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: 000-29959

Cassava Sciences, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**91-1911336**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification Number)*

6801 N. Capital of Texas Highway, Building 1; Suite 300 , Austin , TX 78731
(512) 501-2444
(Address, including zip code, of registrant's principal executive offices and 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, $0.001 par value	SAVA	NASDAQ Capital Market
Warrants, exercisable for shares of Common Stock	SAVAW	NASDAQ Capital 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 Section 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. (Check one):

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 USC. 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 Act). Yes ☐ No ☑

The aggregate market value of the voting and non-voting common equity held by non-affiliates was approximately $ 967 million computed by reference to the last sales price of $24.52 as reported on the Nasdaq Capital Market, as of the last business day of the Registrant's most recently completed second fiscal quarter, June 30, 2023. The number of shares outstanding of the Registrant's common stock, par value $0.001 per share, on February 26, 2024 was 43,225,211 .

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's proxy statement for its 2024 Annual Meeting of Stockholders (the “Proxy Statement”), to be filed with the U.S. Securities and Exchange Commission, no later than 120 days after the Registrant’s fiscal year ended December 31, 2023, are incorporated by reference to Part III of this Annual Report on Form 10-K.

CASSAVA SCIENCES, INC.

FORM 10-K
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PART I

FORWARD-LOOKING STATEMENTS AND NOTICES

This Annual Report on Form 10-K, including the portions of our definitive Proxy Statement incorporated by reference herein, contains "forward-looking statements" within the meaning of the Private Securities Reform Act of 1995. We intend that such forward-looking statements be protected by the safe harbor created thereby. All statements other than statements of present or historical facts contained in this Annual Report, including statements anticipating or otherwise relating to our future results of operations and financial position, future results of ongoing clinical trials, business strategy, plans and objectives for future operations, and anticipated events or trends, are forward-looking statements. In some cases, forward-looking statements are identified by terms such as "aim," "anticipate," "believe," "could," "drive," "estimate," "expect," "forecast," "future," "goal," "intend," "may," "objective," "plan," "potential," "project," "seek," "should," "strategy," "will" and "would" or the negatives of these terms or other comparable terminology.

Examples of forward-looking statements include, but are not limited to, statements about:

- the expected safety profile or treatment benefits, if any, of simufilam for people with Alzheimer's disease in our on-going Phase 3 studies;
- our reliance on third-party contractors to conduct all of our clinical and non-clinical trials and to make drug supply on a large-scale for our Phase 3 clinical program, or their ability to do so on-time or on-budget;
- limitations around data interpretation from results of any of the three clinical phases of our 2-year safety study of simufilam in patients with Alzheimer's disease, as compared to clinical results from randomized controlled trials;
- the ability of clinical scales to assess cognition or health in our trials of Alzheimer's disease;
- any significant changes we may make, or anticipate making, to the design of any of our on-going Phase 3 studies of simufilam in patients with Alzheimer's disease;
- our ability to initiate, conduct or analyze additional clinical and non-clinical studies with our product candidates targeted at Alzheimer's disease and other neurodegenerative diseases;
- the impact of pre-clinical findings on our ability to develop our product candidates;
- the interpretation of results from our pre-clinical or early clinical studies, such as Phase 1 and Phase 2 studies;
- our plans to further develop SavaDx, our investigational blood-based diagnostic product candidate;
- our ability or willingness to expand therapeutic indications for simufilam outside of Alzheimer's disease;
- the safety, efficacy, or potential therapeutic benefits of our product candidates;
- our use of exploratory 'research use only' non-safety related biomarkers in our clinical studies;
- our ability to file for and obtain regulatory approval of our product candidates;
- our strategy and ability to establish an infrastructure to commercialize any product candidates, if approved;
- the potential future revenues of our product candidates, if approved and commercialized;
- the market acceptance of our product candidates, if approved and commercialized;
- the pricing and reimbursement of our product candidates, if approved and commercialized;
- the utility of protection, or the sufficiency, of our intellectual property;
- our potential competitors or competitive products for the treatment of Alzheimer's disease;
- our need to raise new capital from time to time to continue our operations or to expand our operations;
- our use of multiple third-party vendors and collaborators, including a Clinical Research Organization (CRO), to conduct clinical and non-clinical studies of our lead product candidate;
- expectations regarding trade secrets, technological innovations, licensing agreements and outsourcing of certain business functions;
- our expenses or incurred costs increasing by material amounts in excess of budgeted amounts due to unexpected cost overruns, inflation, imperfect forecasting, increased scope of activities or other causes;
- fluctuations in our financial or operating results;
- our operating losses, anticipated operating and capital expenditures and legal expenses;
- expectations regarding the issuance of shares of common stock, options or other equity to employees or directors pursuant to equity compensation awards, net of employment taxes;
- expectations regarding the issuance of shares of common stock to holders of outstanding warrants that are exercised for cash;
- the development and maintenance of our internal information systems and infrastructure;
- our ability to minimize the likelihood and impact of adverse cybersecurity incidents in our information systems and infrastructure;

- our need to hire additional personnel and our ability to attract and retain such personnel;
- existing or emerging regulations and regulatory developments in the United States and other jurisdictions in which we operate;
- our plans to expand the size and scope of our operations;
- the sufficiency of our cash resources to continue to fund our operations;
- potential future agreements with third parties in connection with the commercialization of our product candidates;
- the accuracy of our estimates regarding expenses, capital requirements, and needs for additional financing;
- assumptions and estimates used for our disclosures regarding stock-based compensation;
- the expense, timing and outcome of pending or future litigation or other legal proceedings and claims, including U.S. government inquiries; and
- litigation, claims or other uncertainties that may arise from allegations made against us or our collaborators.

The forward-looking statements in this Annual Report are based on our beliefs, assumptions and expectations of our future performance, events and developments, based on currently available information and plans. Forward-looking statements involve risks and uncertainties, and our actual results and the timing of events may differ materially from those discussed in the forward-looking statements. Such forward-looking statements include, but are not limited to, those described in “Item 1A. Risk Factors”, and investors should consider such risks before investing in our Company. Accordingly, you should not place undue reliance upon any forward-looking statements.

We cannot assure you that we will realize the results or developments we expect or anticipate or, even if substantially realized, that they will affect us or our operations in the way we expect.

The forward-looking statements included in this Annual Report on Form 10-K are made only as of the date hereof. We undertake no obligation to publicly update or revise any forward-looking statement as a result of new information, future events or otherwise, except as required by law.

In addition, statements that “we believe” or similar statements reflecting our beliefs, views, and opinions on the relevant subject are based upon information available to us as of the date of this Annual Report. While 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 an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and involve a number of assumptions and limitations, and you are cautioned not to unduly rely upon these statements.

Our research programs in neurodegeneration have historically benefited from scientific and financial support from the National Institutes of Health (NIH). The contents of this Annual Report are solely our responsibility and do not represent any views of NIH, the Department of Health and Human Services, or any other agency of the United States government, or any of our vendors, collaborators or unrelated third-parties.

All our pharmaceutical assets under development are investigational product candidates. These have not been approved for use in any medical indication by any regulatory authority in any jurisdiction and their safety, efficacy or other desirable attributes, if any, have not been established in any patient population. Consequently, none of our product candidates are approved or available for sale anywhere in the world.

Our clinical results from earlier-stage clinical trials may not be indicative of future results from later-stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements or any scientific data we present or publish.

All of our earlier-stage clinical trials, i.e., all studies that are not in Phase 3 stage of development, involve a relatively small number of patients and limited data. Information and results generated from our early-stage studies do not constitute, and should not be interpreted as, evidence of safety or efficacy for simufilam in Alzheimer’s disease. Rigorous evidence for drug safety and efficacy is required for regulatory approval and is derived from one or more large, randomized, placebo-controlled Phase 3 studies. The design and limited size of our early-stage studies may introduce clinical or statistical bias or may generate results that may not fully distinguish between drug effects, if any, placebo effects and random variation. Different methods of statistical analysis on clinical data from the same study may lead to objectively different numerical results. These and other statistical and clinical features of our early-stage clinical studies add complexity or limitations to the scope of data interpretation. In addition, ‘top-line results’ is a summary of the clinical data prior to the completion of a full and final audit or quality-control of the clinical database. We generally communicate top-line results so that our stakeholders have timely access to a summary of a study’s findings prior to us receiving the final dataset. Final data may change from initial top-line data.

Unless otherwise noted, all clinical data in this Annual Report is statistically non-significant at a standard probability level of $p<0.05$. In addition, from time to time, our scientific research may include the use of exploratory biomarkers, typically labelled 'research use only.' They are understood to mean non-safety-related, investigational diagnostic products that are in the research phase of development and have not been approved by any regulatory agency to be effective, sensitive, specific, accurate, predictive or linked to a specific diagnosis or indication. At present there is no sufficiently reliable evidence that any observed treatment effect on such biomarkers is reasonably likely to predict clinical benefit.

National Clinical Trial ("NCT") is an eight-digit identification number that http://www.ClinicalTrials.gov assigns a clinical study when it is registered with the National Library of Medicine, which is operated by the United States government.

Item 1. *Business*

Overview

Cassava Sciences, Inc. is a clinical-stage biotechnology company based in Austin, Texas. Our mission is to detect and treat neurodegenerative diseases, such as Alzheimer's disease. Our novel science is based on stabilizing – but not removing – a critical protein in the Alzheimer's brain. Our lead therapeutic drug candidate, simufilam, is under clinical evaluation for the proposed treatment of Alzheimer's disease dementia in Phase 3 clinical studies.

For over 12 years, we have combined state-of-the-art technology with new insights in neurobiology to develop novel solutions for Alzheimer's disease and other neurodegenerative diseases. Our strategy is to leverage our unique scientific/clinical platform to develop a first-in-class program for treating neurodegenerative diseases, such as Alzheimer's—a degenerative disease of the brain, where a patient's cognition and health functions decline over time as the disease progresses and the patient moves from mild to moderate to, eventually, severe Alzheimer's disease.

We currently have two biopharmaceutical assets under development:

- our lead therapeutic product candidate, called simufilam, is a novel oral treatment for Alzheimer's disease dementia; and
- our lead investigational diagnostic product candidate, called SavaDx, is a novel way to detect the presence of Alzheimer's disease from a small sample of blood.

Our scientific approach for the treatment of Alzheimer's disease seeks to simultaneously suppress *both* neurodegeneration and neuroinflammation. We believe our ability to potentially improve multiple vital functions in the brain represents a new, different and crucial approach to address Alzheimer's disease.

Our lead product candidate, simufilam, is a proprietary small molecule drug. Simufilam was discovered and designed in-house and was characterized by our academic collaborators during research activities that were conducted from approximately 2008 to date.

Simufilam targets an altered form of a protein called filamin A (FLNA) in the Alzheimer's brain. Published studies have demonstrated that the altered form of FLNA causes neuronal dysfunction, neuronal degeneration and neuroinflammation. Specifically, we believe simufilam disrupts amyloid binding to the α7 nicotinic acetylcholine receptor (α7nAChR), which underlies our drug's primary mechanism of action in Alzheimer's disease. More recent data also suggest a meaningful impact of simufilam on mTOR signaling. Because mTOR contributes to age-related cellular changes, simufilam's suppression of mTOR overactivation, concurrent with improved insulin sensitivity, may slow certain aging processes and attenuate this pathological feature, potentially benefiting brain function and memory in Alzheimer's disease and in aging.

We own exclusive, worldwide rights to our drug and diagnostic assets and related technologies, without royalty obligations to any third party. Our patent protection with respect to simufilam and use of simufilam for Alzheimer's disease and other neurodegenerative diseases currently runs through 2039 and includes nine issued U.S. patents. Corresponding foreign filings have been made for each of the U.S. filings.

We are currently conducting two randomized placebo-controlled Phase 3 clinical trials of oral simufilam in patients with Alzheimer's disease dementia. Both trials are fully enrolled. The trials have randomized a total of approximately 1,900 patients with mild to moderate Alzheimer's disease at baseline. All efficacy data from our Phase 3 program remain blinded. There are no interim analyses on efficacy outcomes.

Our first Phase 3 study, called RETHINK-ALZ, is designed to evaluate the safety and efficacy of simufilam 100 mg tablets versus placebo over 52 weeks (NCT04994483). Top-line results of our 52-week Phase 3 study are anticipated approximately year-end 2024.

Our second Phase 3 study, called REFOCUS-ALZ, is designed to evaluate the safety and efficacy of oral simufilam 100 mg and 50 mg tablets versus placebo over 76 weeks (NCT05026177). Top-line results of our 76-week Phase 3 study are anticipated approximately mid-year 2025.

Risk is Fundamental to the Drug Development Process

We are in the business of new drug discovery and development. Our research and development activities are long, complex, costly and involve a high degree of risk. Holders of our common stock should carefully read this Annual Report in its entirety, including "Item 1A. Risk Factors". *Because risk is fundamental to the process of drug discovery and development, you are cautioned to not invest in our publicly traded securities unless you are prepared to sustain a total loss of the money you have invested.*

About Alzheimer's Disease

Alzheimer's is a degenerative disease of the brain that affects cognition, function and behavior. Over time, a patient's cognition and health functions decline as the disease takes its toll. With disease progression, patients move from mild to moderate to, eventually, severe Alzheimer's disease. Cognitive decline becomes more pronounced, and presumably more difficult to treat, in advanced stages of the disease.

An estimated 6.7 million Americans age 65 and older were living with Alzheimer's dementia in 2023, according to the Alzheimer's Association. According to the same source, in 2011, the largest ever demographic generation of the American population — the baby-boom generation — started reaching age 65. By 2030, the segment of the U.S. population age 65 and older will have grown substantially, and the projected 74 million older Americans will make up over 20% of the total population. Because age is a well-known risk factor for Alzheimer's dementia, new cases of Alzheimer's dementia are expected to climb with the growth in the number of elderly Americans.

Our Scientific Approach is Different

Given the biopharmaceutical industry's challenging track record in Alzheimer's research and drug development, we believe there is an urgent need to consider innovative approaches to combat this disease.

For more than twelve years, we have developed a new and promising scientific approach for the treatment and diagnosis of neurodegenerative diseases, such as Alzheimer's disease. Importantly, we do not seek to clear amyloid out of the brain. Rather, our novel science is based on stabilizing – but not removing – a critical protein in the brain.

Our scientific approach is to treat neurodegeneration by targeting an altered form of a scaffold protein called FLNA. Through years of basic research, we and our academic collaborators identified FLNA as a structurally altered protein that enables neurodegeneration and neuroinflammation pathways in the Alzheimer's brain. We have shown that the altered form of FLNA is pervasive in the Alzheimer's brain and essentially undetectable in healthy control brains.

Using scientific insight and lab techniques, we believe we have elucidated this protein dysfunction. Through this work, we have produced experimental evidence that altered FLNA plays a critical role in Alzheimer's disease. We engineered a family of high-affinity, small molecules to target this structurally altered protein and restore its normal shape and function. This family of small molecules, including our lead therapeutic product candidate, simufilam, was designed in-house and characterized by our academic collaborators.

Our lead drug candidate, simufilam, is a small molecule (oral) drug with a novel mechanism of action. The target of simufilam is altered FLNA, the structurally altered protein in the brain that we seek to stabilize. Importantly, since simufilam has a unique mechanism of action, we believe its potential therapeutic effects may be additive or synergistic with existing drug treatments for Alzheimer's disease dementia.

Our science is based on stabilizing a critical protein in the brain

Proteins are essential for cell function because they participate in virtually every biological process. If protein function is impaired, the health consequences can be devastating. Technological advances in medicine and improvements in lifestyle are making our lives longer. But with age, genetic mutations and other factors conspire against healthy cells, resulting in altered proteins. Sometimes a cell can rid itself of altered proteins. However, when disease changes the shape and function of critical proteins, multiple downstream processes are impaired. There are many clinical conditions in which proteins become structurally altered and impair the normal function of cells, tissues and organs, leading to disease. Conversely, restoring altered proteins back to health –called proteostasis – is a well-accepted therapeutic strategy in clinical medicine.

For over 100 years, scientists have ascribed various neurodegenerative diseases to proteins that misfold and are rendered pathological. In Alzheimer's disease, certain proteins, such as amyloid and tau, lose their normal shape and function. Such misfolded proteins can break down or aggregate in clumps and form plaque or tangles in the brain. Destruction of neuronal synapses, accelerated death of neurons, and dysfunction of the brain support cells, are all widely believed to be direct consequences of misfolded proteins.

FLNA is a scaffolding protein found in high levels in the brain. A healthy scaffolding protein brings multiple proteins together, coordinating their interaction. However, an altered form of FLNA protein is found in the Alzheimer's brain. Our experimental evidence shows that altered FLNA protein contributes to Alzheimer's disease by disrupting the normal function of neurons, leading to neurodegeneration and brain inflammation. Our product candidate, simufilam, aims to counter the altered and toxic form of FLNA in the brain, thus restoring the normal function of this critical protein.

One drug, multiple effects

Simufilam binds to altered FLNA with very high (femtomolar) affinity. We believe simufilam improves brain health by reverting altered FLNA back to its native, healthy conformation, thus countering downstream toxic effects of altered FLNA. This drug effect restores the normal function of key brain receptors, including: the alpha-7 nicotinic acetylcholine receptor; the N-methyl-D-aspartate (NMDA) receptor; and the insulin receptor. These receptors have pivotal roles in brain cell survival, cognition and memory. In addition, recent data suggest a beneficial impact of simufilam on mTOR signaling.

We have generated and published experimental evidence of improved brain health by restoring altered FLNA with simufilam. In animal models, treatment with simufilam resulted in dramatic improvements in brain health, such as reduced amyloid and tau deposits, improved receptor signaling and improved learning and memory. In addition, simufilam has another beneficial treatment effect of significantly reducing inflammatory cytokines in the brain. In animal models of disease, treatment with simufilam greatly reduced levels of IL-6 and suppressed TNF-alpha and IL-1beta levels by 86% and 80%, respectively, illustrating a powerful anti-neuroinflammatory effect.

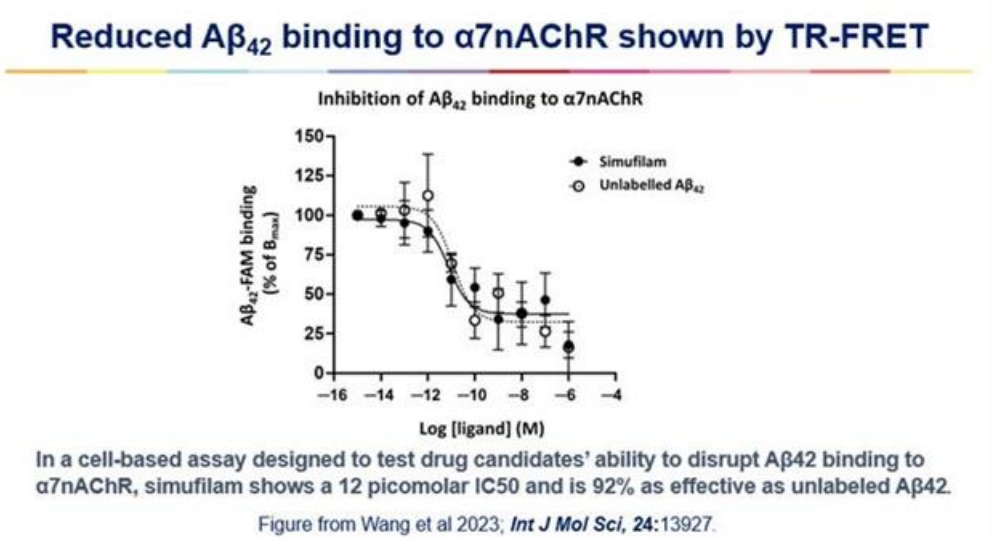
By restoring function to multiple receptors and exerting powerful anti-inflammatory effects, we believe our approach has potential to slow the progression of Alzheimer's disease in patients. We also believe our scientific approach may broaden the range of possible treatment approaches for this complex disease.

Our science is published in multiple peer-reviewed journals. In addition, our research has been supported by NIH under multiple research grant awards. Each grant was awarded following an in-depth, peer-reviewed evaluation of our approach for scientific and technical merit by a panel of outside experts in the field.

Publication Confirming Mechanism of Action of Simufilam

In September 2023, we announced the publication of new research that confirms the biological activity of simufilam. Researchers at the Cochin Institute (Paris, France) used a highly precise cell-based assay based on TR-FRET to show that simufilam interrupts amyloid binding to the α7 nicotinic acetylcholine receptor (α7nAChR). We believe disruption of amyloid binding to α7nAChR underlies simufilam's primary mechanism of action in Alzheimer's disease. The research paper was co-authored by Hoau-Yan Wang and Zhe Pei of the City University of New York, Erika Cecon, Julie Dam and Ralf Jockers of the Institut Cochin, and Lindsay Burns of Cassava Sciences, and appeared in a special issue of *International Journal of Molecular Sciences,* a peer-reviewed journal. See Figure 1.

Figure 1. Experiment conducted by Erika Cecon, Université Paris Cité, Institut Cochin in an assay she developed: Cecon et al 2019; *Br J Pharmacol;* 176:3475-3488. Data shown are means of pooled data from 4 separate experiments ±SEM.



Publication Showing Simufilam Suppresses Overactive mTOR

In June 2023, we announced the publication of new research that showed the effects of simufilam on the mechanistic Target of Rapamycin (mTOR). Scientific literature shows overactive mTOR plays a key role in aging, Alzheimer's disease and other conditions. When functioning normally, mTOR monitors cellular needs and is activated by insulin. The new published research shows mTOR is overactive in lymphocytes isolated from blood collected from Alzheimer's patients versus healthy controls. After oral administration of simufilam 100 mg twice daily to Alzheimer's patients for 28 days, lymphocytes showed normalized mTOR activity and restored sensitivity to insulin.

