discretion, up to 100% of their pretax compensation up to the Internal Revenue Service annual limit. The Company made matching contributions of $0.5 million and $0.4 million during the years ended December 31, 2023 and 2022, respectively.

12. Net Loss Per Share Attributable to Common Stockholders

The following outstanding shares of potentially dilutive securities were excluded from the computation of the diluted net loss per share attributable to common stockholders for the periods presented because their effect would have been anti-dilutive:

	Year Ended December 31,	
	2023	2022
Stock options to purchase common stock	6,820,869	4,033,522
Non-vested Restricted Stock Units	310,087	236,339
Employee stock purchase plan	3,495	5,148
Total	7,134,451	4,275,009

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 disclosure controls and procedures are designed to ensure that information we are required to disclose in 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 such information is accumulated and communicated to our management, including our chief executive officer and chief financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Our management, with the participation and supervision of our chief executive officer and our chief financial officer, have evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of the end of the period covered by this Annual Report on Form 10-K. Based on such evaluation, our chief executive officer and chief financial officer have concluded that as of such date, our disclosure controls and procedures were, in design and operation, effective at a reasonable assurance level.

Management's annual report on internal control over financial reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rule 13a-15(f) and Rule 15d-15(f). Our management conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2023 based on the criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. As a result of that assessment, our management has concluded that our internal control over financial reporting was effective as of December 31, 2023.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm on our internal control over financial reporting due to an exemption established by the JOBS Act for emerging growth companies.

Changes in Internal Control

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the period covered by this Annual Report on Form 10-K that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on the Effectiveness of Controls

The effectiveness of any system of internal control over financial reporting, including ours, is subject to inherent limitations, including the exercise of judgment in designing, implementing, operating, and evaluating the controls and procedures, and the inability to eliminate misconduct completely. Accordingly, in designing and evaluating the disclosure controls and procedures, management recognizes that any system of internal control over financial reporting, including ours, no matter how well designed and operated, can only provide reasonable, not absolute assurance of achieving the desired control objectives. Moreover, 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. We intend to continue to monitor and upgrade our internal controls as necessary or appropriate for our business but cannot assure you that such improvements will be sufficient to provide us with effective internal control over financial reporting.

Item 9B. Other Information.

During our last fiscal quarter, no director or officer, as defined in Rule 16a-1 (f) of the Exchange Act, adopted or terminated a “Rule 10b5-1 trading arrangement” or any “non-Rule 10b5-1 trading arrangement,” each as defined in Item 408 of Regulation S-K.

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

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

We maintain a Code of Business Conduct and Ethics that incorporates our code of business conduct and ethics applicable to all employees, including all directors and executive officers. Our Code of Business Conduct and Ethics is published on our Investors website at https://investors.athira.com/ under "Governance." We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding amendments to, or waiver from, a provision of our Code of Business Conduct and Ethics by posting such information on the website address and location specified above.

The remaining information required by this Item 10 of Form 10-K will be included in our definitive proxy statement to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2023 in connection with the solicitation of proxies for our 2024 Annual Meeting of Stockholders (2024 Proxy Statement) and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item 11 of Form 10-K will be included in our 2024 Proxy Statement and is incorporated herein by reference.

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

The information required by this Item 12 of Form 10-K, including with respect to our equity compensation plans, will be included in our 2024 Proxy Statement and is incorporated herein by reference.

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

The information required by this Item 13 of Form 10-K will be included in our 2024 Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this Item 14 of Form 10-K will be included in our 2024 Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) List the following documents filed as a part of the report:

(1) All financial statements;

See Index to Financial Statements in Part II, Item 8 of this Annual Report on Form 10-K.

(2) Financial Statement Schedules

All financial statement schedules have been omitted because the required information was not applicable or was not present in amounts sufficient to require submission of the schedules, or because the information required is included in the financial statements or the accompanying notes.

(3) Exhibits

The exhibits listed in the following Index to Exhibits are filed, furnished or incorporated by reference as part of this Annual Report on Form 10-K.