These data suggest a meaningful impact of simufilam on mTOR signaling. The suppression of overactive mTOR signaling and its improved responsiveness to insulin represents a mechanistic benefit of simufilam beyond the disruption of pathogenic signaling pathways of soluble amyloid. These improvements in mTOR signaling may also result from reversing an altered conformation of FLNA, allowing FLNA to dissociate from the insulin receptor when insulin binds and initiates signaling. Because mTOR contributes to age-related cellular changes, simufilam's suppression of mTOR overactivation, concurrent with improved insulin sensitivity, may slow certain aging processes and attenuate this pathological feature of Alzheimer's disease, potentially benefiting brain function and memory in Alzheimer's disease and in aging. This mTOR research paper was co-authored by Hoau-Yan Wang, Zhe Pei and Kuo-Chieh Lee of the City University of New York, Boris Nikolov, Tamara Doehner and John Puente, who are investigators in the clinical trial protocols, and Lindsay Burns of Cassava Sciences, and appeared in *Frontiers in Aging*, a peer-reviewed journal.

Simufilam Drug Development

IND submission to FDA, Drug Safety in Early Clinical Studies

For over a decade, we conducted basic research, in vitro studies and preclinical studies in support of a successful Investigational New Drug (IND) submission to FDA for simufilam, including requisite studies around safety pharmacology, toxicology, genotoxicity and bioanalytical methods. In 2017 we filed an IND with FDA for simufilam.

Following FDA acceptance of our IND in 2017, we investigated the safety, dosing and pharmacokinetic profile of simufilam in healthy human volunteers. The design of our first-in-human Phase 1 study was based on regulatory feedback, clinical and scientific rationale and observations from previously conducted preclinical and in vitro studies. In a Phase 1 study, simufilam was evaluated in 24 healthy human volunteers (18 simufilam, 6 placebo) in a single site in the U.S. for safety, tolerability and pharmacokinetics. Study subjects were administered a single oral dose of 50, 100 or 200 mg of simufilam or placebo. Drug appeared safe and well-tolerated. Importantly, simufilam showed no treatment-related adverse effects and no dose-limiting safety findings. Pharmacokinetic measurements demonstrated that simufilam, a small molecule, was rapidly absorbed. Dose-proportionality was observed over the full dose range of 50 to 200 mg.

Phase 2 Clinical Studies

In 2019, we completed a first-in-patient, clinical-proof-of-concept, open-label Phase 2a study of simufilam in the U.S., with substantial support from the National Institute on Aging (NIA), a division of the NIH. In this small study of thirteen patients with mild-to-moderate Alzheimer's disease, treatment with simufilam for 28 days significantly improved certain exploratory biomarkers of Alzheimer's pathology, neurodegeneration and neuroinflammation ($p<0.001$). Drug was safe and well-tolerated. Biomarkers effects were seen in all patients in both cerebrospinal fluid (CSF) and plasma.

In September 2020, we reported final results of a Phase 2b study with simufilam in Alzheimer's disease. In this clinical study funded by the NIH, Alzheimer's patients treated with 50 mg or 100 mg of simufilam twice-daily for 28 days showed statistically significant ($p<0.05$) improvements in CSF biomarkers of disease pathology, neurodegeneration and neuroinflammation, versus Alzheimer's patients who took placebo. Simufilam treatment also significantly reduced levels of plasma P-tau181 in sample testing conducted by Quanterix Corporation, a third-party vendor. In addition, Alzheimer's patients treated with simufilam showed improvements in validated tests of episodic memory and spatial working memory, versus patients on placebo. Cognitive improvements correlated most strongly with decreases in levels of P-tau181. Drug was safe and well-tolerated.

Given the absence of observable dose-limiting effects in our Phase 1 or Phase 2 studies, and in light of the strong scientific rationale and multiple peer-reviewed publications and research grant awards, we determined that simufilam demonstrated favorable proof-of-principle for further evaluation as an investigational drug for the treatment of Alzheimer's disease.

24-Month Clinical Safety Study

Much of the strategic value of our 24 month clinical safety study is to support simufilam's long-term safety profile in patients. We believe a well-designed, long-term, safety study is a prudent risk-management undertaking. Clinical results may serve to help inform and manage the inherent risks and uncertainties of drug development while we undertake a large, expensive Phase 3 clinical testing program.

In March 2020, we initiated a clinical safety study of simufilam, our lead drug candidate, in patients with Alzheimer's disease (NCT04388254). This study was funded in part by a research grant award from NIH. This study was designed to evaluate the long-term clinical safety and tolerability of simufilam in patients with Alzheimer's disease over 24 months. The study included a pre-specified exploratory efficacy endpoint of mean change in ADAS-Cog11 scores, a cognitive scale widely used in Alzheimer's clinical research. This study enrolled over 200 patients with mild-to-moderate Alzheimer's disease ((Mini-Mental State Examination (MMSE) 16-26) who were recruited from 16 U.S. clinical sites. Alzheimer's is a progressive disease, with severity of disease typically assessed by MMSE score. In this study, mild patients are MMSE 21-26, and moderate patients are MMSE 16-20.

We conducted the 24-month safety study in three continuous phases:

- a 12-month, open-label treatment phase, followed by
- a 6-month randomized, placebo-controlled withdrawal phase (previously referred to as the "Cognition Maintenance Study" or CMS), followed by
- 6 additional months of open-label treatment.

Study participants received simufilam oral tablets 100 mg twice-daily in the open-label treatment phases, and simufilam or matching placebo during the randomized withdrawal phase. In an open-label study design, both the health providers and the patients are aware of the drug treatment being given.

All study participants who completed 12 months of open-label simufilam treatment were eligible to participate in the 6-month randomized, placebo-controlled withdrawal phase. Likewise, all study participants who completed the randomized, placebo-controlled withdrawal phase were eligible for 6 additional months of open-label treatment.

Study Results for the 12-month, Open-label Treatment Phase

In January 2023, we announced positive top-line results for the 12-month, open-label treatment phase of the safety study. The pre-specified, exploratory efficacy endpoint was change in baseline on ADAS-Cog11, a cognitive scale widely used in Alzheimer's clinical research. Other exploratory endpoints included the Mini-Mental State Examination (MMSE) to assess disease stage by cognitive impairment; the Neuropsychiatric Inventory (NPI) to assess dementia related behavior; and the Geriatric Depression Scale (GDS). Endpoints were measured at baseline (study entry) and month 12.

Top-line Results – **mean scores, baseline to month 12** (*lower is better, except for MMSE)***:***

- ADAS-Cog11 scores changed from 19.1 (±9.2) to 19.6 (±13.3)
- MMSE scores changed from 21.5 (±3.6) to 20.2 (±6.4)
- NPI10 scores changed from 3.2 (±4.6) to 2.9 (±4.6)
- GDS scores changed from 1.8 (±1.8) to 1.4 (±1.9)

Response Analysis – ***baseline to month 12***

- ADAS-Cog scores improved in 47% of patients; this group had a mean change of -4.7 (±3.8) points (lower is better).
- In an additional 23% of patients, ADAS-Cog declined less than 5 points; this group had a mean change of 2.5 (±1.4) points.
- Patients with an NPI10 score of zero increased from 42% to 54%, indicating reduced dementia-related neuropsychiatric symptoms after 1 year on simufilam.

The Full Analysis Set (FAS) population (N=216) was used for the statistical analysis of efficacy endpoints. Mild and moderate sub-groups showed notable differences on changes in ADAS-Cog mean scores, baseline to month 12 (lower is better):

- In the *mild* sub-group (MMSE 21-26), mean ADAS-Cog scores improved, from 15.0 (±6.3) to 12.6 (±7.8)
- In the *moderate* sub-group (MMSE 16-20), mean ADAS-Cog scores worsened, from 25.7 (±9.2) to 30.1 (±13.1)

We believe the improvement in ADAS-Cog over 1 year in mild patients taking simufilam is well outside the expected range of historic placebo decline rates from numerous other studies. Figure 2: historical declines on ADAS-Cog in early disease (MCI + mild) and mild disease.

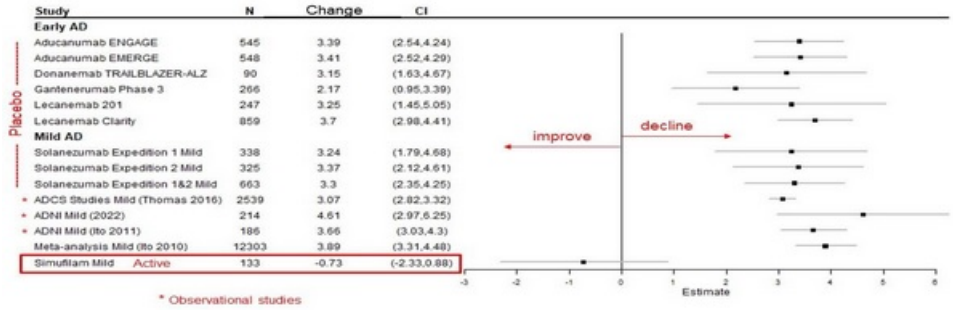


Figure 1: *Statistical model of simufilam versus historical 1-year placebo declines on ADAS-Cog in early disease and mild disease. Forest plot by Pentara Corporation, independent biostatisticians. Data was sourced from non-randomized studies (i.e., ADNI) and randomized, controlled trials conducted by other sponsors in patients with early (i.e., MCI + mild) and mild Alzheimer's disease.*

Safety Data - Simufilam 100 mg tablets twice daily appeared safe and well tolerated in this treatment phase of the open-label study. There were no drug-related serious adverse events. Three treatment-emergent adverse events (TEAEs) occurred in 7% or more of study patients: COVID-19 (12%), urinary tract infection (10%) and headache (9%). Reported TEAEs are based on all study patients who received at least one dose of drug.

Biomarker Data - In this open-label treatment phase of the study, exploratory biomarkers were analyzed from CSF collected from 25 patients who agreed to undergo a lumbar puncture at baseline and again after 6 months of treatment. CSF samples were analyzed blind to timepoint by our academic collaborator at City University of New York.

P-values shown below are baseline vs. 6-month levels by paired t-test:

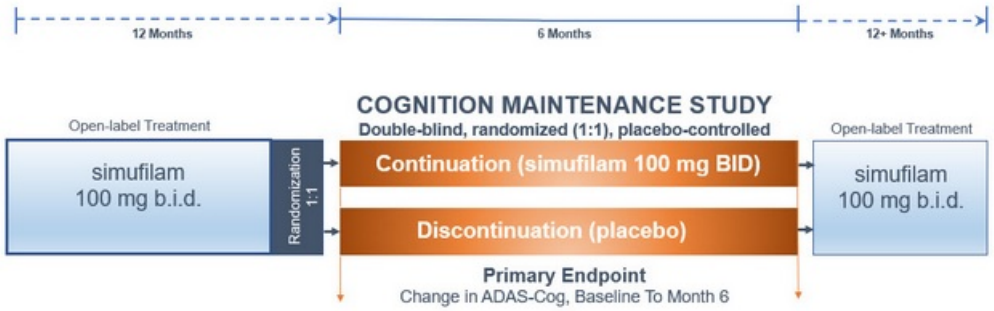
- CSF biomarkers of disease pathology, t-tau and p-tau181, decreased 38% and 18%, respectively (both p<0.00001)
- CSF biomarkers of neurodegeneration, neurogranin and neurofilament light chain (NfL), decreased 72% and 55%, respectively (both p<0.00001)
- CSF biomarkers of neuroinflammation, sTREM2 and YKL-40, decreased 65% and 44% (both p<0.00001)

Study Results for the 6-month, Randomized Withdrawal Study Phase ("Cognition Maintenance Study")

In May 2021, we initiated the randomized, withdrawal phase of the 24 month safety study, which has been previously referred to as the 'Cognition Maintenance Study' or CMS. The CMS has a randomized, withdrawal study design. The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) explains that in a randomized withdrawal study, "*subjects receiving a test treatment for a specified time are randomly assigned to continued treatment with the test treatment or to placebo (i.e., withdrawal of active therapy) … Any difference that emerges between the group receiving continued treatment and the group randomized to placebo would demonstrate the effect of the active treatment*."

The design of randomized, withdrawal phase of the study was intended to evaluate simufilam's effects on cognition and health outcomes in Alzheimer's patients who continue with drug treatment versus patients who discontinue drug treatment. This was a double-blind, randomized, placebo-controlled study of simufilam in patients with mild-to-moderate Alzheimer's disease. Study patients were randomized (1:1) to simufilam or placebo for six months. To enroll in the CMS, patients must have previously completed 12 months or more of open-label treatment with simufilam. Final enrollment was 157 patients. See Figure 3.

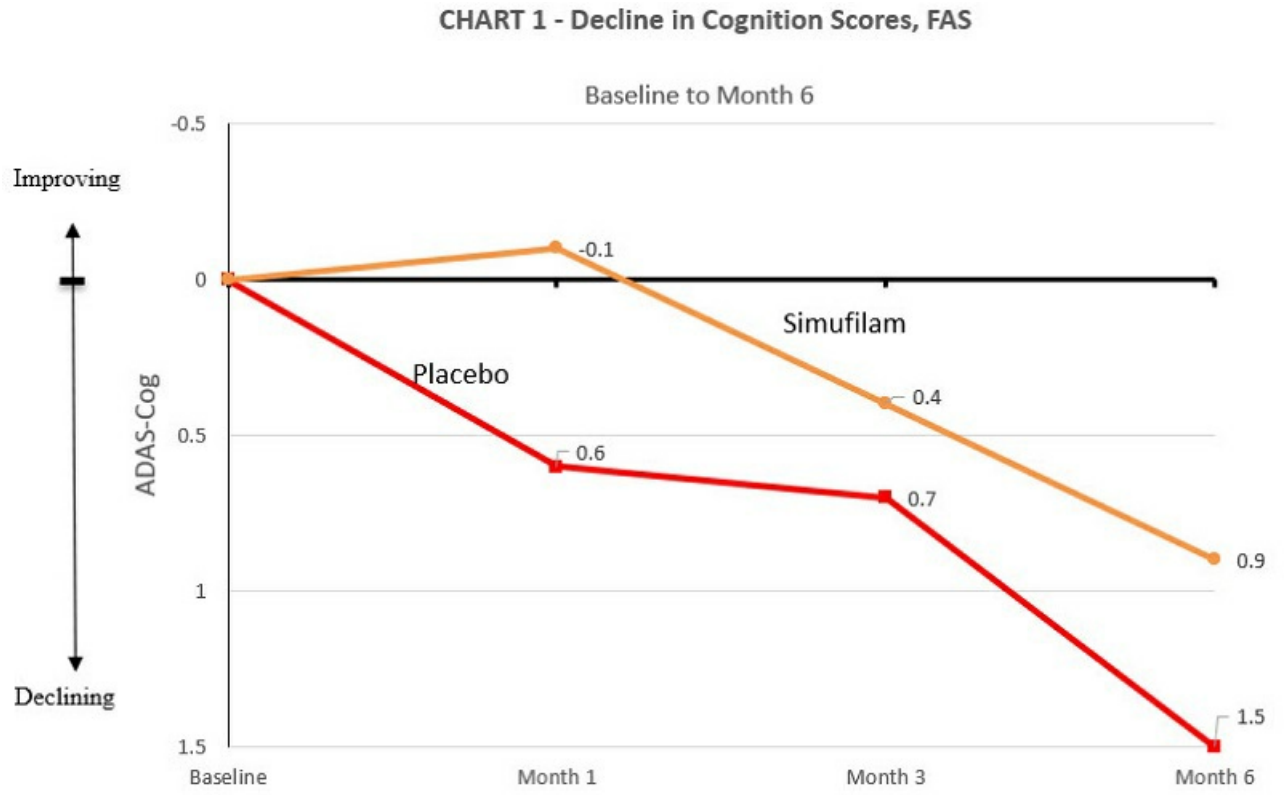
Figure 3. Design of the Randomized Withdrawal Phase (CMS)



Top-line Results - Simufilam treatment for 6 months slowed cognitive decline by 38% compared to placebo in mild-to-moderate Alzheimer's disease (MMSE 16-26) patients. The placebo arm declined 1.5 points on ADAS-Cog, and this arm declined at all measured timepoints. The simufilam arm declined 0.9 points on ADAS-Cog, a 38% difference in favor of drug at month 6 (95% CI, – 2.1 to 1.0; not significant for sample sizes). See Table 1 and Chart 1.

Table 1: Results of Randomized Withdrawal Study – cognitive change, full analysis set (FAS)

Full Analysis Set	**Simufilam 100 mg (N = 78)**	**Placebo (N = 77)**	**Numerical Difference**	**Percent Difference**
6-month Change in ADAS-Cog	0.9 point Decline	1.5 point Decline	–0.6	38% in favor of drug

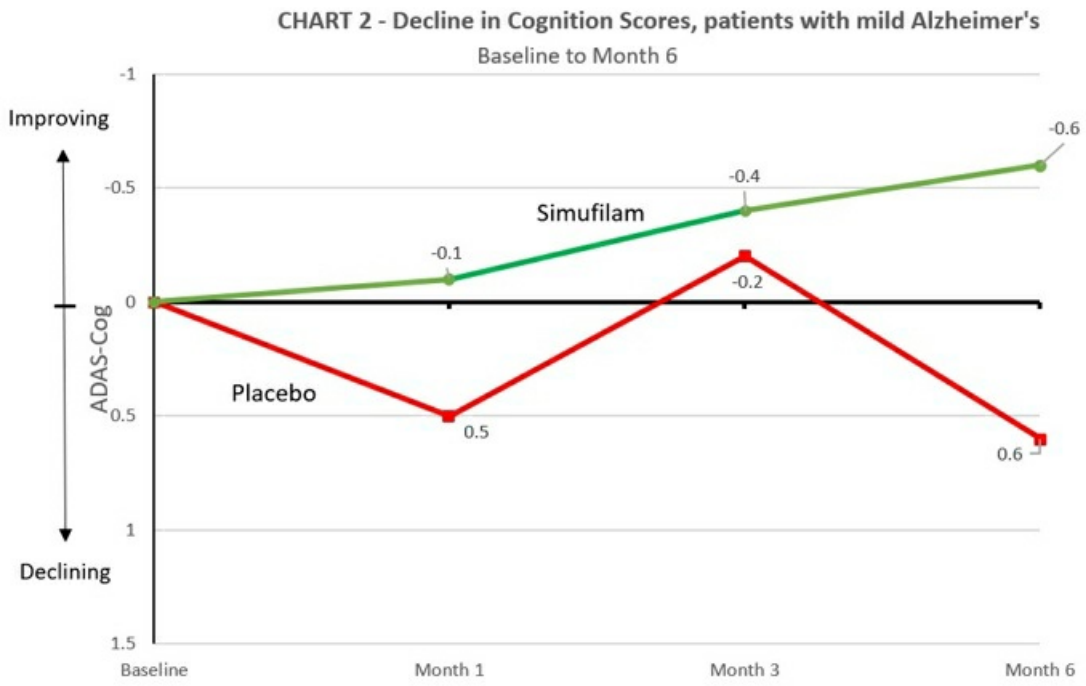


Upon randomization into the randomized, withdrawal phase, mean baseline MMSE scores were 18.6 and 18.1 for the simufilam and placebo arms, respectively. Mean baseline ADAS-Cog scores were 19.3 and 21.9 for the simufilam and placebo arms, respectively.

Simufilam Drug Effects Favored Patients with Mild Alzheimer's Disease – Simufilam treatment for 6 months slowed cognitive decline > 200% compared to placebo in mild Alzheimer's disease. Patients with mild Alzheimer's (MMSE 21-26) on placebo declined 0.6 points on ADAS-Cog over 6 months as a group. Patients with mild Alzheimer's on simufilam improved 0.6 points over 6 months as a group, a 205% difference in favor of drug (95% CI, – 2.6 to 0.4; not significant for sample sizes). See Table 2 and Chart 2.

Table 2: Results of Randomized Withdrawal Study – cognitive change, mild patients

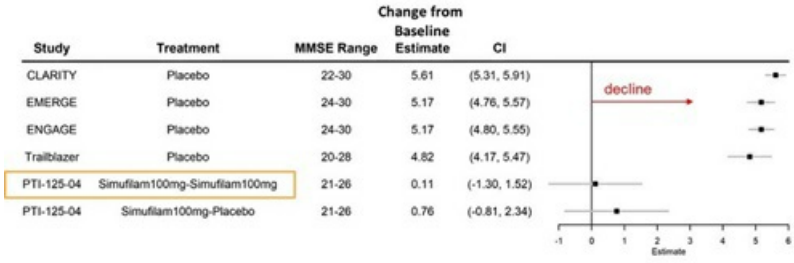
Mild Patients	**Simufilam 100 mg (N= 40)**	**Placebo (N= 36)**	**Numerical Difference**	**Percent Difference**
6-month Changes in ADAS-Cog	0.6 point Improvement	0.6 point Decline	–1.1	205% in favor of drug



Upon randomization into the randomized, withdrawal phase of the study, mean baseline MMSE scores for mild patients were MMSE 24.0 and MMSE 24.1 for the simufilam and placebo arms, respectively. Mean baseline ADAS-Cog scores for mild patients were 11.0 and 11.2 for the simufilam and placebo arms, respectively.

Simufilam for 18 months stabilized cognition in mild Alzheimer's disease – After taking open-label simufilam for 12 months, 76 patients with mild Alzheimer's disease (MMSE 21-26) enrolled in the randomized, withdrawal phase and were randomized to receive either simufilam (N=40) or placebo (N=36) for 6 months. Mild patients randomized to simufilam in the CMS showed no material decline in ADAS-Cog scores over 18 months as a group, indicating stable cognition. Mild patients randomized to placebo in the randomized, withdrawal phase (and therefore withdrawn from simufilam treatment for 6 months) declined by 0.8 points in ADAS-Cog over 18 months as a group. See Figure 4.

Figure 4. Historical declines on ADAS-Cog over 18 months in Alzheimer's disease (MMSE 20-30), placebo arms vs simufilam treatment.



Study	Treatment	MMSE Range	Change from Baseline Estimate	CI
CLARITY	Placebo	22-30	5.61	(5.31, 5.91)
EMERGE	Placebo	24-30	5.17	(4.76, 5.57)
ENGAGE	Placebo	24-30	5.17	(4.80, 5.55)
Trailblazer	Placebo	20-28	4.82	(4.17, 5.47)
PTI-125-04	Simufilam100mg-Simufilam100mg	21-26	0.11	(-1.30, 1.52)
PTI-125-04	Simufilam100mg-Placebo	21-26	0.76	(-0.81, 2.34)

Figure 4: Forest plot by Pentara Corporation, independent biostatisticians. Data was sourced from the placebo groups in randomized, controlled trials of monoclonal antibodies conducted by other sponsors in Alzheimer's disease (MMSE 20-30). Results shown for CLARITY P3 trial of lecanemab; EMERGE and ENGAGE P3 studies of aducanumab; and TRAILBLAZER P3 trial of donanemab; in this figure, the randomized, withdrawal phase is referred to as the 'PTI-125-04' study; 'Simufilam100mg-Simufilam100mg' refers to patients who received simufilam in both the open-label phase and the randomized, withdrawal phase; 'Simufilam100mg-Placebo' refers to patients who received simufilam in the open-label phase and placebo in the randomized, withdrawal phase.

Safety Data – Simufilam 100 mg tablets twice daily appeared safe and well tolerated in the 6-month the randomized, withdrawal phase of the 24 month safety study.

Discussion –Patients who completed 12 months of open-label simufilam treatment were invited to participate in the randomized, withdrawal phase. It is not known how long a washout period may be needed to remove lingering drug effects, if any, from prior treatment with open-label simufilam for 12 months. In this small randomized, withdrawal study phase in patients with mild-to-moderate Alzheimer's disease, simufilam slowed cognitive decline by 38% on ADAS-Cog over six months (not statistically significant), with good drug safety. Effects were pronounced in mild patients. Mean baseline MMSE and ADAS-Cog scores were approximately balanced given the small size of each arm.

Study Results for the 24-Month Safety Study

In February 2024, we reported top-line results of the 24-month clinical safety study. Average changes in ADAS-Cog scores, baseline to month 24, indicate the following:

- Patients with mild Alzheimer's disease who received simufilam treatment continuously for two years (n=47) had no decline in ADAS-Cog scores (± 1.51 SE) as a group.
- Patients with mild Alzheimer's who received simufilam treatment non-continuously (n=40) declined 1 point on ADAS-Cog (± 1.65 SE) as a group. Non-continuous treatment consisted of one year on open-label drug, six months on placebo and six months back on open-label drug.
- In patients with mild Alzheimer's, the largest separation between the continuous and non-continuous treatment groups occurred at the end of the 6-month randomized, placebo-controlled withdrawal phase.
- Patients with moderate Alzheimer's who received simufilam treatment continuously for two years (n=32) declined 11.05 points on ADAS-Cog (± 1.91 SE) as a group.

Patients with mild Alzheimer's disease (n=87) started the 24 months study with MMSE 21-26, with ten exceptions. Patients with moderate Alzheimer's started the 24 months study with MMSE 16-20, with one patient who entered with MMSE 15.

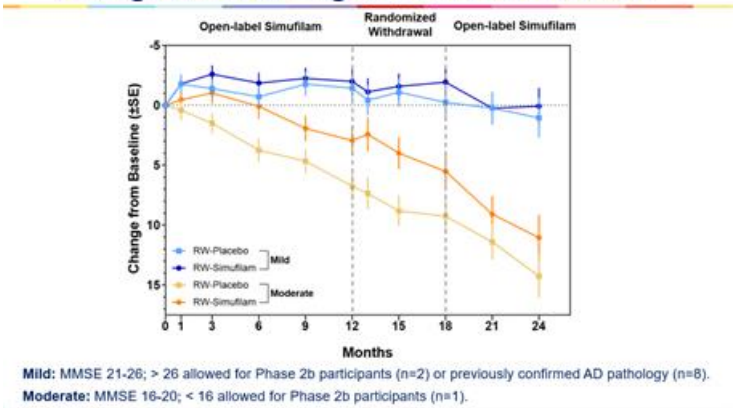
The pre-specified cognition endpoints were analyzed on the Full Analysis Set (FAS) by an independent consulting firm that specializes in complex statistical analysis of clinical trial results. The FAS population consists of all study participants who received at least one dose of treatment and have both baseline and at least one post-baseline assessment. (Because FAS data is specific to each phase of a study, the FAS for the 24-month study may differ from the FAS for other study phases).

Mild patients who received simufilam for 24 continuous months (n=47) showed an average change of 0.07 points on ADAS-Cog11 (± 1.51 SE), baseline to month 24, as a group.

Mild Alzheimer's patients who received 12 months of open-label simufilam, followed by placebo in the 6-month randomized, placebo-controlled withdrawal phase, followed by an additional 6 months of open-label simufilam (n=40), declined by an average of 1.04 points on ADAS-Cog11 (± 1.65 SE), baseline to month 24, as a group. See Figure 4B.

Figure 4

Change in ADAS-Cog11 in Mild vs. Moderate



Mild: MMSE 21-26; > 26 allowed for Phase 2b participants (n=2) or previously confirmed AD pathology (n=8).
Moderate: MMSE 16-20; < 16 allowed for Phase 2b participants (n=1).

Mean ADAS-Cog scores at baseline were approximately balanced in the group of mild Alzheimer's patients who received drug continuously versus non-continuously (15.2 and 14.6, respectively).

Safety Data – Oral simufilam 100 mg tablets twice daily appeared safe and well tolerated in this study. There were no drug-related serious adverse events. The most common treatment-emergent adverse events (TEAEs) were Covid-19 and urinary tract infection.

End-of-Phase 2 (EOP2) Meeting with FDA

In January 2021, we held an End-of-phase 2 (EOP2) meeting for simufilam with the U.S. Food and Drug Administration (FDA). The purpose of this EOP2 meeting was to gain general agreement around key elements of a pivotal Phase 3 program to treat Alzheimer's disease dementia. FDA attendees included Robert Temple, MD, Deputy Center Director for Clinical Science and Senior Advisor in the Office of New Drugs; Billy Dunn, MD, Director, Office of Neuroscience; Eric Bastings, MD, Director, Division of Neurology, and others.

In February 2021, we announced the successful completion of our EOP2 meeting. Official meeting minutes confirm that we and FDA are aligned on key elements of a Phase 3 clinical program for simufilam. FDA agreed that the completed Phase 2 program, together with an ongoing and well-defined Phase 3 clinical program, are sufficient to potentially show evidence of clinical efficacy for simufilam in Alzheimer's disease. There was also agreement that the use of separate clinical scales to assess cognition (ADAS-cog[1]) and function (ADCS-ADL[2]) are appropriate endpoints of efficacy. iADRS [3] is an efficacy endpoint that combines scores for ADAS-cog and ADCS-ADL, and thereby provide a single composite measure of cognition and health function. Other endpoints include the NPI[4].

[1] ADAS-Cog = The Alzheimer's Disease Assessment Scale – Cognitive Subscale, a measure of cognition

[2] ADCS-ADL = Alzheimer's Disease Cooperative Study – Activities of Daily Living, a measure of health function

[3] iADRS = integrated Alzheimer's Disease Rating Scale, a composite measure of cognition and health function

[4] NPI = Neuropsychiatric Inventory, a clinical tool that assesses the presence and severity of dementia-related behavior

Special Protocol Assessments

In August 2021, we announced we had reached agreement with FDA under a Special Protocol Assessment (SPA) for both Phase 3 studies. These SPA agreements document that FDA has reviewed and agreed upon the key design features of our Phase 3 study protocols of simufilam for the treatment of patients with Alzheimer's disease.

An SPA agreement indicates concurrence by the FDA with the adequacy and acceptability of specific critical elements of overall protocol design (e.g., entry criteria, dose selection, endpoints, etc.). These elements are critical to ensure that our planned Phase 3 studies of simufilam in Alzheimer's disease can
potentially be considered adequate and well-controlled studies in support of a future regulatory submission and marketing application.

The first clinical study protocol under the SPA is titled " *A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, 52-Week Study Evaluating the Safety and Efficacy of One Dose of Simufilam in Subjects with Mild-to-Moderate Alzheimer's Disease*."

The second clinical study protocol under the SPA is titled " *A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, 76-Week Study Evaluating the Safety and Efficacy of Two Doses of Simufilam in Subjects with Mild-to-Moderate Alzheimer's Disease*."

Phase 3 Clinical Program Overview

Our Phase 3 program consists of two large, double-blind, randomized, placebo-controlled studies of simufilam in patients with mild-to-moderate Alzheimer's disease dementia. Both studies are designed to measure changes in cognition and function during their treatment period. Some highlights of this clinical program are summarized in Figure 5.

Premier Research International is the CRO supporting the conduct of our Phase 3 clinical program. Our Phase 3 clinical sites are currently located in the United States, Canada, Puerto Rico, Australia, and South Korea.

Figure 5. Summary of Our Phase 3 Clinical Program

RETHINK-ALZ and REFOCUS-ALZ

In Fall 2021, we announced initiation of two Phase 3 studies of simufilam in mild-to-moderate Alzheimer's disease dementia. In November 2023, we had announced the completion of patient enrollment in both Phase 3 studies. A total of approximately 1,900 patients are randomized into these studies. Approximately 70% of randomized patients entered our Phase 3 studies with mild Alzheimer's disease (MMSE 20 to 27).

The first Phase 3 study, called RETHINK-ALZ, is designed to evaluate the safety and efficacy of oral simufilam 100 mg over 52 weeks (NCT04994483). Details of the RETHINK-ALZ Phase 3 study include:

- Approximately 800 patients are randomized into this study.
- Patients are randomized (1:1) to simufilam 100 mg tablets or matching placebo twice daily.
- Patients are treated for 52 weeks.
- Efficacy endpoints are ADAS-Cog12, a cognitive scale, and ADCS-ADL, a functional scale and iADRS, (which is a combination of scores from ADAS-Cog & ADCS-ADL). All three clinical measurements are standard psychometric assessment tools in trials of Alzheimer's disease.
- Other endpoints include plasma biomarkers of disease and NPI, a clinical tool that assesses the presence and severity of dementia-related behavior.
- No interim analyses on efficacy are planned.

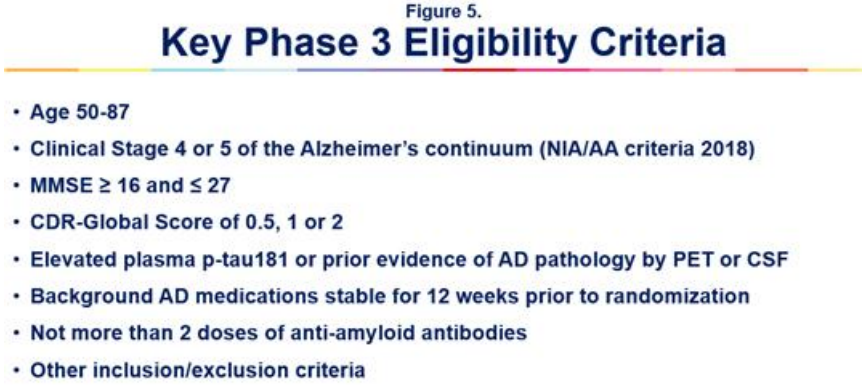
Our second Phase 3 study, called REFOCUS-ALZ, is designed to evaluate the safety and efficacy of oral simufilam 100 mg and 50 mg over 76 weeks (NCT05026177). Details of the REFOCUS-ALZ Phase 3 study include:

- Approximately 1,100 patients are randomized into this study.
- Patients are randomized (1:1:1) to simufilam 100 mg tablets, 50 mg tablets, or matching placebo twice daily.
- Patients are treated for 76 weeks.
- Efficacy endpoints are ADAS-Cog12, a cognitive scale, and ADCS-ADL, a functional scale and iADRS, (which is a combination of scores from ADAS-Cog & ADCS-ADL). All three clinical measurements are standard psychometric assessment tools in trials of Alzheimer's disease.
- Other endpoints include biomarkers of disease, MRI imaging and NPI, a clinical tool that assesses the presence and severity of dementia-related behavior.
- No interim analyses on efficacy are planned.

Phase 3 Entry Criteria

In our Phase 3 clinical studies, eligibility criteria are the requirements that patients must meet to be included in a study. These requirements help make sure that study participants are substantially and closely matched as a group in terms of specific factors such as age, disease or stage of disease, general health, and other key factors. Eligibility criteria can consist of inclusion criteria, which are required for a person to participate in the study, or exclusion criteria, which prevent a person from participating. See Figure 5A.

Figure 5.



Use of Plasma Phosphorylated-tau181 (p-tau181)

We believe plasma p-tau181 is a biomarker qualifier of Alzheimer's neuropathology. RETHINK-ALZ and REFOCUS-ALZ Phase 3 studies use a 'research use only', non-safety related exploratory p-tau181 plasma assay to qualify mild-to-moderate Alzheimer's patients. The plasma assay we use does not rely on age, APOE-gene status or complex algorithms to provide a result. P-Tau181 testing was performed by an independent commercial laboratory.

Data and Safety Monitoring Board (DSMB)

In September 2023, we announced that a routine, scheduled meeting of a DSMB recommended that both of our Phase 3 studies continue as planned, without modification. This DSMB only reviewed patient safety. It did not assess drug efficacy.

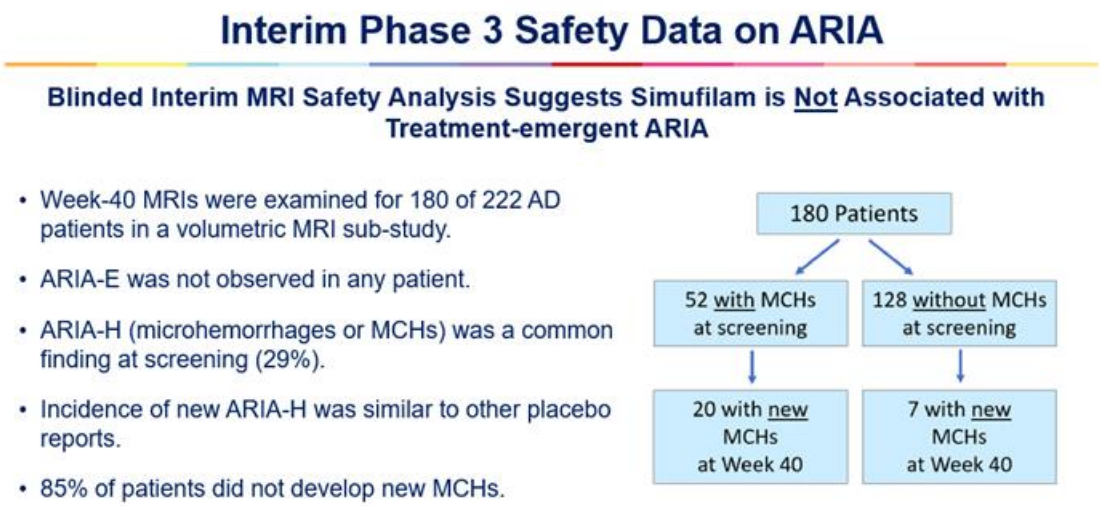
Interim MRI Safety Data

In October 2023, we announced a potentially significant safety finding based on interim magnetic resonance imaging (MRI) brain data from Alzheimer's patients who are enrolled in a Phase 3 clinical trial of simufilam. These MRI data suggest simufilam is not associated with treatment-emergent amyloid-related imaging abnormalities, or ARIA. MRIs were all analyzed for ARIA by independent, board-certified neuroradiologists.

ARIA is a medical term used to describe a spectrum of brain MRI imaging abnormalities, such as brain swelling and brain bleeds. ARIA is a known risk factor for Alzheimer's patients taking the class of drugs known as monoclonal antibodies directed against amyloid. In contrast to that class of drugs, simufilam is a small-molecule (oral) drug candidate.

The new safety finding is based on an independent, interim neuroradiological evaluation of brain MRIs taken at week 40 in a blinded sub-study of 180 Alzheimer's patients enrolled in REFOCUS-ALZ, our on-going 76-week Phase 3 clinical trial of simufilam in mild-to-moderate Alzheimer's. Final MRI data is expected at the conclusion of this Phase 3 study. See Figure 6.

Figure 6.



Status of Phase 3 Clinical Program

Our Phase 3 trials have randomized a total of approximately 1,900 patients with mild to moderate stages of Alzheimer's disease at baseline (MMSE 16-27), with approximately 800 patients randomized in the 52-week study (RETHINK-ALZ) and approximately 1,100 patients randomized in the 76-week study (REFOCUS-ALZ).

Approximately 70% of patients enrolled in our Phase 3 trials are diagnosed with mild Alzheimer's disease (MMSE 20-27), with remaining patients entering the study with moderate disease (MMSE 16-19). Since the distribution of patients randomized in these trials is numerically skewed towards mild patients, we expect to rely predominantly on outcomes from mild patients to evaluate drug safety and efficacy.

Over 340 patients have completed the 52-week RETHINK-ALZ study. Over 215 patients have completed the 76-week REFOCUS-ALZ study, for a total of over 555 completers.

All efficacy data from our Phase 3 program remain blinded. There are no interim analyses on efficacy outcomes.

We anticipate top-line data readout for our 52-week study (RETHINK-ALZ) approximately year-end 2024.

We anticipate top-line data readout for our 76-week study (REFOCUS-ALZ) approximately mid-year 2025.

We have initiated a discussion with the FDA to finalize a statistical analysis plan (SAP), which is a formal document defining the detailed analysis that our independent biostatisticians will undertake as to efficacy data collected in our Phase 3 trials. The SAP includes in-depth technical details and descriptions on the intended clinical trial analysis, the statistical methods and models that will be used, the population being analyzed, the data variables that will be analyzed, how missing data will be accounted for, descriptions of covariates to be included in the statistical model, and other statistical factors, all of which will be prospectively defined, documented and finalized prior to unblinding of any efficacy outcomes.

Open-label Extension Study for the Phase 3 Program

In October 2022, we announced the initiation of an open-label extension study for our Phase 3 program. This study is designed to provide no-cost access to oral simufilam for up to one year to Alzheimer's patients who have successfully completed a Phase 3 study of simufilam and who meet other entry criteria.

We expect the open-label extension study to generate additional long-term clinical safety data for oral simufilam 100 mg twice daily over 52 weeks. There is no obligation for a patient or a physician to participate in the open-label extension study. Each clinical investigational site and each patient chooses whether to participate in this open-label extension study.

Patient enrollment for this study began in November 2022. To date, over 500 patients entered the open-label extension study.

Phase 3 Drug Supply

We have a drug supply agreement with Evonik Industries AG for simufilam. Under the agreement, Evonik supplies and is expected to continue to supply us with large-scale, clinical-grade quantities of simufilam. Evonik is one of the world's largest contract development and manufacturing organizations for pharmaceutical ingredients. Other vendors supply excipients, the finished dosage form (i.e., simufilam tablets), drug packaging, package labeling and other critical components of the supply chain for Phase 3 drug supply.

SavaDx

Our investigational product candidate, called SavaDx, is an early-stage program focused on detecting the presence of Alzheimer's disease from a small sample of blood. For business, technical and personnel reasons, we continue to prioritize the development of simufilam, our novel drug candidate, over SavaDx, our novel diagnostic candidate. SavaDx is a research-use only, non-safety related exploratory biomarker. Development activity related to SavaDx accounts for less than 1% of our research budget.

Working with third parties, we continue to evaluate the use of mass spectrometry to detect FLNA or other proteins of interest. The data and information generated from these evaluations continues to be under review for potential intellectual property rights.

The regulatory pathway for SavaDx may eventually include formal analytical validation studies and clinical studies that support evidence of sensitivity, specificity and other variables in various healthy and diseased patient populations. We have not conducted such studies and do not expect to conduct such studies in 2024.

SavaDx is designed as an antibody-based detection system for altered filamin A (FLNA). Working with third parties, we are evaluating the use of mass spectrometry to detect FLNA, i.e., without the use of antibodies. These evaluations are on-going.

Over the past twelve years, we discovered that altered FLNA is a hallmark feature of brain pathology in patients with Alzheimer's disease. We believe SavaDx may reveal early traces of the disease, potentially even before the overt appearance of disease symptoms, such as memory loss.

A diagnostic test usually measures one or more biomarkers, which are biological indicators of disease. A deep understanding of the biology of disease is required to identify and develop a diagnostic. A valid diagnostic has certain baseline characteristics to be functional and useful for clinical practice. It must detect disease in patients (sensitivity) and, conversely, not detect disease in healthy subjects (specificity); and it is preferably quantitative, giving some indication of severity or stage of disease. Collectively, the ability to selectively detect disease indicators can be useful to provide diagnostic information (i.e., detect the disease) or prognostic information (i.e., predict the disease or its future course).

Currently, the most definitive method to diagnose Alzheimer's disease is through autopsy after death, which is not particularly helpful. Methods to detect Alzheimer's disease during its course can be expensive, invasive, subjective, risky and/or uncomfortable. Importantly, because of the expense and invasiveness of current tests, most people are not tested until they show obvious cognitive decline.