Index to Exhibits

Exhibit Number	Description	Incorporated by Reference			
		Form	File No.	Exhibit	Filing Date
3.1	Amended and Restated Certificate of Incorporation of the Company	10-Q	001-39503	3.1	November 12, 2020
3.2	Amended and Restated Bylaws of the Company	8-K	001-39503	3.1	November 18, 2022
4.1	Specimen Common Stock Certificate of the Registrant	S-1/A	333-248428	4.1	September 14, 2020
4.2	Investors' Rights Agreement, dated May 29, 2020, as amended, by and among the Registrant and the Investors and Key Holders party thereto	S-1/A	333-248428	4.2	September 9, 2020
4.3	Description of Capital Stock				
10.1**	Form of Director and Executive Officer Indemnification Agreement	S-1	333-248428	10.1	August 26, 2020
10.2**	2014 Equity Incentive Plan, as amended	S-1/A	333-248428	10.2	September 9, 2020
10.3**	2020 Equity Incentive Plan	S-1/A	333-248428	10.5	September 9, 2020
10.4**	Form of Stock Option Agreement under the 2020 Equity Incentive Plan	S-1/A	333-248428	10.6	September 9, 2020
10.5**	Form of Restricted Stock Award Agreement under the 2020 Equity Incentive Plan	S-1/A	333-248428	10.7	September 9, 2020
10.6**	Form of RSU Agreement under the 2020 Equity Incentive Plan	S-1/A	333-248428	10.8	September 9, 2020

10.7†	Amended and Restated Standard Exclusive Licensing Agreement with Sublicensing Terms, dated October 28, 2015, by and between the Registrant and Washington State University, and amendments thereto	S-1	333-248428	10.9	August 26, 2020
10.8**	2020 Employee Stock Purchase Plan, as amended and Form of Subscription Agreement Thereunder	10-K	001-39503	10.8	March 23, 2023
10.9	Lease agreement, dated July 20, 2020, by and between the Registrant and North Creek Parkway Center Investors, LP	S-1/A	333-248428	10.11	September 9, 2020
10.10**	Outside Director Compensation Policy, as amended	10-K	001-39503	10.10	March 23, 2023
10.11**	Executive Incentive Compensation Plan	S-1/A	333-248428	10.13	September 9, 2020
10.12**	Confirmatory Employment Letter between the Registrant and Mark Litton, Ph.D.	S-1/A	333-248428	10.15	September 9, 2020
10.13**	Confirmatory Employment Letter between the Registrant and Kevin Church, Ph.D.	S-1/A	333-248428	10.16	September 9, 2020
10.14**	Employment Offer Letter between the Registrant and Andrew Gengos	8-K	001-39503	10.1	May 22, 2023
10.15**	Amended and Restated Change in Control and Severance Agreement between the Registrant and Mark Litton, Ph.D.	8-K	001-39503	10.1	January 31, 2022
10.16**	Change in Control and Severance Agreement between the Registrant and Andrew Gengos	8-K	001-39503	10.2	May 22, 2023
10.17**	Employment Offer Letter between the Registrant and Hans Moebius, Ph.D.	S-1/A	333-248428	10.21	September 14, 2020
10.18**	First Amendment to Employment Agreement between the Registrant and Hans Moebius, Ph.D.	10-K	001-39503	10.27	March 28, 2022
10.19**	Change in Control and Severance Agreement between the Registrant and Hans Moebius, Ph.D.	S-1/A	333-248428	10.22	September 14, 2020
10.20**	Employment Offer Letter between the Registrant and Rachel Lenington	10-Q	001-39503	10.1	August 16, 2021
10.21**	Change in Control and Severance Agreement between the Registrant and Rachel Lenington	10-Q	001-39503	10.2	August 16, 2021
10.22**	Employment Offer Letter between the Registrant and Mark Worthington	10-Q	001-39503	10.3	August 16, 2021
10.23**	Change in Control and Severance Agreement between the Registrant and Mark Worthington	10-Q	001-39503	10.4	August 16, 2021
10.24	First Amendment to Lease by and between the Registrant and Nitrogen Propco 2020, L.P., as successor-in-interest to North Creek Parkway Center Investors, L.P., dated June 28, 2021	10-Q	001-39503	10.5	August 16, 2021