Current approaches for diagnosing Alzheimer's disease include measurement of amyloid-β (specifically, $A\beta_{42}$), total tau (T-tau) or phosphorylated tau (P-tau) levels in CSF or plasma; structural neuroimaging techniques, including magnetic resonance imaging (MRI) or computerized tomography (CT); positron-emission tomography (PET) imaging of brain amyloid (AmyVid®); and batteries of cognitive tests. Usually, a combination of more than one test is necessary to provide a working diagnosis. When such tests and techniques are used together, the totality of data can be sensitive and specific for the detection of Alzheimer's disease. In practice, however, such tests and techniques are only used after overt symptoms of impaired memory.

We believe there is a profound need for a blood-based diagnostic test for Alzheimer's disease. A quick, simple, inexpensive test may benefit the medical community in many ways. Advantages may include confirming the presence of Alzheimer's disease earlier, when lifestyle changes and potential therapeutics may have the most impact, or conversely, to rule out Alzheimer's disease at such early stages. Other potential benefits include discriminating Alzheimer's disease from other causes of dementias; helping to identify stage of Alzheimer's disease; selection and enrollment of appropriate patients into clinical studies of experimental product candidates; and better alignment of a patient's specific diagnosis with a targeted therapeutic.

It is widely accepted that in Alzheimer's disease, pathological changes in the brain occur at least 10-15 years before clinical symptoms appear. These "pre-symptomatic" changes include deposits of certain misfolded or impaired proteins in the brain. Our long-term goal with SavaDx is to identify people with Alzheimer's disease, potentially long before clinical symptoms occur. Early detection may be critical for any intervention to cease – or at least slow down – brain damage before it is too late. Importantly, a non-invasive screen for latent Alzheimer's disease prior to overt symptoms could be conducted as a general health screen, not just in patients at risk by family history or in patients already showing cognitive impairment. Once a disease-modifying treatment is found, early detection is likely to be critically important. Early detection and treatment may also be critical in identifying such a disease-modifying treatment, as many believe one reason for clinical study failures in Alzheimer's disease is that treatment has routinely started too late in the course of disease to make any impact.

Moreover, with repeat measurements over time, SavaDx may provide a probability of cognitive decline or disease progression. Even if SavaDx does not provide a precise numerical cutoff value for Alzheimer's disease, we believe it may be important to incorporate data from SavaDx into the overall diagnostic framework for neurodegeneration, and Alzheimer's disease in particular. As with any diagnosis of disease, some people may embrace a way to detect Alzheimer's disease long before clinical symptoms appear, while others may prefer not to know – at least until better treatments are found.

Diagnostic development program.

Diagnostic development differs from drug development in many important ways. As a result, diagnostic development requires substantial differences in planning, study design and study execution.

Some of the ways that diagnostic development differs from drug development include the following:

- We may need to choose among a wider range of regulatory pathways for approval of SavaDx, depending on factors such as intended use and user, test type and complexity and role in patient-care decisions;
- Drug studies usually deal primarily with one office within FDA, but the regulatory pathway for SavaDx may require us to consider the policies of multiple federal or state regulatory agencies and offices;
- Unlike drug programs, statistical analysis with SavaDx does not focus on efficacy and safety endpoints. Rather, study endpoints for SavaDx will focus on sensitivity (true positives), specificity (true negatives), positive predictive value (percentage of correct positive diagnoses of known positive cases) and negative predictive value (percentage of correct negative diagnoses of known negative cases).

SavaDx is an investigational diagnostic product candidate that has not yet been reviewed by FDA. Early clinical testing consisted of collecting blood samples on a limited scale to test and validate SavaDx using antibodies or mass spectrometry. Our ability to test such samples and generate accurate results depends on multiple factors, many of which are beyond our control. For example, optimal sample collection depends on risk of sample degradation, storage requirements to preserve samples, cost of sample storage and actual vs. predicted time of assay validation.

We have conducted four early validation tests using SavaDx. In three blinded studies of test samples, SavaDx detected more than a 10-fold separation between Alzheimer's patients and normal healthy control subjects (N=232 test samples). In these three proof-of-concept studies, SavaDx demonstrated nearly 100% accuracy and specificity. The three studies deployed a research grade antibody manufactured by an outside vendor.

A fourth blinded study of SavaDx failed to generate meaningful diagnostic data. We believe the fourth study deployed a faulty research antibody sourced from an outside vendor. Commercially available research antibodies can present certain technical flaws, such as improper validation, significant batch-to-batch variations or inconsistent storage, any of which can jeopardize results of studies and experiments.

In July 2021, we announced positive clinical data with SavaDx when used to measure plasma levels of altered filamin A before and after simufilam treatment in patients with Alzheimer's disease. In a Phase 2b randomized, controlled trial sponsored by the National Institutes of Health (NIH), simufilam significantly reduced a plasma marker of altered filamin A in Alzheimer's patients treated for 28 days. Plasma levels of p-tau181 also dropped significantly in these same patients, as measured by Quanterix Corporation, a third-party vendor.

SavaDx is currently designed as an antibody-based detection system for filamin A (FLNA). Working with third parties, we are evaluating the use of mass spectrometry to detect FLNA, i.e., without the use of antibodies. These evaluations are on-going.

The legal system for intellectual property around diagnostic methods is highly complex and uncertain. In the U.S., patent courts have struggled to define a clear means of patent eligibility for modern age diagnostics. Generally, a simple process involving correlations between blood test results and patient health is not eligible for patent claims because such processes incorporate "laws of nature". However, different outcomes from different courts, including Federal Circuit, district court and Patent Trial and Appeal Board decisions, have continued to create a sometimes vague or conflicting legal framework for determining the eligibility of patent claims for diagnostic methods. As a result, we cannot be certain how SavaDx fits into the current U.S. legal framework for obtaining effective patent claims. Furthermore, claims for diagnostic methods can be complicated to enforce.

We currently have no issued patents in the United States with respect to SavaDx.

Expansion of Our Science to Other Indications

Protein misfolds occur in a wide variety of biological processes and diseases. We may leverage our scientific insights in neurodegeneration and neuroinflammation and advanced tools in molecular biology, biochemistry, and imaging to expand our science to other diseases. New indications and new drug development approaches may complement our initial focus on Alzheimer's disease.

Preclinical programs are always visionary, sometimes innovative and often of high biomedical potential. By definition, such programs are exploratory and risky. Most preclinical programs fail for scientific or other reasons, regardless of the amount of effort or resources that are brought to bear. For these reasons, we do not intend to disclose our preclinical programs until they become material to our pipeline of product candidates.

We Own Worldwide Rights to Our Neurodegeneration Program

We own intellectual property, including patents, patent applications, technology, trade secrets and know-how in the U.S. and other countries. The protection of patents, designs, trademarks and other proprietary rights that we own or license is critical to our success and competitive position. We consider the overall protection of our patents and other intellectual property rights to be of material value and act to protect these rights from infringement.

We seek to protect our technology by, among other methods, filing and prosecuting U.S. and foreign patents and patent applications with respect to our technology and products and their uses. The focus of our patent strategy is to secure and maintain intellectual property rights to technology for our program in neurodegeneration.

Simufilam was discovered and designed in-house and was characterized by our academic collaborators during research activities that were conducted from approximately 2008 to date. SavaDx is being developed in-house with outside collaborators. We own exclusive, worldwide rights to those drug and diagnostic assets and related technologies, without royalty obligations to any third party. Our patent protection with respect to simufilam and use of simufilam for Alzheimer's disease and other neurodegenerative diseases currently runs through 2039 and includes nine issued U.S. patents. In addition, we have patent protection with respect to simufilam for use in treating certain cancers that runs through 2033. Our patent estate further includes patents and patent applications for related compounds and treatments. Corresponding foreign filings have been made for each of the U.S. filings.

Our Development Team

Our product development team is led by seasoned professionals with a proven track record of innovation in drug discovery and development, as well as substantial business expertise.

Our Founder and Chief Executive Officer, Remi Barbier, has over 25 years of biopharmaceutical industry experience and has led teams responsible for pioneering several pharmaceutical innovations, including abuse-deterrent technology for opioid drugs; the clinical development of multiple pain drug candidates; an innovative antibody program in cancer; and other programs in neuroscience and other therapeutics areas. Before founding Cassava Sciences, he held leadership roles and was founder or co-founder of three life science companies, all of which are now either publicly traded or were acquired.

Our Chief Medical Officer, James Kupiec, MD, has participated in research programs that led to two FDA drug approvals prior to Cassava Sciences. He previously served at Pfizer, Inc. as VP, Global Clinical Leader for Parkinson's Disease and Clinical Head of the Neuroscience Research Unit. Dr. Kupiec also held leadership roles at Sanofi and Ciba-Geigy Pharmaceuticals and before that was a practicing neurologist.

Lindsay Burns, PhD, SVP, Neuroscience, reports to Dr. Kupiec and has worked on the development of several product candidates in neuroscience and other therapeutics areas while at Neurex (acquired by Elan Pharmaceuticals) and Abgenix (acquired by Amgen).

Michael Zamloot, SVP of Technology Operations, has participated in research programs that led to four FDA drug approvals prior to Cassava Sciences. He previously worked in drug operations and supply chain management at Boehringer Mannheim (acquired by Roche Diagnostics), Athena Neuroscience (acquired by Elan Pharmaceuticals) and Ciba-Geigy (acquired by Novartis).

Michael Marsman, PharmD, SVP of Regulatory Affairs previously held senior positions at Impax Laboratories, Millennium Pharmaceuticals, and Syntex, where he had shared responsibility for the regulatory approval of several high-profile drugs. He also previously led regulatory affairs for our Company for nearly a decade until 2019.

George (Ben) Thornton, PhD, SVP of Technology, has led research and development teams at Johnson & Johnson as well as translated basic science to the clinical setting at biotechnology start-ups such as GeneMedicine and Apovia.

Our management team is further supported by scientific advisors who are leading experts in the field and share our commitment to advancing new treatments for neurodegenerative diseases, including Alzheimer's disease.

Our Strategy

Our goal is to develop product candidates to diagnose and treat neurodegeneration, such as Alzheimer's disease. Key elements of our business strategy to achieve this mission include:

- building a lean company that is narrowly focused on developing innovative product candidates for Alzheimer's disease and other areas of neurodegeneration;
- validating our unique scientific approach with competitive research grants and publishing our scientific data in peer-reviewed journals;
- applying our development capabilities to advance our product candidates through clinical proof-of-concept studies and beyond;
- using our expertise and experience to continue to focus on discovering new indications and product candidates, validated by experimental evidence and leading experts in the field; and
- continuing to outsource preclinical studies, clinical studies and formulation development activities in order to allow more efficient deployment of our resources

We also conduct basic research and development in collaboration with academic and other partners. Our research and development expenses were $89.4 million, $68.0 million and $24.8 million for the year ended December 31, 2023, 2022 and 2021, respectively. See "*Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations*" for additional details regarding our research and development activities.

Competition

The drug discovery and development industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face potential competition from many different sources, including pharmaceutical and biotechnology companies, academic institutions, governmental agencies, and public and private research institutions. Any product candidates that we successfully develop and commercialize, such as simufilam or SavaDx, may compete with existing therapies and new therapies that may become available in the future.

Historically, the drug industry has attempted to treat Alzheimer's disease by developing drugs that block the synthesis of, or remove or disaggregate, beta amyloid and, more recently, another protein in the brain called tau. Essentially, the prevailing doctrine holds that amyloid (or tau) must be cleared out of the brain. This scientific approach has been repeatedly tested by our competitors in late-stage clinical studies using a variety of antibody backbones, epitopes and target conformations in various stages of disease. More recent competitors in Alzheimer's research are focused on modulating proteins in the brain that have anti-inflammatory or other properties.

In contrast, our scientific approach seeks to simultaneously improve neurodegeneration and neuroinflammation. We believe improving multiple vital functions in the brain represents a new, different and crucial approach to address Alzheimer's disease.

Regardless of scientific approach, improvement or stability in cognition and health function remains a key criterion for a new drug in Alzheimer's disease to receive full, unconditional marketing approval from the FDA.

Our competitors may have significantly greater financial resources, an established presence in the market, expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing-approved products. These competitors compete with us in recruiting and retaining qualified scientific and technical personnel, establishing clinical study sites and patient registration for clinical studies, as well as in acquiring or developing technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies, significant financial backing from large investors and/or access to intellectual property from large established companies.

The key competitive factors affecting the success of simufilam, and any other product candidates that we develop to address neurodegenerative disorders, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition, patient and physician acceptance and the availability of reimbursement from government and other third-party payors. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient or are less expensive than products that we may develop.

Our competitors may develop and obtain FDA approval for their products more rapidly than us. For example, the FDA approved Biogen's aducanumab (human monoclonal antibody) for the treatment of Alzheimer's disease using an accelerated approval pathway, although its development and commercialization was subsequently discontinued by Biogen in January 2024. More recently, in January 2023, lecanemab (humanized version of a mouse monoclonal antibody, marketed as Leqembi®), which is a proprietary drug of Eisai R&D Management Co., Ltd. and Biogen, Inc., received marketing approval from the FDA for the treatment of Alzheimer's disease using an accelerated approval pathway and in July 2023, the FDA granted lecanemab full approval for the treatment of Alzheimer's disease. In addition, we believe Eli Lilly's donanemab drug is poised for a potential FDA approval in the first half of 2024 in patients with early Alzheimer's disease. Each of the foregoing drugs is currently delivered by infusion.

Other currently marketed drugs, called cholinesterase inhibitors, focus solely on treating symptoms mostly in patients with mild-to-moderate Alzheimer's disease. The Alzheimer's brain has low levels of a neurotransmitter called acetylcholine. Cholinesterase inhibitors prevent an enzyme in the brain, called acetylcholinesterase, from breaking down acetylcholine. Currently marketed cholinesterase inhibitors include donepezil (marketed by Eisai Co., Ltd. and Pfizer, Inc. as Aricept®), rivastigmine (marketed by Novartis AG as Exelon®) and galantamine (marketed by Janssen Pharmaceuticals, Inc. as Razadyne®). Cholinesterase inhibitors may benefit some patients for several months, after which the targeted brain receptors are desensitized, and drug efficacy is lost. Another approved medication for treating the symptoms of Alzheimer's disease is memantine, a non-competitive antagonist of NMDA receptors (marketed by Lundbeck as Namenda®).

In recent years, we have observed ramped-up worldwide efforts aimed at developing blood-based techniques to detect and monitor Alzheimer's disease. The key competitive factors affecting the success of SavaDx, and any other product candidates that we develop to diagnose neurodegeneration, if approved, are likely to be their measure of accuracy, such as specificity and sensitivity, as well as their convenience, patient acceptance, price and the availability of reimbursement from government and other third-party payors. Our competitors in the diagnostic area are pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Despite increased research effort, the field has generally been hampered by lack of reproducibility and an unclear path on how to move academic discoveries into clinical utilization.

In addition to blood-based techniques to detect Alzheimer's disease, competitors are examining the use of novel tracing agents and imaging techniques to map the course of neurodegeneration. In 2012, FDA approved Amyvid® (Eli Lilly Pharmaceuticals), which is a radioactive diagnostic agent for brain imaging of amyloid plaque. Amyvid can rule out Alzheimer's disease but does not confirm its presence. That is, a negative scan means little or no plaque is present; however, a positive scan does not necessarily indicate Alzheimer's disease. In addition, Amyvid cannot be used to stage Alzheimer's disease because some people take years to show cognitive decline after amyloid plaque develops, while other others rapidly develop advanced Alzheimer's disease within months.

Manufacturing

Simufilam and any future product candidates must be manufactured for clinical trial use in compliance with current good manufacturing practices (cGMP) regulations. These regulations are extensive, stringent and complex, and may include requirements regarding the organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. Our manufacturing vendors must have facilities to make our product candidates in strict compliance with cGMP requirements and the FDA's or comparable foreign regulatory authorities' satisfaction. Our third-party vendors may also be subject to periodic and unannounced inspections of their respective facilities for general cGMP compliance by the FDA and other foreign authorities. These inspections may include review of procedures and operations used in the testing and manufacture of simufilam to assess compliance with applicable regulations. Failure to comply with statutory and regulatory requirements subjects a manufacturer to possible legal or regulatory action, including warning letters, the seizure or recall of products, injunctions, consent decrees placing significant restrictions on or suspending manufacturing operations and civil and criminal penalties. Contract manufacturers often encounter difficulties involving production yields, quality control and quality assurance, as well as shortages of qualified personnel. Any of these actions or events could have a material impact on the availability of simufilam. Our suppliers may be forced to stop producing, storing, shipping or testing our drug product candidates if they fall out of compliance with government regulations and standards.

Although we are ultimately responsible for the manufacture of simufilam and any other future product candidates, we have limited or no control over our suppliers' compliance, or lack thereof, with the multitude of regulations and standards that affect our drug products. We cannot control decisions by our suppliers that affect their ability or willingness to continue to supply us on acceptable terms, or at all.

We do not own or lease any manufacturing facilities. We outsource formulation, manufacturing and related activities to third parties. For the foreseeable future, we will continue to rely on third parties to conduct certain quality control and assurance testing, shipping or storage of our product candidates.

We currently rely on one non-affiliated contract development and manufacturing organization (CDMO)—Evonik Corporation—to manufacture simufilam and expect to continue to do so. In 2021, we entered into an agreement with Evonik Corporation to supply large-scale, clinical-grade quantities of drug substance for simufilam.

We believe our manufacturing strategy will continue to provide sufficient drug supply for our Phase 3 program, including both drug substance (i.e., active ingredient) and drug product (i.e., oral tablets). The goal of our manufacturing strategy is to ensure the integrity of the supply chain for drug substance in compliance with FDA standards. We believe raw materials for our drug product are readily available from reliable sources.

Government Regulation

Our operations are subject to various levels of governmental controls and regulations in the United States and in other countries where we operate, including Canada, South Korea and Australia. We attempt to comply with all legal requirements in the conduct of our operations and employ business practices that we consider to be prudent under the circumstances in which we operate. Government authorities in the U.S. (federal, state and local), Canada, South Korea, Australia and other countries regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug and diagnostic products. Generally, before a new drug or diagnostic can be marketed, considerable data demonstrating its quality, safety and efficacy and/or specificity must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by each regulatory authority.

U.S. Drug Development

In the U.S., FDA regulates drugs under the Food, Drug, and Cosmetic Act (FDCA). Both drugs and diagnostics also are subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or post-market may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Product candidates must be approved by FDA before they may be commercialized in the U.S. The drug approval process generally includes the following sequence of steps:

- Completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with good laboratory practice;
- Submission to FDA of an IND, which must become effective before human clinical studies may begin;
- Approval by an independent institutional review board (IRB) or ethics committee before each study may be initiated;
- Performance of adequate and well-controlled human clinical studies in accordance with applicable IND regulations, code of good clinical practice (cGCP), requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- Submission to FDA of a new drug application (NDA);
- A determination by FDA within 60 days of its receipt of an NDA to accept the filing for review;
- Satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug will be produced to assess compliance with cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- Potential FDA audit of the preclinical study and/or clinical study sites that generated the data in support of the NDA;
- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug in the U.S.; and
- Compliance with any post-approval requirements, including the potential requirement to conduct post-approval studies.

The data required to support an NDA are generated in two distinct developmental stages: preclinical and clinical. The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for any future product candidates will be granted on a timely basis, or at all.

Preclinical Studies and IND

The preclinical developmental stage generally involves laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which support subsequent clinical testing. As sponsor, we must submit the results of the preclinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to FDA as part of the IND. An IND is a request for authorization from FDA to administer an investigational product to humans and must become effective before human clinical studies may begin.

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as in vitro and animal studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including cGCP regulations for safety/toxicology studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, to FDA as part of an IND. Some long-term preclinical testing, such as long-term toxicity tests, animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by FDA, unless before that time FDA raises concerns or questions about any aspect of the program. In such a case, the IND sponsor and FDA must resolve any outstanding concerns before the clinical study can begin.

Clinical Studies

The clinical stage of development involves the administration of the investigational product to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the study sponsor's control, in accordance with cGCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical studies are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to FDA as part of the IND. Furthermore, each clinical study must be reviewed and approved by an IRB for each institution at which the clinical study will be conducted to ensure that the risks to individuals participating in the clinical studies are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical study subject or his or her legal representative and must monitor the clinical study until completed. There also are requirements governing the reporting of ongoing clinical studies and completed clinical study results to public registries.

A sponsor who wishes to conduct a clinical study outside of the U.S. may, but need not, obtain FDA authorization to conduct the clinical study under an IND. If a foreign clinical study is not conducted under an IND, the sponsor may submit data from the clinical study to FDA in support of an NDA. The FDA may accept a well-designed and well-conducted foreign clinical study not conducted under an IND if the study was conducted in accordance with cGCP requirements and FDA is able to validate the data through an onsite inspection if deemed necessary. We currently have clinical sites outside of the U.S. in Canada, Puerto Rico, South Korea and Australia.

Clinical studies in the U.S. generally are conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3, and may overlap.

- Phase 1 clinical studies generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical studies is to assess the absorption, metabolism, pharmacologic action, tolerability and safety of a drug candidate.
- Phase 2 clinical studies involve studies in disease-affected patients to determine the proper dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, possible adverse effects and safety risks are identified, and a preliminary evaluation of efficacy may be observed.
- Phase 3 clinical studies generally involve enrolling many patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. These studies may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

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

Progress reports detailing the results of the clinical studies, among other information, must be submitted at least annually to FDA. Written safety reports and the investigations for serious and unexpected adverse events, or any other findings suggesting a significant risk to humans exposed to the drug must be submitted to FDA.

Phase 1, Phase 2, and Phase 3 clinical studies may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical study 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 study at its institution if the clinical study is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical studies are overseen by an independent group of qualified experts organized by the clinical study sponsor, known as a Data and Safety Monitoring Board (DSMB). This group provides authorization for whether a study may move forward at designated check-points based on access to certain data from the trial. Concurrent with clinical studies, companies usually complete additional animal studies and must develop additional information about the chemistry and physical characteristics of the drug as well as 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 and, among other things, companies must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that our product candidates do not undergo unacceptable deterioration over their shelf life.

NDA Review Process

Following completion of the clinical studies, data is analyzed to assess whether the investigational product is safe and effective for the proposed indicated use or uses. The results of preclinical studies and clinical studies are then submitted to FDA as part of an NDA, along with proposed labeling, chemistry and manufacturing information to ensure product quality and other relevant data. In short, the NDA is a request for approval to market a drug for one or more specified indication and must contain proof of safety and efficacy for a drug's purity and potency. The application may include both negative and ambiguous results of preclinical studies and clinical studies, as well as positive findings. Data may come from company-sponsored clinical studies intended to test the safety and efficacy of a product's use or from several alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of FDA. FDA approval of an NDA must be obtained before a drug may be marketed in the U.S.

Under the Prescription Drug User Fee Act (PDUFA), as amended, each NDA must be accompanied by a user fee. FDA adjusts the PDUFA user fees on an annual basis. According to FDA's fiscal year 2024 fee schedule, effective through September 30, 2024, the user fee for an application requiring clinical data, such as an NDA, is approximately $4.0 million. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. 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 all submitted NDAs before it accepts them for filing and may request additional information rather than accept the NDA for filing. The FDA must decide whether to accept an NDA for filing within 60 days of receipt. Once the submission is accepted for filing, FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by FDA under PDUFA, FDA has 10 months, from the filing date, in which to complete its initial review of a new molecular-entity NDA and respond to the applicant, and six months from the filing date of a new molecular-entity NDA designated for priority review. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often extended by FDA requests for additional information or clarification.

Before approving an NDA, FDA may conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMP requirements. The FDA will not approve the product unless it determines that the manufacturing processes and facilities fully comply with cGMP requirements and are adequate to assure consistent production of the product within required specifications. The FDA also may audit data from clinical studies to ensure compliance with cGCP requirements. Additionally, FDA may refer applications for novel product candidates which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions, if any. The FDA is not bound by recommendations of an advisory committee, but it considers such recommendations when making decisions on approval. The FDA likely will reanalyze the clinical study data, which could result in extensive discussions between FDA and the applicant during the review process. After FDA evaluates an NDA, it will issue either an approval letter or a Complete Response Letter (CRL). An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A CRL indicates that FDA's review of the application is complete and the application cannot be approved in its present form. A CRL usually describes the specific deficiencies in the NDA identified by FDA. The CRL may require additional clinical data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time-consuming requirements related to clinical studies, preclinical studies or manufacturing. If a CRL is issued, the applicant may either resubmit the NDA, addressing all the deficiencies identified in the CRL, or withdraw the application. Even if such data and information are submitted, FDA may decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical studies are not always conclusive and FDA may interpret data differently than we interpret the same data.

Commercialization Plan

Our product candidates have not received marketing approval from the FDA, and we do not expect to have any approved product candidates in the near term. We currently have no company experience in marketing drugs and have no personnel, capabilities or infrastructure in sales, marketing, third-party payor programs or commercial product distribution. When and if any of our product candidates are approved for commercialization, we will need to develop a commercialization infrastructure for any such product in the U.S. and potentially in certain other key markets. As a matter of strategy, we may also rely on partnerships or collaborations with larger biopharmaceutical companies to provide commercialization infrastructure, such as sales and marketing and commercial distribution.

Advertising and Promotion

The FDA and other federal regulatory agencies closely regulate the marketing and promotion of drugs through, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet. None of our product candidates can be commercially promoted before receiving FDA approval. After approval, product promotion can include only those claims relating to safety and effectiveness that are consistent with the labeling approved by FDA. Healthcare providers are permitted to prescribe drugs for "off-label" uses — that is, uses not approved by FDA and therefore not described in the drug's labeling — because FDA does not regulate the practice of medicine. However, FDA regulations impose stringent restrictions on manufacturers' communications regarding off-label uses. Failure to comply with applicable FDA requirements and restrictions in this area may subject us to adverse publicity and enforcement action by FDA, the U.S. Department of Justice, or the Office of the Inspector General of Health and Human Services, as well as state authorities. This could subject us to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which we promote or distribute our product candidates.

Post-Approval Requirements

After a product candidate receives regulatory approval, it is often subject to pervasive and continuing regulation by FDA, including, among other things, requirements relating to drug listing and registration, recordkeeping, periodic reporting, product sampling and distribution, adverse event reporting and advertising, marketing and promotion restrictions.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-market testing, known as Phase 4 testing, or FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control, drug manufacture, packaging, and labeling procedures must continue to conform to cGMP after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with FDA and certain state agencies. Registration may result in periodic announced or unannounced inspections by FDA or these state agencies, during which the agency inspects manufacturing facilities to assess compliance with cGMP. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and quality control to maintain compliance with cGMP. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered. In addition, other regulatory actions may be taken, including, among other things, warning letters, the seizure of products, injunctions, consent decrees placing significant restrictions on or suspending manufacturing operations, refusal to approve pending applications or supplements to approved applications, civil penalties, and criminal prosecution.

The FDA may require post-approval clinical studies to help assure continued safety or effectiveness of the approved drug. The FDA may also require a labeling change if it becomes aware of new safety information that it believes should be included in the labeling of a drug.

In addition to the FDA, manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in the U.S., including the Centers for Medicare and Medicaid Services, other divisions of the Department of Health and Human Services, the Department of Justice, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency, the Affordable Care Act (ACA) and state and local governments.

For example, in the United States, sales, marketing and scientific and educational programs must also comply with state and federal fraud and abuse laws. These laws include the federal Anti-Kickback Statute, which makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Violations of this law are punishable by prison, criminal fines, administrative civil money penalties and exclusion from participation in federal healthcare programs. Moreover, the ACA provides that 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.

Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the ACA. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals or refusal to allow a firm to enter into supply contracts, including government contracts. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

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

The Hatch-Waxman Amendments

Orange Book Listing

In seeking approval for our product candidates through an NDA, we will be required to list with FDA each patent whose claims cover the drug product. Upon receiving regulatory approval, each of the patents listed in the application for this drug is then published in FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the "Orange Book." Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an abbreviated NDA, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredient in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, preclinical or clinical tests to prove the safety or efficacy of their drug product. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to make certain certifications to FDA concerning any patents listed for the approved product in FDA's Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a section viii statement certifying that its proposed ANDA label does not contain (or carves out) any language regarding the patented method-of-use rather than make certifications concerning a listed method-of-use patent. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA applicant. The ANDA application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

Disclosure of Clinical Study Information

Sponsors of clinical studies of FDA-regulated products, including drugs, are required to register and disclose certain clinical study information. Information related to the product, patient population, phase of investigation, clinical study sites and investigators, and other aspects of the clinical study is then made public as part of the registration. Sponsors are also obligated to post certain information regarding the results of their clinical studies after completion. Disclosure of the results of these studies can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Other Regulatory Requirements

We may be subject to federal, state and local environmental laws and regulations, including the Environmental Protection Act and the Clean Air Act. Although we believe that our safety procedures for handling and disposing of controlled materials comply with the standards prescribed by state and federal regulations, accidental contamination or injury from these materials may occur. In the event of such an occurrence, we could be held liable for any damages that result and any such liability could exceed our resources.

We may also be subject to regulations under other federal, state, and local laws, including the Occupational Safety and Health Act, national restrictions on technology transfer, and import, export, and customs regulations. It is possible that any portion of the regulatory framework under which we operate may change and that such change could have a negative impact on our current and anticipated operations. Failure to comply with these requirements could result, among other things, in suspension of regulatory approval, recalls, injunctions or civil or criminal sanctions.

Third-Party Payor Coverage and Reimbursement

The commercial success of our product candidates, if approved, will depend, in part, upon the availability of coverage and adequate reimbursement from third-party payors at the federal, state and private levels. Third-party payors include governmental programs such as Medicare or Medicaid, private insurance plans and managed care plans. These third-party payors may deny coverage or reimbursement for our product candidates in whole or in part if they determine that our product candidates are not medically appropriate or necessary. Also, third-party payors attempt to control costs by limiting coverage through the use of formularies and other cost-containment mechanisms and the amount of reimbursement for particular procedures or drug treatments.

Some third-party payors also require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. While we cannot predict whether any proposed cost-containment measures will be adopted or otherwise implemented in the future these requirements or any announcement or adoption of such proposals could have a material adverse effect on our ability to obtain adequate prices for our approved product candidates to operate profitably.

Human Capital

Our approach to human capital resource management starts with our mission to detect and treat neurodegenerative diseases, such as Alzheimer's disease. Our industry exists in a complex regulatory environment. The unique demands of our industry, together with the challenges of running an enterprise focused on the discovery, development, manufacture and commercialization of innovative medicines, require talent that is highly educated and/or has significant industry experience. Additionally, for certain key functions, we require specific scientific expertise to oversee and conduct research and development activities and the complex manufacturing requirements for biopharmaceutical products.

Our employees are an essential asset, and we consider our ability to recruit, train, retain and motivate our employees to be critical to our success. We are an equal opportunity employer, and we are fundamentally committed to creating and maintaining a work environment in which employees are treated with respect and dignity. All human resources policies, practices and actions related to hiring, promotion, compensation, benefits and termination are administered in accordance with the principal of equal employment opportunity, meaning that they are made on the basis of individual skills, knowledge, abilities, job performance and other legitimate criteria and without regard to race, color, religion, sex, sexual orientation, gender expression or identity, ethnicity, national origin, ancestry, age, mental or physical disability, genetic information, any veteran status, any military status or application for military service, or membership in any other category protected under applicable law. By focusing on employee retention and engagement, we also improve our ability to support our clinical trials, our pipeline, business and operations, and also protect the long-term interests of our stockholders. Our success also depends on our ability to attract, engage and retain a diverse group of employees.

Our base pay program aims to compensate management and staff members relative to the value of the contributions of their role, which takes into account the skills, knowledge and abilities required to perform each position, as well as the experience brought to the job. We also provide cash incentive programs to reward our management team and staff members in alignment with achievement of Company-wide goals that are designed to drive aspects of our strategic priorities that support and advance our strategy across our Company. Our management team and staff members are eligible for the grant of equity awards under our long-term incentive program that are designed to align their long-term interests with that of our stockholders.

Our benefit programs are generally broad-based, promote health and overall well-being and emphasize saving for retirement. All management team and regular staff members are eligible to participate in the same core health and welfare and retirement savings plans. Other employee benefits may include medical plans, dental plans, vacation and sick-pay plans, flexible spending accounts, life and accident insurance and short and long-term disability benefits.

Our Compensation Committee provides oversight of our executive compensation plans, policies and programs.

As of December 31, 2023, we had 29 full-time employees. None of our employees is represented by a labor union or covered under a collective bargaining agreement. We also engage numerous consultants to perform services on retainer, per diem or an hourly basis. We consider our relationship with our employees to be good.

Lawsuit Against Perpetrators of "Short and Distort" Campaign

On November 3, 2022, we announced that we had filed a lawsuit in federal court against certain individuals who executed a "short and distort" campaign against Cassava Sciences. The 150+ page complaint alleges that the defendants' disinformation campaign caused a precipitous decline in Cassava Sciences' stock price, a multi-billion dollar decline in its market capitalization, and delayed the Company's work in developing a treatment for Alzheimer's disease. The complaint identifies over 1,000 false and defamatory statements made by the defendants in submissions to the U.S. Food and Drug Administration as well as "reports" and presentations that defendants published online or on social media. Between January 3 and 23, 2024, the Magistrate Judge assigned to the case recommended that the District Court grant defendants' various motions to dismiss the complaint. The Company has timely filed objections to those recommendations with the District Court. The matter is pending in federal district court for the Southern District of New York.

Internal Investigation

Beginning in August 2021, certain individuals, later revealed to be short sellers of the Company's securities, publicly alleged that the Company and certain of its employees and third-party collaborators had engaged in research misconduct in connection with the development of simufilam. These allegations related in part to research that was conducted at the City University of New York ("CUNY") pursuant to research contracts with the Company.

The Company takes allegations of research misconduct seriously. Accordingly, the Company's Board of Directors engaged the law firm Orrick Herrington & Sutcliffe LLP to investigate these allegations. The investigation had access to Company personnel, communications, documents, data, and information, and counsel was assisted by technical experts with relevant experience and knowledge. The investigation has found no evidence to substantiate allegations that the Company or its employees engaged in or were aware of research misconduct.

Publication Corrections

An erratum or corrigendum is a correction of a published text, generally a human, production or author's error, that was not caught in proofing. Such errors generally do not impact data conclusions. We note the following corrections in our published works.

In July 2021, we presented clinical data for SavaDx in a poster presentation titled, " *SavaDx, a Novel Plasma Biomarker to Detect Alzheimer's Disease, Confirms Mechanism of Action of Simufilam*" at the Alzheimer's Association International Conference (AAIC) in Denver, CO and virtually. Publication correction: The AAIC data and data analysis are correct, however, visual errors that were not caught in proofing were disclosed by the Company in September 2021. This error does not impact data conclusions.

In 2017, we published in Neurobiology of Aging an article titled " *PTI-125 binds and reverses an altered conformation of filamin A to reduce Alzheimer's disease pathogenesis*" (Vol 55, July 2017, Pages 99–114). Publication correction: Figure 12 contains an image showing 12 control bands. It should show 13. The data analysis was based on all 13 control bands. Other human errors in this publication have been noted and corrected. These errors do not impact data conclusions.

In 2012, we published in the Journal of Neuroscience an article titled *, "Reducing Amyloid-Related Alzheimer's Disease Pathogenesis by a Small Molecule Targeting Filamin A*" (JNeurosci 2012;32:9773-9784). Publication correction: A duplicated panel appears in Figure 8B of the article. This error does not impact data conclusions and the publisher printed a correction.

Corporate Information

We were incorporated as a Delaware corporation in May 1998 under the name Pain Therapeutics, Inc. In March 2019, we changed our company name to Cassava Sciences, Inc. Our principal offices are located at 6801 N. Capital of Texas Highway, Building 1; Suite 300, Austin, TX, 78731. Our telephone number is 512-501-2444. Our website address is www.CassavaSciences.com. Information contained on our website is not a part of this Annual Report on Form 10-K and the inclusion of our website address in this Annual Report on Form 10-K is an inactive textual reference only.

We use Cassava Sciences, the Cassava Sciences logo, artwork and other marks as trademarks in the United States and other countries. Solely for convenience, trademarks and trade names referred to in this Annual Report, including logos, artwork, and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights, or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other entities' trade names, trademarks, or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

We file electronically with the Securities and Exchange Commission, or SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of the site is http://www.sec.gov.

You may obtain a free copy of our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and amendments to those reports on the day of filing with the SEC on our website at http://www.cassavasciences.com, by contacting our corporate offices by calling 512-501-2450 or by sending an e-mail message to IR@cassavasciences.com.

Item 1A. ***Risk Factors***

RISK FACTORS

Investing in our securities involves a high degree of risk. This section includes a discussion of what we believe to be the material factors that make an investment in our Company speculative or risky. The risks described in this section are not the only risks we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations and the market price of our securities.

You should carefully consider the risks described below, as well as other information contained in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our securities. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations, and growth prospects. In such an event, the market price of our securities could decline, and you may lose all or part of your investment.

Risks Related to the Discovery, Development, and Commercialization of Our Product Candidates

- *We have concentrated a substantial portion of our research and development efforts on the treatment of Alzheimer's disease, an area of research that has seen significant failure rates. Further, our product candidates are based on new scientific approaches and novel technology, which makes it difficult to predict the time and cost of product candidate development and likelihood of success.*
- *We are heavily dependent on the success of simufilam, our lead product candidate which is still under development. If this product candidate fails one or both of our ongoing Phase 3 trials, or does not receive regulatory approval, we will be unable to generate product revenue and our business will be harmed.*
- *We have a limited operating history in our business targeting Alzheimer's disease and no history of product approvals for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability.*
- *We cannot give any assurance that we will file for regulatory approval for any of our product candidates, or that if we file for approval, our product candidates will receive regulatory approval, which is necessary before they can be commercialized.*
- *There can be no assurance that promising results of smaller Phase 1 and Phase 2 clinical trials or 24-month safety study with simufilam will be reproduced in our large Phase 3 studies.*
- *Clinical results observed in our smaller Phase 1 and Phase 2 clinical trials or 24-month safety study with simufilam are not regulatory evidence of drug safety or efficacy.*
- *We may encounter substantial delays in our clinical studies or may not be able to conduct or complete our clinical studies on the timelines we expect, if at all.*
- *If physicians and patients do not accept and use our drugs, we will not achieve sufficient product revenues and our business will suffer.*
- *We currently have no in-house capabilities to manufacture or commercialize our product candidates, and we rely on a third-party commercial drug manufacturing organization for clinical drug supplies. If we are unable to develop our own manufacturing, sales, marketing and distribution capabilities, or if we are not successful in contracting with third parties for these services on favorable terms, or at all, our product revenues could be adversely impacted.*
- *We may need to rely on clinical results generated predominately, or even solely, from patients with mild Alzheimer's disease to show evidence of efficacy in our Phase 3 clinical trials, if any, and this may present more or different challenges in our efforts to develop simufilam.*
- *Our clinical studies may fail to demonstrate substantial evidence of the safety and efficacy of our product candidates, which would prevent, delay, or limit the scope of regulatory approval and commercialization.*

Risks Related to Government Regulation and Other Legal Compliance Matters

- *Our financial condition and operating results could be adversely impacted by unfavorable results of legal proceedings, government investigations or allegations and other claims, many of which arose following a short selling attack campaign against our Company that commenced in 2021.*
- *If we are ultimately unable to file for and obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.*
- *Our ability to market and promote our product candidates will be determined and limited by FDA-approved labeling.*
- *If we fail to comply or stay in compliance with the complex set of federal, state, local and foreign laws and regulations that apply to our business, we could suffer severe consequences that could materially and adversely affect our operating results and financial condition.*
- *Government agencies may establish and promulgate usage guidelines that could limit the use of our product candidates.*

Risks Related to Our Intellectual Property

- *If we are unable to obtain and maintain sufficient patent protection for any product candidates we develop, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize any product candidates we may develop may be adversely affected.*
- *Issued patents covering our product candidates and other technologies could be found invalid or unenforceable if challenged in court or before administrative bodies in the U.S. or abroad.*
- *If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be materially harmed.*
- *If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be materially harmed.*

Risks Related to Our Business and Operations

- *Our reputation and operations could be adversely impacted by allegations of wrongdoing, regardless of their merits.*
- *Our ability to continue to operate without any significant disruptions will, in part, depend on our ability to source materials and clinical supplies via our product supply chains.*
- *Our reliance on third parties for both the supply and manufacture of materials for our product candidates carries the risk that we will not have sufficient quality or quantities of such materials or product candidates, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.*
- *We expect to significantly grow the size and capabilities of our organization and we may experience difficulties in effectively managing this growth.*
- *Our internal computer systems, or those used by third parties on whom we rely, may fail or suffer other breakdowns, cyberattacks, or information security breaches that could compromise the confidentiality, integrity, and availability of such systems and data, result in material disruptions of our development programs and business operations, risk disclosure of confidential, financial, or proprietary information, and affect our reputation.*
- *Business disruptions and lack of appropriate levels of commercial insurance could seriously harm our future revenue and financial condition and increase our costs and expenses.*
- *Social media platforms have significantly altered the dynamics of corporate communications and present risks and challenges, some of which are and may continue to be unknown to us.*

Risks Related to Financial Condition and Capital Requirements

- *We have incurred significant net losses in each period since our inception and anticipate that we will continue to incur net losses for the foreseeable future.*
- *We have broad discretion in the use of our capital resources, including the net proceeds from any of our financing transactions and may not use them effectively.*
- *We have no product revenues and may never achieve revenues or profitability based on product revenues.*

Risks Related to the Ownership of Our Common Stock

- *The market price of our common stock has historically been highly volatile and we expect it to continue to be volatile, which could result in substantial losses for investors who purchase our shares.*
- *Changes in our ownership could limit our ability to utilize net operating loss carryforwards.*
- *Short sellers of our stock may be manipulative and may drive down the market price of our common stock.*

Risks Related to the Discovery, Development, and Commercialization of Our Product Candidates

We have concentrated a substantial portion of our research and development efforts on the treatment of Alzheimer's disease, an area of research that has seen significant failure rates. Further, our product candidates are based on new scientific approaches and novel technology, which makes it difficult to predict the time and cost of product candidate development and likelihood of success.

We have concentrated substantially all of our research and development efforts on experimental methods for the treatment of Alzheimer's disease. Prior efforts by biopharmaceutical companies in the field of neurodegenerative diseases, including efforts to develop new treatments for Alzheimer's disease, have seen many failures and very limited clinical success. Since 2003, many new types and classes of drugs have been developed and tested in Alzheimer's disease, including monoclonal antibodies, gamma secretase modulators and inhibitors, β-site amyloid precursor protein cleaving enzyme (BACE) inhibitors, receptor for advanced glycation end-products (RAGE) inhibitors, nicotinic partial agonists and allosteric modulators, serotonin subtype receptor (5HT6) antagonists, and others, but virtually all of these scientific programs have failed in Phase 3 or earlier testing. Developing and, if approved, commercializing a novel treatment for Alzheimer's disease subjects us to many challenges, including obtaining regulatory approval from FDA and other regulatory authorities who have only a limited set of precedents to rely on. Notwithstanding the substantial challenges historically associated with the development of new treatments for Alzheimer's disease, we seek to improve brain health by addressing the neurodegeneration and neuroinflammation components of Alzheimer's disease. Our lead drug candidate for Alzheimer's disease is based on a new approach of stabilizing—but not removing—a critical protein in the brain. We cannot be certain that our novel technologies will yield clinical results that support the approval of a safe and effective therapeutic product or, if approvable, that such a product will be marketable. In addition, because FDA has limited comparators to evaluate our lead drug candidate, we could experience a longer than expected regulatory review process and increased development costs.