10.25**	Change in Control and Severance Agreement between the Registrant and Kevin Church	10-K	001-39503	10.28	March 28, 2022
10.26	Controlled Equity Offering Sales Agreement℠, dated January 6, 2023, among the Registrant, Cantor Fitzgerald & Co. and BTIG, LLC	8-K	001-39503	1.01	January 6, 2023
10.27**	Executive Transition Agreement between the Registrant and Hans Moebius dated January 5, 2024	8-K	001-39503	10.1	January 8, 2024
21.1	List of Subsidiaries of the Registrant	S-1/A	333-24828	21.1	September 9, 2020
23.1	Consent of Independent Registered Public Accounting Firm				
24.1	Power of Attorney (included in signature pages hereto)				
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				
31.2	Certification of Principal Accounting and Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				
32.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				
32.2*	Certification of Principal Accounting and Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				
97	Amended and Restated Compensation Recovery Policy				
101.INS	Inline XBRL Instance Document				
101.SCH	Inline XBRL Taxonomy Extension Schema Document				
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document				
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document				
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document				

101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted in Inline XBRL and included in Exhibit 101)

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* The certifications filed as Exhibits 32.1 and 32.2 are not deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 and are not to be incorporated by reference into any filing of the Company under the Securities Act of 1933 or the Securities Exchange Act of 1934, whether made before or after the date hereof irrespective of any general incorporation by reference language contained in any such filing, except to the extent that the registrant specifically incorporates it by reference.

** Indicates a management contract or compensatory plan.

† Pursuant to Item 601(b)(10) of Regulation S-K, certain portions of this exhibit have been omitted by means of marking such portions with asterisks because the Registrant has determined that the information is not material and would likely cause competitive harm to the Registrant if publicly disclosed.

Item 16. Form 10-K Summary

Not applicable.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

Athira Pharma, Inc.

Date: February 22, 2024

By: /s/ Mark Litton
Mark Litton
President and Chief Executive Officer (*Principal Executive Officer*)

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Mark Litton and Andrew Gengos, and each one of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in their name, place and stead, in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with Exhibits thereto and other documents in connection therewith with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or substitute or substitutes may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Annual Report on Form 10-K has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Mark Litton Mark Litton	President, Chief Executive Officer and Director (*Principal Executive Officer*)	February 22, 2024
/s/ Andrew Gengos Andrew Gengos	Chief Financial Officer and Chief Business Officer (*Principal Financial and Accounting Officer*)	February 22, 2024
/s/ Kelly A. Romano Kelly A. Romano	Chairwoman of the Board of Directors	February 22, 2024
/s/ Joseph Edelman Joseph Edelman	Director	February 22, 2024
/s/ John M. Fluke, Jr. John M. Fluke, Jr.	Director	February 22, 2024
/s/ James A. Johnson James A. Johnson	Director	February 22, 2024
/s/ Barbara Kosacz Barbara Kosacz	Director	February 22, 2024
/s/ Michael Panzara Michael Panzara	Director	February 22, 2024
/s/ Grant Pickering Grant Pickering	Director	February 22, 2024

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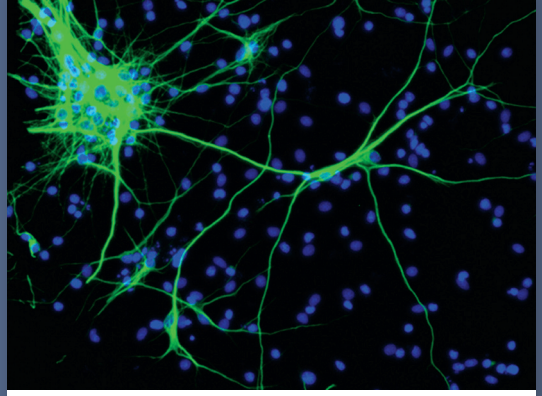

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