We are heavily dependent on the success of simufilam, our lead product candidate which is still under development. If this product candidate fails one or both of our on-going Phase 3 clinical trials, or does not receive regulatory approval, we will be unable to generate product revenue and our business will be harmed.

In recent years, we have invested a significant portion of our efforts and financial resources in the development of simufilam and, to a much lesser extent, SavaDx, for the treatment and detection of Alzheimer's disease, respectively. Our business is substantially dependent on our ability to successfully complete clinical development and obtain regulatory approval for simufilam, which may never occur. The results of clinical studies are subject to a variety of factors, and there can be no assurance that simufilam will advance to regulatory approval, be approved by applicable regulatory agencies, or be successfully commercialized.

We expect that a substantial portion of our efforts and expenditures over the next few years will continue to be devoted to simufilam and, to a much lesser extent, SavaDx. This will require additional clinical development, management of clinical and manufacturing activities, regulatory approval in one or more national jurisdictions and obtaining commercial-scale manufacturing supply. Substantial investment and significant efforts will be required before we can generate any revenues from any commercial sales of our product candidates. We cannot be certain that we will be able to successfully complete any of these activities.

We have a limited operating history in our business targeting Alzheimer's disease and no history of product approvals for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability.

We are a clinical-stage biopharmaceutical company with a limited operating history in our business targeting Alzheimer's disease. Since we commenced operations in 1998, we have had no product candidates approved for commercial sale and have not generated any revenue from product sales. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. To date, we have not completed a pivotal Phase 3 clinical study in Alzheimer's disease, obtained marketing approval for any product candidates, or conducted sales and marketing activities necessary for successful product commercialization. Our long operating history as a company without product revenue makes any assessment of our future success and viability subject to significant uncertainty.

We will continue to encounter risks and difficulties frequently experienced by clinical-stage biopharmaceutical companies in rapidly evolving fields. We have not yet demonstrated an ability to successfully overcome such risks and difficulties. If we do not successfully address these risks and difficulties, our business, results of operations and financial condition will suffer materially.

We cannot give any assurance that any of our product candidates will receive regulatory approval, which is necessary before they can be commercialized.

To date, we have invested substantial effort and financial resources to identify, procure intellectual property for, and develop our programs in neurodegeneration, including conducting preclinical and clinical studies for our product candidates, simufilam and SavaDx, and providing general and administrative support for these operations. Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize our product candidates, and we may fail to do so for many reasons, including the following:

- our product candidates may not successfully complete preclinical studies or clinical studies;
- a product candidate may, on further study, be shown to have harmful side effects or other characteristics that indicate it is unlikely to be safe or effective or otherwise does not meet applicable regulatory criteria;
- our competitors may develop products or therapies that render our product candidates obsolete or less attractive;
- the product candidates that we develop may not be sufficiently covered by intellectual property;
- the product candidates that we develop may be challenged by third parties' patents or other intellectual property or exclusive rights;
- the market for our product candidates may change so that the continued development of a product candidate is no longer reasonable or commercially attractive;
- our product candidates may not be capable of being produced in commercial quantities at an acceptable cost, or at all;
- if a product candidate obtains regulatory approval, we may be unable to establish sales and marketing capabilities, or successfully market such approved product candidate, to gain market acceptance; and
- a product candidate may not be accepted as safe, effective or useful by patients, the medical community or third-party payors, if applicable.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

We may not be successful in our efforts to further develop our product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. SavaDx is in the early stages of development. Simufilam, our late-stage product candidate, will require successful completion of our ongoing Phase 3 program, management of preclinical, clinical, and manufacturing activities, regulatory approval, adequate manufacturing supply, a commercial organization, and significant marketing efforts before we generate any revenue from product sales, if at all.

We have never completed a product development program in neurodegeneration. Further, we cannot be certain that any of our product candidates will be successful in clinical studies, and we may terminate existing or future clinical studies prior to their completion.

If any of our product candidates successfully complete clinical studies, we may seek regulatory approval to market our product candidates in the U.S., Japan, Canada, the United Kingdom or the European Union, and in additional foreign countries where we believe there is a viable commercial opportunity. We may never receive regulatory approval to market any product candidates anywhere even if such product candidates successfully complete clinical studies, which would adversely affect our viability. To obtain regulatory approval in countries outside the U.S., we would need to comply with numerous and varying regulatory requirements of such other countries regarding safety, efficacy, manufacturing and controls, clinical studies, commercial sales, pricing, and distribution of our product candidates. Even if we are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. If we are unable to obtain approval for our product candidates in multiple jurisdictions, our business, financial condition, results of operations, and our growth prospects could be negatively affected.

Even if we receive regulatory approval to market any of our product candidates, whether for the treatment or diagnosis of neurodegenerative diseases or other diseases, we cannot provide assurance that any such product candidate will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives.

Investment in biopharmaceutical product development involves significant risk that any product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval, and become commercially viable. We cannot provide any assurance that we will be able to successfully advance any of our product candidates through the development process or, if approved, successfully commercialize any of our product candidates.

There can be no assurance that promising results of smaller Phase 1 and Phase 2 clinical trials or a 24-month Safety Study with simufilam will be reproduced in our large Phase 3 studies.

Results of our Phase 1, Phase 2 and 24-month Safety Study with simufilam are not predictive of the future results of Phase 3 clinical trials. Simufilam may fail to show the desired safety and efficacy in Phase 3 clinical trials despite having progressed successfully through preclinical studies and initial clinical trials. Many biopharmaceutical companies have suffered significant setbacks in Phase 3 clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. We cannot be certain that our product candidates will not face similar setbacks.

In addition, conclusions based on data from analyses of Phase 1 and Phase 2 clinical studies and open-label results may not be reproduced when implemented in large, well-controlled, randomized clinical trials. Particular caution should be exercised when interpreting preliminary data, data relating to a small number of patients and data from open-label uncontrolled studies, which are generally not capable of providing interpretable evidence of efficacy. Results of our small, “first-in-human” Phase 1 study was designed to assess the initial safety characteristics of simufilam in healthy human volunteers and this study was not designed to, and did not, evaluate safety, tolerability and efficacy of simufilam in patients. Similarly, our Phase 2 clinical studies with simufilam were designed to assess the safety characteristics of simufilam in patients. Our Phase 2 program was not designed to, and did not, evaluate large-scale or long-term safety, tolerability and efficacy of simufilam in patients. There can be no assurance that future large, well-controlled, multi-dose studies will demonstrate the safety, tolerability or efficacy of simufilam to treat patients with any indication, including Alzheimer’s disease.

Even if our clinical trials for simufilam are completed as planned, we cannot be certain that their results will support the substantial evidence of safety and efficacy needed to obtain regulatory approval. The failure of simufilam to show safety, tolerability or efficacy in any future clinical studies would significantly harm our business.

Clinical results observed our smaller Phase 1 and Phase 2 clinical trials or 24-month Safety Study with simufilam are not regulatory evidence of drug safety or efficacy.

Data results from our non-Phase 3 studies do not constitute, and should not be interpreted as, regulatory evidence of safety or efficacy for simufilam in Alzheimer's disease. Rigorous evidence for drug safety and efficacy is derived from one or more large, randomized, placebo-controlled studies. The size and open-label design of portions of our non-Phase 3 studies may introduce clinical or statistical bias or may generate results that may not fully distinguish between drug effects and random variation. Different methods of statistical analysis on clinical data from the same study may lead to objectively different numerical results. These and other statistical and clinical features of our non-Phase 3 studies add complexity or limitations to the scope of data interpretation.

We may encounter substantial delays in our clinical studies or may not be able to conduct or complete our clinical studies on the timelines we expect, if at all.

Clinical testing is expensive, time consuming, and subject to uncertainty. We cannot guarantee that any clinical studies will be conducted as planned, enroll patients as planned or be completed on schedule, if at all. Moreover, even after our studies begin, safety or other issues may arise that could suspend or terminate such clinical studies. A failure of one or more clinical studies can occur at any stage of testing, and our ongoing or future clinical studies may not be successful. Events that may prevent successful or timely initiation or completion of clinical studies include:

- inability to generate sufficient or necessary preclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of clinical studies or to support the filing of a New Drug Application for simufilam;
- delays in confirming target engagement, patient selection, or other relevant biomarkers to be utilized in preclinical and clinical product candidate development;
- delays in reaching a consensus with regulatory agencies on study design;
- delays in reaching an agreement on acceptable terms with prospective clinical study sites, the terms of which can be subject to extensive negotiation and may vary significantly among different clinical study sites;
- delays in identifying and recruiting suitable clinical investigators;
- delays in obtaining required IRB approval for each clinical study site or adverse action by one or more IRBs;
- a new safety finding that presents unreasonable risk to clinical study participants;
- a negative finding from an inspection of our clinical research organization (CRO), clinical study operations or study sites;
- the finding that the investigational protocol or plan is deficient to meet its stated objectives;
- delays in identifying, recruiting, and enrolling suitable patients to participate in our clinical studies, and delays caused by patients withdrawing from clinical studies, or failing to return for post-treatment follow-up;
- delays caused by disease epidemics, pandemics, such as COVID-19, or other health crises;
- difficulty collaborating with patient groups and investigators;
- failure by our CRO or other third parties, or us to adhere to clinical study requirements;
- failure to perform in accordance with FDA's or any other regulatory authority's Code of Good Clinical Practice (GCP) requirements, or other regulatory guidelines in other countries;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional studies;
- the cost of clinical studies of our product candidates being greater than we anticipate;
- clinical studies of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical studies or abandon product development programs; and
- delays in manufacturing, testing, releasing, validating, or importing/exporting sufficient stable quantities of our product candidates for use in clinical studies or the inability to do any of the foregoing.

Any inability to successfully initiate or complete clinical studies could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, we may be required to, or we may elect, to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical study delays could also shorten any periods during which our products have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

Delays in the completion of any clinical study of our product candidates will increase our costs, slow down our product candidate development and approval process and delay, or potentially jeopardize our ability to commence product sales and generate revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical studies may also ultimately lead to the denial of regulatory approval of our product candidates or the termination of such clinical studies prior to their completion, either of which could adversely affect our business.

We have conducted, and continue to conduct, portions of our Phase 3 clinical trials outside the United States, and the FDA may not accept data from trials conducted in foreign locations.

We have conducted, and we expect to continue to conduct, portions of our Phase 3 clinical trials outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be conducted and performed by qualified investigators in accordance with ethical principles. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. In general, the patient population for any clinical trials we conduct outside the United States must be representative of the population for which we intend to label the product in the United States. In addition, while Phase 3 clinical trials conducted outside the United States are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. We cannot assure you that the FDA will accept data from portions of our Phase 3 trials conducted outside the United States. If the FDA does not accept such data from such clinical trials, we would likely need to conduct additional trials, which would be costly and time-consuming and delay or permanently halt our development of simufilam, our lead investigational product.

The FDA or other regulatory agencies may put a clinical hold on our clinical studies, which would cause our business to suffer.

A clinical hold is an order issued by FDA or another regulatory agency to suspend an ongoing clinical trial, typically due to newly identified deficiencies with, or the need for additional information regarding, the subject study or drug candidate. For example, we are aware that in 2022, FDA placed clinical holds on drug candidates for Alzheimer's disease from two competitors, Cortexzyme Inc. and Denali Therapeutics Inc. The grounds for imposition of a clinical hold are complex, variable and fact specific. If FDA imposes a clinical hold on us, no new patients may be enrolled in the subject study and study patients already in such study may be taken off our drug candidate unless treatment is specifically permitted by FDA in the interest of patient safety. If we are issued a clinical hold, FDA would expect us to address the cited deficiencies or provide the requested additional information, in each case, through the submission of a detailed, written response. A clinical hold would require us to spend significant resources, potentially over an extended period of time, to address the root causes of FDA's concerns, even if we disagreed with the FDA's assessment of asserted deficiencies. If we were unable to find and successfully address such root causes or if our response were deemed inadequate to lift the clinical hold, this could adversely affect our business. If we were subjected to a clinical hold that remained in effect for one year or longer, the FDA may consider the IND for the affected product candidate to fall into Inactive Status, which may result in termination of the corresponding clinical program. To the extent we are not successful in lifting any clinical hold that the FDA might impose, our results of operations and business will be materially adversely affected.

If physicians and patients do not accept and use our drugs, we will not achieve sufficient product revenues and our business will suffer.

Even if FDA approves our drugs, physicians and patients may not accept and use them. Acceptance and use of our drugs will depend on a number of factors including:

- when the drug is launched into the market and related competition;

- approved label claims;
- perceptions by members of the healthcare community, including physicians, about the safety, side effects and effectiveness of our drugs;
- perceptions by physicians regarding the cost-benefit of our product candidates;
- published studies demonstrating the cost effectiveness of our drugs relative to competing products;
- availability of reimbursement for our products from government or healthcare payers;
- effectiveness of marketing and distribution efforts by us and other licensees and distributors.

Because we expect to rely on sales generated by our current lead product candidates for substantially all of our revenues for the foreseeable future, the failure of any of these drugs to find market acceptance would harm our business and could require us to seek additional financing.

We may not be successful in developing our product candidates in neurodegeneration.

In addition to the risks associated with our Phase 3 clinical trials for simufilam, SavaDx and our future product candidates in neurodegeneration are still in development. Such early stage product candidates will take several years to develop and must undergo extensive clinical and scientific validations. Even if we are successful in developing any of our product candidates through clinical and scientific validation, we may not be able to develop a drug or a diagnostic that:

- meets applicable regulatory standards, in a timely manner or at all;
- successfully competes with other technologies and tests;
- avoids infringing the proprietary rights of others;
- is adequately reimbursed by third-party payors;
- can be performed at commercial levels or at reasonable cost; or
- can be successfully marketed.

To the extent we are not successful in developing our new product candidates in neurodegeneration, our results of operations and business will be materially adversely affected.

Interim, "top-line" and preliminary data from our clinical trials that we announce or publish from time to time are likely to change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final dataset.

From time to time, we may publish "top-line" or preliminary data from our clinical trials. 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 at the time of its initial release. As a result, the top-line 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. Such data from clinical trials may materially change as more study data become available. Preliminary or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, preliminary top-line data should be viewed with caution until the final data is available. Differences between preliminary or top-line data and final data could significantly harm our business prospects and may cause the trading price of our securities to fluctuate significantly.

Furthermore, other parties, 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 than us, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is typically selected from a more extensive amount of available information. You or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the preliminary or topline data that we report differ from later, final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize our product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects.

We currently have no in-house capabilities to manufacture or commercialize our product candidates and we rely on third-party commercial drug manufacturers for clinical drug supplies. If we are unable to develop our own manufacturing, sales, marketing and distribution capabilities, or if we are not successful in contracting with third parties for these services on favorable terms, or at all, our product revenues could be adversely impacted.

We rely on various third parties to manufacture, fill, label, store, test and ship our product candidates. We plan to continue to outsource formulation, manufacturing and related activities. These suppliers must comply with cGMP regulations enforced by FDA and other government agencies, and are subject to ongoing periodic unannounced inspection, including preapproval inspections by FDA and corresponding state and foreign government agencies to ensure strict compliance with cGMP and other standards. These manufacturers may subsequently be stopped from producing, manufacturing, filling, labeling, storing, testing and shipping our product candidates due to their non-compliance with federal, state or local regulations. We do not have control over our suppliers' compliance with these regulations and standards and we cannot control decisions by our suppliers that affect their ability or willingness to continue to supply us on acceptable terms, or at all.

Disputes in the past have arisen with some of these third parties with respect to fulfilling certain conditions and obligations. There can be no guarantee that such disputes will not arise again in the future, which may lead to termination of an agreement. If an agreement is terminated, we would not be able to commercialize our product candidates until another manufacturer is identified and we have entered into a manufacturing agreement with such manufacturer. We may not be able to replace a commercial supplier on commercially reasonable terms, or at all. Replacing any of our commercial suppliers would be expensive and time consuming. Failure by any of our suppliers to perform as expected could delay or prevent the commercialization or potential regulatory approval of our product candidates for an extended period of time, result in shortages, cost overruns or other problems and would materially harm our business.

We currently have no sales, marketing or distribution capabilities. We have not established commercial strategies regarding any of our product candidates. In order to commercialize our products, if any are approved by FDA, we will either have to develop such capabilities internally or collaborate with third parties who can perform these services for us.

If we decide to commercialize any of our drugs ourselves, we may not be able to

- hire and retain the necessary experienced personnel;
- build sales, marketing and distribution operations in a cost-effective manner which are capable of successfully launching new drugs;
- obtain access to adequate numbers of physicians to prescribe our products; or
- generate sufficient product revenues.

In addition, establishing such operations on our own will take time and involve significant expense. If our commercial operations lack complementary products, we may not be able to compete in a cost-effective manner with competitors with more products to sell. If we engage third-party collaborators to perform any commercial operations, our future revenues may depend significantly upon the performance of those collaborators. If we decide to enter into new co-promotion or other licensing arrangements with third parties, we may be unable to locate acceptable collaborators because the number of potential collaborators is limited and because of competition from others for similar alliances. Even if we are able to identify one or more acceptable new collaborators, we may not be able to enter into any collaborative arrangements on favorable terms, or at all.

In addition, due to the nature of the market for our product candidates, it may be necessary for us to license all or substantially all of our product candidates to a single collaborator, thereby eliminating our opportunity to commercialize these other products independently. If we enter into any such new collaborative arrangements, our revenues are likely to be lower than if we marketed and sold our products ourselves.

In addition, any revenues we receive would depend upon our collaborators' efforts which may not be adequate due to lack of attention or resource commitments, management turnover, change of strategic focus, business combinations or other factors outside of our control. Depending upon the terms of our collaboration, the remedies we have against an under-performing collaborator may be limited. If we were to terminate the relationship, it may be difficult or impossible to find a replacement collaborator on acceptable terms, or at all.

We rely on third parties to conduct our studies and some aspects of our research, and such third parties may not perform satisfactorily, which could delay or harm our studies, research, and testing.

We substantially rely and expect to continue to rely on third parties, such as contract research organizations (CROs), clinical data management organizations, medical institutions, and clinical investigators, to conduct some aspects of our research and preclinical testing and our clinical studies. For example, Pentara Corporation, an independent consulting firm that specializes in complex statistical analysis of clinical trials, has conducted statistical analysis relating to cognition endpoints in our clinical studies. Any of these third parties may terminate their engagements with us or be unable to fulfill their contractual obligations. If we need to enter into alternative arrangements, it will delay our product development activities.

Our reliance on these third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that all of our clinical studies are conducted in accordance with the general investigational plan and protocols for the trial. Moreover, FDA requires us to comply with the norms of Good Clinical Practice (GCPs) for conducting, recording, and reporting the results of clinical studies to assure that data and reported results are credible, reproducible, and accurate and that the rights, integrity, and confidentiality of study participants are protected. We also are required to register ongoing clinical studies and post the results of completed clinical studies on a government-sponsored database within certain timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions.

If our third-party vendors do not successfully carry out their contractual duties, meet expected deadlines, or conduct studies in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for any product candidates we may develop and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. For example, one of our vendors failed to fully comply with certain Good Laboratory Practice (GLP) norms in its research facility, which required us to repeat a lab study at a different research site.

We also rely on other third parties to label, store and distribute drug supplies for our clinical studies. Any performance failure on the part of our distributors, including with the shipment of any drug supplies, could delay clinical development or marketing approval of any product candidates we may develop or commercialization of our product candidates, producing additional losses and depriving us of potential product revenue.

We may not be successful in our efforts to expand our technology or product candidates in other indications.

Our drug development strategy is to clinically test and seek regulatory approval for our product candidates in Alzheimer's disease dementia, our primary indication. We may expand our research efforts outside of this primary indication and into other areas of clinical medicine based on genetic, biological or mechanistic overlap with the primary indication. Conducting clinical studies for additional indications for our product candidates will require substantial technical, financial and human resources and is prone to the inherent risks of failure in drug development. We cannot provide any assurance that we will be successful in our effort to expand our technology or our product candidates in additional indications, even if we obtain approval for our product candidate in Alzheimer's disease.

If we fail to successfully identify and develop additional product candidates, our commercial opportunity will be limited to Alzheimer's disease or other neurodegenerations.

Identifying, developing, obtaining regulatory approval for, and commercializing additional product candidates requires substantial expertise and funding and is prone to the risks of failure inherent in drug development. We cannot provide any assurance that we will be able to successfully identify or acquire additional product candidates, advance any additional product candidates through the development process, or assemble sufficient resources to identify, acquire, or develop additional product candidates. If we are unable to successfully identify, acquire, develop, and commercialize additional product candidates, our commercial opportunity may be limited.

We have never obtained FDA approval for a diagnostic test and we may not be able to secure such approval in a timely manner or at all.

We are developing an investigational blood-based diagnostic test for Alzheimer's disease, called SavaDx, which will require FDA approval prior to commercialization. Our diagnostic product candidate, marketing, sales and development activities and manufacturing processes are subject to extensive and rigorous regulation by FDA pursuant to the FDCA, by comparable agencies in foreign countries, and by other regulatory agencies and governing bodies. Under the FDCA, a diagnostic must receive FDA clearance or approval before it can be commercially marketed in the United States. The process of obtaining marketing approval or clearance from FDA or by comparable agencies in foreign countries for new products could:

- take a significant period of time;
- require the expenditure of substantial resources;
- involve rigorous preclinical testing, as well as increased post-market surveillance;
- require changes to products; and
- result in limitations on the indicated uses of products.

If we do not compete effectively with scientific and commercial competitors, we may not be able to successfully develop our diagnostic test for Alzheimer's disease.

The field of clinical laboratory testing is highly competitive. Diagnostic tests are characterized by rapid technological change. Our competitors in the United States and abroad are numerous and include, among others, major diagnostic companies, reference laboratories, molecular diagnostic firms, universities and other research institutions. Most of our potential competitors have considerably greater financial, technical, marketing and other resources than we do, which may allow these competitors to discover important biological markers and determine their function before we do. We could be adversely affected if we do not discover proteins or biomarkers and characterize their function, develop diagnostic and pharmaceutical and clinical services based on these discoveries, obtain required regulatory and other approvals and launch these tests and their related services before our competitors. We also expect to encounter significant competition with respect to any diagnostic tests that we may develop or commercialize. Those companies that bring to market new diagnostic tests before we do may achieve a significant competitive advantage in marketing and commercializing their tests. We may not be able to develop additional diagnostic tests successfully and we may not obtain or enforce patents, if any, covering these tests that provide protection against our competitors. Moreover, our competitors may succeed in developing diagnostic tests that circumvent our technologies or tests. Furthermore, our competitors may succeed in developing technologies or tests that are more effective or less costly than those developed by us or that would render our technologies or tests less competitive or obsolete. We expect competition to intensify in the fields in which we are involved as technical advances in these fields occur and become more widely known and changes in intellectual property laws generate challenges to our intellectual property position.

We will need to develop our own proprietary antibodies or find alternative approaches that do not involve antibodies to advance our SavaDx and our diagnostic program.

To date, most of our tests with SavaDx have relied on the use of commercially available antibodies, which are complex molecules that can recognize and bind to an intended protein. Commercially available antibodies can present technical challenges, such as improper validation, significant batch-to-batch variations or inconsistent storage, any of which can jeopardize our studies and experiments. We are also evaluating an alternative approach to detect Alzheimer's disease using mass spectrometry to detect FLNA, i.e., without the use of antibodies. The complexity of such an alternative approach also gives rise to many technical issues that are challenging to solve. We cannot be certain that we will be able to successfully complete the development of a detection system for Alzheimer's disease that does or does not involve antibodies.

Our Phase 2 clinical studies with simufilam in patients with Alzheimer's disease are generally not designed to show a statistically meaningful difference in cognition or other health functions between those patients who receive placebo and those who receive drug.

Clinical research data is often analyzed with statistical probability (p-value) to address the question of whether a clinical observation is related to a treatment effect, a random effect or something else. This, in turn, requires a clinical study to incorporate a sufficiently large sample patient population to infer the appropriate statistical analysis. By design, our Phase 2 clinical studies with simufilam generally do not include a sufficiently large patient population to generate statistical probability on measures of cognition or other health functions. This feature may make it difficult for investors to properly interpret whether clinical observations in those Phase 2 studies with simufilam are important or meaningful. Conversely, our clinical studies may generate statistically significant data (i.e., $p<0.05$) on exploratory biomarkers, or other endpoints, that have unknown or no clinical importance. In general, the distinction between statistically significant data and clinically meaningful data is a complex area of research that continues to evolve and may be subject to differences of opinion among scientists, clinicians, biostatisticians and other professionals, as well as among government regulators.

In our open-label study, we observed apparent differences in treatment effects by stage of disease. These observations may or may not replicate in any of our subsequent clinical studies.

Alzheimer's dementia is a progressive, degenerate disease. Severity of disease is typically assessed by stage of disease progression, a continuum that ranges from, approximately, mild cognitive impairment (MCI), to early stage, to mild, to moderate and finally to severe disease. Over time, cognition progressively worsens in the mild-to-moderate stages of Alzheimer's as the disease takes its toll. However, we do not have a clear understanding of how our drug candidate simufilam may impact patients by stage of disease, if at all. For example, in our open-label and small placebo-controlled studies, we observed apparent differences in treatment effects by stage of disease. While we believe our data in mild patients may emphasize the importance of treating patients early in the disease, such observations may or may not replicate in any of our subsequent clinical studies.

We expect to rely on clinical results generated predominately, or even solely, from patients with mild Alzheimer's disease to show evidence of efficacy in our Phase 3 clinical trials, if any. Our reliance on patients with mild disease may narrow our ability to broadly market simufilam to the Alzheimer's disease community, if our drug candidate receives regulatory approval.

Our Phase 3 trials have randomized a total of approximately 1,900 patients with mild to moderate stages of Alzheimer's disease at baseline (MMSE 16-27). Approximately 70% of these patients are diagnosed with mild Alzheimer's disease (MMSE 20-27). Since the distribution of patients randomized into these trials is numerically skewed towards mild patients, we expect to rely predominantly, or even solely, on outcomes from mild patients to show evidence of drug efficacy, if any, in our Phase 3 trials. Our reliance on mild Alzheimer's patients to show evidence of drug efficacy in our Phase 3 trials may not allow us to meet the regulatory standards required to gain a broad label indication in Alzheimer's disease, and this may limit our ability to broadly market simufilam to the Alzheimer's disease community, if our drug candidate receives regulatory approval and becomes commercially available.

We may encounter difficulties keeping patients enrolled in our Phase 3 clinical studies, and our clinical development activities could thereby be delayed or otherwise adversely affected.

The successful completion of clinical studies in accordance with their protocols depends, among other things, on our ability to keep patients enrolled in our Phase 3 studies until study conclusion. Patients who are enrolled in our Phase 3 studies may terminate their participation for a many reasons, including:

- moving away from a clinical site;
- inability to keep appointments due to loss of mobility or caregiver;
- perceptions as to the efficacy of treatment, or lack thereof, including those who are randomized to placebo;
- side-effects associated with treatment;
- loss of interest or motivation to continue participation in clinical research;
- patient non-compliance or protocol deviations;
- interest in other available therapies and product candidates;
- withdrawal of patient consents; and
- the emergence of severe or debilitating health issues unrelated to study participation, such as a fall resulting in a fractured hip.

Our clinical studies may fail to demonstrate substantial evidence of the safety and efficacy of our product candidates, which would prevent, delay, or limit the scope of regulatory approval and commercialization.

Before obtaining regulatory approvals for any of our product candidates, we must demonstrate through lengthy, complex, and expensive preclinical experiments and clinical studies that our product candidates are both safe and effective for use in an intended population. Each product candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use, as determined by the FDA in the United States.

New drug discovery, development and commercialization involves a high degree of risk. The process is expensive and complex and can take many years to complete, and its outcome is inherently uncertain. It can take over 10 to 15 years and cost over $1 to $2 billion for each new drug candidate to achieve regulatory approval. Only a small number of research and development programs achieve regulatory approval and subsequent commercialization of a drug product. We believe that in recent decades about 90 to 95% of novel drug candidates under development by the biopharmaceutical industry have failed to achieve regulatory approval and subsequent commercialization. Failure can occur at any time during the drug discovery and development process and such failures may be due to lack of clinical efficacy, adverse safety profile, regulatory hurdles, excessive costs, lack of perceived market opportunity, lack of resources, insufficient reimbursement from insurers, inability to compete or for other reasons. Many biopharmaceutical companies have suffered significant setbacks in Phase 3 clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Seasoned professionals with a prior track record of innovation in drug discovery and development, as well as substantial business expertise, routinely fail to achieve regulatory approval of new product candidates.

The results of our preclinical studies with our product candidates may not be predictive of the results of early-stage or later-stage clinical studies, and results of early clinical studies of our product candidates may not be predictive of the results of later-stage clinical studies. The results of clinical studies in one set of patients or disease indications may not be predictive of those obtained in another. In some instances, there can be significant variability in safety or efficacy results between different clinical studies of the same product candidate due to numerous factors, including changes in study procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen, and other clinical study protocols and the rate of dropout among clinical study participants. Our open-label extension study may also extend the timing and overall cost of our clinical development program substantially. Product candidates in later stages of clinical studies may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical studies.

We may suffer significant setbacks in our ongoing Phase 3 clinical studies due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier studies. Clinical trials in neurodegenerative diseases, including Alzheimer's disease, have much higher historically failure rates than in many other disease areas. Most new product candidates for neurodegeneration that begin clinical studies are never approved by regulatory authorities for commercialization.

We have limited experience in designing clinical studies in neurodegeneration and may be unable to design and execute a clinical study to support marketing approval. We cannot be certain that our current clinical studies or any other future clinical studies will be successful. Additionally, any safety concerns observed in any one of our clinical studies in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications, which could have a material adverse effect on our business, financial condition, and results of operations.

In addition, even if such clinical studies are successfully completed, we cannot guarantee that FDA or foreign regulatory authorities will interpret the results as we do, and more studies could be required before we submit our product candidates for approval. To the extent that the results of the studies are not satisfactory to 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 studies in support of potential approval of our product candidates. Even if regulatory approval is secured for any of our product candidates, the terms of such approval may limit the scope and use of our product candidates, which may also limit its commercial potential.

If our drug candidate causes or contributes to a death or a serious injury before or after approval, we will be subject to medical reporting regulations, which can result in voluntary corrective actions or agency enforcement actions.

Our drug candidate in Alzheimer's disease is aimed at elderly patients with dementia, some of whom may be frail due to advanced age or underlying health issues. Under FDA medical reporting regulations, we are required to report to the FDA information that our drug candidate has or may have caused or contributed to a death or serious injury. Any such serious adverse event involving our drug could result in future FDA action, such as an inspection, enforcement action or warning, or in more serious cases, a complete shutdown of our clinical program. In the context of our ongoing clinical trials, we report adverse events to the FDA in accordance with applicable national and local regulations. Any corrective action, whether voluntary or involuntary, and either pre- or post-market, needed to address any serious adverse events will require the dedication of our time and capital, distract management from operating our business, and may harm our reputation and financial results.

The market opportunities for simufilam and SavaDx, if approved, may be smaller than we anticipate.

If our clinical development programs succeed, we expect to seek regulatory approval of simufilam and SavaDx for patients with Alzheimer's disease. Our projections of the number of patients with Alzheimer's disease is based on our beliefs and estimates. These estimates have been derived from a variety of outside sources, including scientific literature, patient foundations and market research, and may prove to be incorrect. The actual number of patients may turn out to be lower than expected. Additionally, the potential patient population for our current programs or future product candidates may be limited. Even if we obtain regulatory approval and capture significant market share for any product candidate, the potential target populations may be smaller than anticipated, and we may never achieve profitability without obtaining marketing approval for additional indications.

We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that additional competitors may achieve regulatory approval before us or develop therapies that are safer, more advanced, or more effective than ours, any of which may harm our business operations.

Drug discovery and development is highly competitive. Moreover, the neurodegenerative field is characterized by intense and increasing competition, and a strong emphasis on intellectual property. We may face competition with respect to any of our product candidates that we seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

In addition to Biogen, Eisai and Eli Lilly, several pharmaceutical and biotechnology companies are currently pursuing the development of products for the treatment of neurodegenerative diseases, including Alzheimer's disease. Many of these current or potential competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical studies, obtaining regulatory approvals, and marketing approved products than we do.

Our commercial opportunity could be reduced or eliminated if other competitors develop and commercialize products that are safer, are more effective, have fewer or less severe side effects, are more convenient, achieve greater acceptance among physicians and patients, or are less expensive than any products that we may develop. Furthermore, currently approved products could be discovered to have application for treatment of neurodegenerative disease indications, which could give such products significant advantages over any of our product candidates. Competitors other than Biogen, Eisai and Eli Lilly 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. Additionally, products or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, we could face litigation or other proceedings with respect to the scope, ownership, validity, and/or enforceability of our patents relating to our competitors' products and our competitors may allege that our products infringe, misappropriate, or otherwise violate their intellectual property. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

Risks Related to Government Regulation and Other Legal Compliance Matters

Our financial condition and operating results could be adversely impacted by unfavorable results of legal proceedings, government investigations or allegations and other claims, many of which arose following a short selling attack campaign against our Company that commenced in 2021.

We are, and may in the future be, subject to various investigations and legal proceedings.

In recent years, there has been a trend of increasing government investigations, legal proceedings and law enforcement activities against companies, executives and others operating in our industry, including those arising from whistleblower programs operated by the SEC and DOJ and the *qui tam* provisions of the False Claims Act.

We are currently managing inquiries from U.S. government agencies, as well as civil claims under federal and state laws, relating to and/or arising out of research and development of our product candidates, including grant applications, securities disclosures and other aspects of our business. For additional information regarding legal proceedings, see "Item 8. Financial Information—8.A. Consolidated Statements and Other Financial Information—Legal Proceedings". New claims or inquiries may arise in the future.

In response to government document requests and other claims asserted against us, we established a comprehensive document retention policy that strictly governs how we handle, store and protect our documents and data. Failure to comply with our document retention policy would expose us to risk of enforcement actions and penalties under applicable laws.

Legal proceedings are inherently unpredictable, and large judgments or penalties sometimes occur. As a consequence, we may in the future incur judgments or penalties that could involve large cash payments, including the potential repayment of amounts allegedly obtained improperly and other penalties, including enhanced damages. While we maintain insurance coverage for certain types of claims, such insurance coverage may be insufficient to cover all losses or all types of claims that may arise.

In addition, such proceedings against us or against third parties with whom we collaborate or otherwise do business may affect our reputation, inhibit our ability to raise fund in the capital markets, create a risk of potential exclusion from government reimbursement or grant programs and may lead to additional civil litigation. Even meritless claims could subject us to adverse publicity, hinder us from securing insurance coverage in the future or require us to incur significant legal costs. As a result, having taken into account all relevant factors, we may in the future enter into settlements of such claims without bringing them to final legal adjudication by courts or other such bodies, despite having potentially significant defenses against them, in order to limit the risks they pose to our business and reputation. Such settlements may require us to pay significant sums of money and to enter into corporate integrity or similar agreements intended to regulate company behavior for a period of years, which can be costly to operate under.

As a result, significant claims or legal proceedings to which we are a party, any judgments or settlements against us or involving third parties associated with us relating to such claims or proceedings, and any accruals that we may take with respect to potential judgments or settlements, could have a material adverse impact on our business, financial condition or results of operations, as well as on our reputation.

Additional future litigation involving us could be costly and time-consuming to defend.

Innovative drug development is highly litigious, and we may, from time to time, become subject to or involved in additional legal proceedings, claims and allegations that arise in the ordinary course of business or pursuant to governmental or regulatory enforcement activity. Regardless of merit, any lawsuits against or involving us, individually or in the aggregate, may have a material adverse effect on our business, financial condition, results of operations or cash flows. In addition, any litigation to which we subsequently become a party might result in substantial costs and divert management's attention, time and resources, which might seriously harm our business, financial condition, results of operations and cash flows. Our insurance policies might not cover such claims, might not provide sufficient payments to cover all of the costs to resolve one or more such claims, and might not continue to be available on terms acceptable to us. In particular, any claim could result in potential liability for us if the claim is outside the scope of the indemnification agreement we have with our third-party partners, or our third-party partners do not abide by the indemnification agreement as required, or the liability exceeds the amount of any applicable indemnification limits or available insurance coverage. A claim brought against us that is uninsured or underinsured could result in unanticipated costs and could have a material adverse effect on our financial condition, results of operations, cash flows or reputation.

If we are ultimately unable to file for and obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.

The time required to obtain approval by FDA and comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical studies, 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. 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 preclinical, clinical, or other studies. We have not obtained regulatory approval for any product candidate, including our product candidates aimed at Alzheimer’s disease, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Applications for our product candidates could fail to receive regulatory approval in an initial or subsequent indication for many reasons, including but not limited to the following:

- FDA or comparable foreign regulatory authorities may disagree with the design, implementation, or results of our clinical studies;
- FDA or comparable foreign regulatory authorities may determine that our product candidates are not safe and effective, only moderately 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 program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- we may be unable to demonstrate to FDA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio when compared to the standard of care is acceptable;
- FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical studies;
- the data collected from clinical studies of our product candidates may not be sufficient to support the submission of a new drug application (NDA), or other submission or to obtain regulatory approval in the United States or elsewhere;
- FDA or 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 FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical studies, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations, and growth prospects.

Our ability to market and promote our product candidates will be determined and limited by FDA-approved labeling.

The commercial success of our product candidates will depend upon our ability to obtain FDA-approved labeling effectively describing their features. If a product receives regulatory approval, the approval may be significantly limited to specific disease stages, patient populations and dosages, or the indications for use may otherwise be limited, which could restrict the availability of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling or may condition the approval of the NDA on other changes to the proposed labeling or a commitment to conduct one or more post-market studies or clinical trials. For example, the FDA may require Phase 4 testing which involves clinical trials designed to further assess a drug's safety and effectiveness.

Our failure to achieve FDA approval of product labeling containing appropriate information will prevent us from advertising and promoting the key features of our product candidates in order to differentiate them from other similar products. On the other hand, limitations required by the FDA for the product labeling of our product candidates may restrict the patient populations to which our product candidate is available. Either of these results would make our products less competitive in the market the commercial value of the product.

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

We are exposed to the risk of fraud, misconduct, or other illegal activity by our employees, independent contractors, consultants, commercial partners, and vendors. Misconduct by these parties could include intentional, reckless, and negligent conduct that fails to:

- comply with the laws of FDA and other comparable foreign regulatory authorities;
- provide true, complete, and accurate information to FDA and other comparable foreign regulatory authorities;
- comply with manufacturing standards we have established;
- comply with healthcare fraud and abuse laws in the U.S. and similar foreign fraudulent misconduct laws;
- report financial or clinical information or data accurately or to disclose unauthorized activities to us; or
- otherwise comply with applicable criminal, civil or regulatory laws governing their conduct.

Activities subject to laws also involve the improper use of information obtained in the course of patient recruitment for clinical studies, which could result in regulatory sanctions and cause serious harm to our reputation. Further, it is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws. 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 fines or other sanctions.

If we fail to comply or stay in compliance with the complex set of federal, state, local and foreign laws and regulations that apply to our business, we could suffer severe consequences that could materially and adversely affect our operating results and financial condition.

We are obligated to comply with the laws of all countries and jurisdictions in which we operate. These laws cover an extremely wide and growing range of activities. Such legal requirements can vary from country to country, and new requirements may be imposed on us from time to time as government and public expectations regarding acceptable corporate behavior change, and enforcement authorities modify interpretations of legal and regulatory provisions and change enforcement priorities. In addition, we rely on numerous associates, independent contractors, consultants, commercial partners and vendors who may put our reputation, business and operations at risk of material impairment if they engage, or are alleged to engage, in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, in violation of such laws and public expectations.

The laws and regulations that govern our operations include, among others:

- the Clinical Laboratory Improvement Amendments (CLIA) of 1988, which are United States federal regulatory standards that apply to all clinical laboratory testing performed on humans in the United States, requires that laboratories obtain certification from the federal government, and state licensure laws;
- FDA laws and regulations , including those relating to off-label marketing;
- the Health Insurance Portability and Accountability Act (HIPAA), which imposes comprehensive federal standards with respect to the privacy and security of protected health information and requirements for the use of certain standardized electronic transactions, including penalties for violators, enforcement authority to state attorneys general and requirements for breach notification;
- state laws regulating testing and protecting the privacy of test results, as well as state laws protecting the privacy and security of health information and personal data and mandating reporting of breaches to affected individuals and state regulators;
- the federal anti-kickback law, or the Anti-Kickback Statute, which prohibits knowingly and willfully offering, paying, soliciting, receiving, or providing remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual, or the furnishing, arranging for, or recommending of an item or service that is reimbursable, in whole or in part, by a federal health care program;
- the federal False Claims Act (FCA), which imposes liability on any person or entity that, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment to the federal government and which, under its *qui tam* provisions, allows private litigants (called “relators”) to file claims under seal on behalf of the government and to receive a percentage of recoveries obtained as a result;
- the federal Civil Monetary Penalties Law, which prohibits, among other things, the offering or transfer of remuneration to a Medicare or state health care program beneficiary if the person knows or should know it is likely to influence the beneficiary’s selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state health care program, unless an exception applies;
- other federal and state fraud and abuse laws, such as anti-kickback laws, prohibitions on self-referral, and false claims acts, which may extend to services reimbursable by any third-party payor, including private insurers;
- the Foreign Corrupt Practices Act (FCPA) and other worldwide anti-bribery laws, including those that prohibit companies and their intermediaries from making improper payments to government officials or other third parties for the purpose of obtaining or retaining business, and laws that prohibit commercial bribery;
- import, export control and economic sanctions laws and regulations in the U.S. and elsewhere;
- Federal securities laws, including provisions of the Exchange Act and Dodd-Frank Act under which whistleblowers that report alleged violations of wrongdoing can obtain up to 30% of related recoveries;
- the federal Physician Payments Sunshine Act, which requires manufacturers to track and report to the federal government certain payments and other transfers of value made to physicians and teaching hospitals and ownership or investment interests held by physicians and their immediate family members;
- section 216 of the federal Protecting Access to Medicare Act of 2014 (PAMA), which requires applicable laboratories to report private payer data in a timely and accurate manner every three years (and in some cases annually);

- state laws that impose reporting and other compliance-related requirements; and
- similar foreign laws and regulations that will apply to us in foreign countries in which we may choose to operate in the future.

Government agencies may establish and promulgate usage guidelines that could limit the use of our product candidates.

Government agencies, professional and medical societies, and other groups may establish usage guidelines that apply to our product candidates. These guidelines could address such matters as usage and dose, among other factors. Application of such guidelines could limit the clinical use or commercial appeal of our product candidates.

Our product candidates may cause undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences.

During the conduct of clinical trials, study participants report changes in their health to their doctor, including illnesses, injuries and discomforts. Often, it is not possible to determine whether our product candidate caused these conditions. Regulatory authorities may draw different conclusions and may require us to pause our clinical trials or require additional testing to confirm these determinations, if they occur. In addition, we have not yet completed long-term safety studies with simufilam to determine if this product candidate is safe for humans. Adverse events or other undesirable side effects caused by simufilam could cause us or regulatory authorities to interrupt, delay, or halt clinical studies and could result in a more restrictive label or the delay or denial of regulatory approval by FDA or other comparable foreign regulatory authorities. Drug-related side effects could affect patient recruitment, the ability of enrolled patients to complete the study, and/or result in potential claims.

We may be subject to legal liability associated with clinical trials.

Our business requires us to engage in the conduct of clinical studies in human volunteers and in patients in the United States and abroad. There are circumstances under which a participant in one of our clinical trials could impose liability on us. For example, a clinical investigator who is a participant in one of our studies may intentionally or unintentionally deviate from a clinical protocol and cause harm to a clinical trial participant, or a clinical trial participant may seek to compel us to continue to supply drug to them after the completion of a study but prior to FDA approval.

Claims may be brought against us for negligence, breach of contract, harm, injury or death, or other legal theories based on the nature of a study. Clinical trial liability is a complex and somewhat unsettled area of law and may vary by state and by country where we conduct clinical studies. Furthermore, claims may be brought against us by a clinical investigator, a clinical trial participant, or another party associated with a clinical study, long after the completion of a clinical study. Defense of such actions is a fact-intensive process that could be costly and involve significant time and attention of our management and other resources, may result in monetary liabilities or penalties, and may require us to change our business in an adverse manner.

Our insurance policies may be inadequate and potentially expose us to unrecoverable risks.

Although we maintain product liability insurance coverage, such insurance may not be adequate to cover all liabilities that we may incur. We anticipate that we may need to increase our insurance coverage each time we commence a clinical trial and if we successfully commercialize any product candidate. Insurance availability, coverage terms and pricing continue to vary with market conditions. We endeavor to obtain appropriate insurance coverage for insurable risks that we identify; however, we may fail to correctly anticipate or quantify insurable risks, we may not be able to obtain appropriate insurance coverage and insurers may not respond as we intend to cover insurable events that may occur. We do not carry a separate cybersecurity commercial insurance policy covering the potential financial losses that may occur in the event we experience a cybersecurity incident. Conditions in the insurance markets relating to nearly all areas of traditional corporate insurance change rapidly and may result in higher premium costs, higher policy deductibles and lower coverage limits. For some risks, we may not have or maintain insurance coverage because of cost or availability.

We are and will be required to maintain product liability insurance pursuant to certain of our development and commercialization agreements. We may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. A successful product liability claim or series of claims brought against us could adversely affect our results of operations, business, and reputation. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, withdrawal of clinical study participants, costs due to related litigation, distraction of management's attention from our primary business, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our product candidates, and decreased demand for our product candidates, if approved for commercial sale.

If our product candidates receive regulatory approval, we and our collaborators will be subject to ongoing FDA obligations and continued regulatory review, such as continued safety reporting requirements, and we and our collaborators may also be subject to additional FDA post-marketing obligations or new regulations, all of which may result in significant expense and limit our and our collaborators' ability to commercialize our potential drugs.

Any regulatory approvals that our product candidates receive may also be subject to limitations on the indicated uses for which the drug may be marketed or contain requirements for potentially costly post-marketing follow-up studies. In addition, if FDA approves any of our product candidates, the labeling, packaging, adverse event reporting, storage, advertising, promotion and record keeping for the drug will be subject to extensive regulatory requirements. The subsequent discovery of previously unknown problems with the drug, including but not limited to adverse events of unanticipated severity or frequency, or the discovery that adverse events previously observed in preclinical research or clinical studies that were believed to be minor actually constitute much more serious problems, may result in restrictions on the marketing of the drug, and could include withdrawal of the drug from the market.

The FDA's policies may change, and additional government regulations may be enacted that could prevent or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. If we are not able to maintain regulatory compliance, we may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution. Any of these events could prevent us from marketing our products and our business could suffer.

Enacted and future legislation may increase the difficulty and cost for us to commercialize our product candidates and may reduce the prices we are able to obtain for our product candidates.

Legislative and regulatory changes and future changes regarding the healthcare system could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities or affect our ability to profitably sell any product candidates for which we obtain marketing approval.

In the U.S., the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (the Medicare Modernization Act) established the Medicare Part D program and provided authority for limiting the number of drugs that will be covered in any therapeutic class thereunder. The Medicare Modernization Act, including its cost reduction initiatives, could limit the coverage and reimbursement rate that we receive for any of our approved products. Private payors may follow Medicare coverage policies and payment limitations in setting their own reimbursement rates resulting in similar limits in payments from private payors.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act, among other things, imposes a significant annual fee on companies that manufacture or import branded prescription product candidates. It also contains substantial provisions intended to, among other things, broaden access to health insurance, reduce or constrain the growth of health care spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, and impose additional health policy reforms, any of which could have a material adverse effect on our business. A significant number of provisions are not yet, or have only recently become, effective, but the Affordable Care Act may result in downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

The Affordable Care Act, as well as other healthcare reform measures that have been and 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 product, and could seriously harm our future revenues. 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 compromise our ability to generate revenue, attain profitability or commercialize our products. The Affordable Care Act is a highly complex piece of legislation that continues to evolve. We do not and cannot understand or anticipate the full impact and potential implications of the Affordable Care Act on our business or on our drugs.

The purported goal of the Inflation Reduction Act (IRA) of 2022 is to lower healthcare costs for Americans, and includes several provisions aimed at reducing drug spending and increasing access to pharmaceuticals. Specifically, the IRA introduces drug-price negotiations by requiring the federal government to negotiate “maximum fair prices” with drug manufacturers for certain brand-name, single-source drugs covered under Medicare Part B and Part D. In addition, the IRA penalizes price increases and expands required discounts on branded, single-source drugs. The IRA is a highly complex piece of legislation that continues to evolve. We do not and cannot understand or anticipate the full impact and potential implications of the IRA on our business or on our drugs, however, we currently believe the IRA may reduce the prices we are able to obtain for our product candidates, if approved in the United States.

Our relationships with customers and payors will be subject to applicable anti-kickback, fraud and abuse, transparency, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm, administrative burdens, and diminished profits and future earnings.

Healthcare providers, physicians and payors play a primary role in the recommendation and prescription of any product candidates for which we may obtain marketing approval. Our current or future arrangements with 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 any product candidates for which we may obtain marketing approval. Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. Restrictions under applicable federal, state and foreign healthcare laws and regulations may affect our ability to operate and expose us to areas of risk, including:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the FCA, which imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA;
- HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute to defraud any healthcare benefit program or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and its implementing regulations, which also imposes obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- federal laws requiring drug manufacturers to report information related to payments and other transfers of value made to physicians and other healthcare providers, as well as ownership or investment interests held by physicians and their immediate family members, including under the federal Open Payments program, commonly known as the Sunshine Act, as well as other state and foreign laws regulating marketing activities; and
- state and foreign equivalents of each of the above laws, including state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers; state laws which 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 restricting payments that may be made to healthcare providers; 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 often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Nonetheless, it is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain sufficient patent protection for any product candidates, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize any product candidates we may develop may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the U.S. and other countries with respect to our proprietary product candidates and other technologies we may develop. We seek to protect our proprietary position by filing patent applications in the U.S. and abroad relating to our core programs and product candidates, as well as other technologies that are important to our business. Given that our product candidates are in early or clinical stages of development, our intellectual property portfolio with respect to certain aspects of our product candidates is also at an early stage. We have filed or intend to file patent applications on aspects of our technology and core product candidates; however, there can be no assurance that any such patent applications will issue as granted patents. Furthermore, in some cases, we have filed only provisional patent applications on certain aspects of our technology and product candidates and each of these provisional patent applications is not eligible to become an issued patent until, among other things, we file a non-provisional patent application within 12 months of the filing date of the applicable provisional patent application. Any failure to file a non-provisional patent application within this timeline could cause us to lose the ability to obtain patent protection for the inventions disclosed in the associated provisional patent applications.

Furthermore, in some cases, we may not be able to obtain issued claims covering compositions relating to our core programs and product candidates, as well as other technologies that are important to our business, and instead may need to rely on filing patent applications with claims covering a method of use and/or method of manufacture for protection of such core programs, product candidates, and other technologies. There can be no assurance that any such patent applications will issue as granted patents, and even if they do issue, such patent claims may be insufficient to prevent third parties, such as our competitors, from utilizing our technology. Any failure to obtain or maintain patent protection with respect to our core programs and product candidates could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

U.S. intellectual property rights around diagnostic methods is a complex, evolving area of law and effective patent claims may not be available to us for our investigational diagnostic product candidate, SavaDx, in the United States.

The legal system for intellectual property around diagnostic methods is highly complex, remains uncertain and continues to evolve. In the U.S., patent courts have struggled to define a clear means of patent eligibility for modern age diagnostics. Case law interpretations from the U.S. Supreme Court have left certain important scientific advances in the area of diagnostics without effective patent claims. In 2012, the Supreme Court held that a simple process involving correlations between blood test results and patient health is not eligible for patent claims because such processes incorporate “laws of nature”. Since then, different outcomes from different courts, including Federal Circuit, District Court and Patent Trial and Appeal Board decisions, have continued to create a sometimes vague or conflicting legal framework for determining the eligibility of patent claims for diagnostic methods. As a result, we cannot be certain how SavaDx fits into the current U.S. legal framework for obtaining effective patent protection. We currently have no U.S. patents or patent applications with respect to SavaDx, and we believe it may be protected in the United States only by trade secrets, know-how and other proprietary rights technology. Furthermore, claims for diagnostic methods can be complicated to enforce. For patent infringement to occur with a protected diagnostic, the patented method must generally either be performed by one person in its entirety or performed by multiple parties all under the control or direction of a single party. Accordingly, even if effective patent claims are issued for SavaDx, it may be impractical, impossible or even undesirable to enforce potential infringement claims.

Issued patents covering our product candidates and other technologies could be found invalid or unenforceable if challenged in court or before administrative bodies in the U.S. or abroad.

If we initiated legal proceedings against a third party to enforce a patent covering our product candidates or other technologies, the defendant could counterclaim that the asserted patent is invalid or unenforceable. In patent litigation in the U.S. and in other jurisdictions, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may raise claims challenging the validity or enforceability of our patents before administrative bodies in the U.S. or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, 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 in such a way that they no longer cover our product candidates or other technologies. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we or our licensing partners 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 product candidates or other technologies. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations, and growth prospects.

If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration, and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Act). The Hatch-Waxman Act permits a patent term extension of up to five years as compensation for patent term lost during 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, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar extensions as compensation for patent term lost during regulatory review processes are also available in certain foreign countries and territories, such as in Europe under a Supplementary Patent Certificate. However, we may not be granted an extension in the U.S. and/or foreign countries and territories because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, 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 a patent term extension or the term of any such extension is shorter than what we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and growth prospects could be materially harmed.

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

In addition to seeking patents for our product candidates and other technologies, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology, and other proprietary information and to maintain our competitive position. We consider trade secrets and know-how to be one of our primary sources of intellectual property. Trade secrets and know-how can be difficult to protect. We expect our trade secrets and know-how to over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel from academic to industry scientific positions.

We seek to protect these trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, CROs, CDMOs, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants as well as train our employees not to bring or use proprietary information or technology from former employers to us or in their work, and remind former employees when they leave their employment of their confidentiality obligations. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. Despite our efforts, 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 illegally 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 U.S. are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

If any of our patent applications do not issue as patents in any jurisdiction, we may not be able to compete effectively.

Changes in either the patent laws or their interpretation in the U.S. and other countries may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our patents with respect to our product candidates. With respect to our intellectual property related to our product candidates, we cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors or other third parties.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, or enforce all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into nondisclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, outside scientific collaborators, CROs, CDMOs, consultants, advisors, and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in any of our patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

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 technology and product candidates would be adversely affected.

The patent position of biotechnology and pharmaceutical 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 may not result in patents being issued which protect our product candidates or other technologies or which effectively prevent others from commercializing competitive technologies and 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 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 to which we have rights may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether product candidates or other technologies will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents 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 growth prospects.

The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our patents may be challenged in the courts or patent offices in the U.S. and abroad. We may be subject to a third-party pre-issuance submission of prior art to the United States Patent and Trademark Office (USPTO) or become involved in opposition, derivation, revocation, reexamination, post-grant and *inter partes* review, or interference proceedings 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, such patent rights, allow third parties to commercialize our product candidates or other technologies 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, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our priority of invention or other features of patentability with respect to our patents and patent applications. 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 or identical technology and products, or limit the duration of the patent protection of our product candidates and other technologies. 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. If we are unsuccessful in any such proceeding or other priority or inventorship dispute, we may be required to obtain and maintain licenses from third parties, including parties involved in any such interference proceedings or other priority or inventorship disputes. Such licenses may not be available on commercially reasonable terms or at all or may be non-exclusive. If we are unable to obtain and maintain such licenses, we may need to cease the development, manufacture, and commercialization of one or more of the product candidates we may develop. The loss of exclusivity or the narrowing of our owned and licensed patent claims could limit our ability to stop others from using or commercializing similar or identical technology and products.

In addition, given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product 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.

We may not be able to protect our intellectual property and proprietary rights throughout the world.

Filing, prosecuting, and defending patents on our product candidates and other technologies in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the U.S.

Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products, and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the U.S. These products may compete with our products, and our patents 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 certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary 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 at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by government 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 government fees on patents and applications will be due to be paid to the USPTO and various government patent agencies outside of the U.S. over the lifetime of our owned or licensed patents and applications. The USPTO and various non-U.S. government agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

Changes in either the patent laws or interpretation of the patent laws in the U.S. could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the U.S., the first to invent the claimed invention was entitled to the patent, while outside the U.S., the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act (the America Invents Act) enacted in September 2011, the U.S. transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This requires us to be cognizant of the time from invention to filing of a patent application. Since patent applications in the U.S. and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we were the first to either (i) file any patent application related to our product candidates or other technologies or (ii) invent any of the inventions claimed in our patents or patent applications.

The America Invents Act also significantly affects the way patent applications are prosecuted and as well as patent litigation. This includes allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings as compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

In addition, the patent positions of companies in the development and commercialization of pharmaceuticals are particularly uncertain. Various U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

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

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

We may not be successful in obtaining necessary rights to our product candidates or other technologies.

Many pharmaceutical companies, biotechnology companies, and academic institutions that compete with us in the field of neurodegeneration therapy may have patents filed and are likely filing patent applications potentially relevant to our business. In order to avoid infringing these third-party patents, we may find it necessary or prudent to obtain licenses to such patents from such third-party intellectual property holders. We may also require licenses from third parties for certain technologies for use with future product candidates. In addition, with respect to any patents we co-own with third parties, we may wish to obtain licenses to such co-owner's interest to such patents. However, we may be unable to secure such licenses or otherwise acquire any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for our future product candidates. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several 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 rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

We may be subject to claims that our employees, consultants, or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property which may prevent or delay the development of our product candidates.

The field of developing innovations for neurodegenerative diseases is highly competitive and dynamic. Due to the focused research and development that is taking place by several companies, including us and our competitors, the intellectual property landscape in this field is in flux, and it may remain uncertain in the future. Additionally, no products utilizing our underlying science and technology have yet reached the market. As such, there may be significant intellectual property related litigation and proceedings relating to our, and other third party, intellectual property and proprietary rights in the future.

Many of our employees, consultants, and advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors and potential competitors. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. 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. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

Our commercial success depends in part on our ability to develop, manufacture, market, and sell any product candidates that we develop and to use our proprietary technologies without infringing, misappropriating, and otherwise violating the patents and other intellectual property rights of third parties. There is a substantial amount of complex litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may become party to, or threatened with, such actions in the future, regardless of their merit. As discussed above, recently, due to changes in U.S. law referred to as patent reform, new procedures including *inter partes* review and post-grant review have been implemented. As stated above, this reform adds uncertainty to the possibility of challenge to our patents in the future.

Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates and other technologies may give rise to claims of infringement of the patent rights of others. Although we believe that we do not infringe on any third parties' patents or other intellectual property, we cannot assure you that our product candidates and other technologies that we have developed, are developing or may develop in the future will not infringe existing or future patents owned by third parties. We may not be aware of patents that have already been issued to a third party, such as a competitor in the fields in which we are developing product candidates, who might assert infringement of patents it may hold by our current or future product candidates or other technologies, including claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover our product candidates or other technologies. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our product candidates or other technologies, could be found to be infringed by our product candidates or other technologies. In addition, 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 product candidates or other technologies may infringe.

Engaging in litigation to defend against third parties alleging that we have infringed, misappropriated, or otherwise violated their patents or other intellectual property rights is very expensive, particularly for a company of our size, and time-consuming. Some of our competitors may be able to sustain the costs of litigation or administrative proceedings more effectively than we can because of greater financial resources. Patent litigation and other proceedings may also absorb significant management time. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings against us could impair our ability to compete in the marketplace. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time consuming, and unsuccessful.

Competitors may infringe on our patents or the patents of our licensing partners, or we may be required to defend against claims of infringement. In addition, our patents or the patents of our licensing partners also may become involved in inventorship, priority, or validity disputes. To counter or defend against such claims can be expensive and time consuming. In an infringement proceeding, a court may decide that a patent in which we have an interest is invalid or unenforceable, the other party's use of our patented technology falls under the safe harbor to patent infringement, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our 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 and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Intellectual property rights do not necessarily address all potential threats.

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 make products that are similar to our product candidates or utilize similar technology but that are not covered by the claims of the patents that we may own;
- we might not have been the first to make the inventions covered by the issued patent or pending patent application that we own now or in the future;
- we might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned intellectual property rights;
- it is possible that our current or future pending patent applications will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties;
- our competitors or other third parties 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 harm our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

Risks Related to Our Business and Operations

Our reputation and operations could be adversely impacted by allegations of wrongdoing, regardless of their merits.

We believe that our reputation has significantly contributed to the success of our business. We also believe that maintaining and enhancing our reputation is critical to many of our core operations, such as conducting studies, working with outside vendors, attracting qualified employees, members of our Board of Directors and science collaborators, raising funds for future operations, and working with potential industry and government collaborators. Maintaining and enhancing our reputation will depend largely on our ability to develop innovative drug products, continue to generate credible scientific data and respond appropriately to our critics, which we may not do successfully.

Our reputation may be injured by the dissemination of false statements purporting to be fact, mischaracterizations of our scientific data, or by hostile actions made by or paid for by parties associated with market participants who seek a decline in the price of our securities (“short-sellers”) as well as media coverage of the foregoing. Allegations, mischaracterizations and similar statements may be disseminated directly to third parties with whom we interact, published in forums over which we have no control, such as through online social media channels or publicized as a result of media coverage, and may be adopted by the editors of scientific or technical journals that have published our research, potentially resulting in retractions or expressions of concern by the journals. For example, although no journal has asserted that we or any of our employees or consultants has inappropriately manipulated data or engaged in any misconduct, public short-seller allegations have prompted several journals to reassess certain peer-reviewed articles previously published by researchers associated with us and to retract articles or issue expressions of concern.

Regardless of merit, allegations, mischaracterizations and false statements may spread quickly and erode confidence in our reputation. Maintaining and enhancing our reputation may require us to make substantial investments in legal actions or other activities, and these investments could be expensive, time consuming, and unsuccessful. If we fail to successfully maintain our reputation, or if we incur excessive expenses in this effort, our business, operations, future prospects, cash flows, and financial position may be adversely affected.

Our current dependence on single source suppliers for our drug substance and drug product could materially adversely affect our ability to manufacture our product candidates and materially increase our costs.

We rely on single source suppliers for materials that are critical to the manufacturing of simufilam, our lead product candidate. This reliance subjects us to risks related to our potential inability to obtain an adequate supply of required materials. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct their activities in accordance with regulatory requirements, or if there are disagreements between us and these third parties, we may not be able to complete, or may be delayed in completing, the clinical studies required to support future regulatory submissions and approval of the product candidates we develop. Our operating results could be materially adversely affected if we were unable to obtain adequate supplies of simufilam in a timely manner or if their cost increased significantly due to inflation or other factors.

Further, under certain circumstances, service providers that have contracted with us may be entitled to terminate their engagements with us. In such circumstances, product development activities could be delayed while we seek to identify, validate, and negotiate an agreement with a replacement service provider. In some such cases an appropriate replacement may not be readily available or available on acceptable terms, which could cause additional delays to our development process. It would likely result in production and delivery delays if we needed to find alternative suppliers for simufilam, which could lead to delays in our clinical trials and have a material adverse effect on our business, results of operations and financial condition

Inadequate Congressional funding for the FDA, the SEC and other U.S. government agencies or comparable foreign regulatory authorities, including from government shut downs, or other disruptions to these agencies' operations, could hinder these agencies' ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent government 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 or comparable foreign regulatory authorities 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 enact statutory, regulatory and policy changes. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business.

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, unpredictable and entirely beyond our control.

Disruptions at the FDA and other agencies may also slow the time necessary for us and the FDA to communicate and continue discussions on key aspects of our Phase 3 clinical analysis, or for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, in prior years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA or SEC to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

The FDA may change the statutory requirements for drug approval.

FDA Guidances for Industry are non-binding policy documents that are issued by FDA from time to time to assist sponsors, such as our Company, with the clinical development of drug candidates. Even though such guidance documents do not set legal standards or impose binding requirements they are nonetheless broadly followed by sponsors, including us. In addition, sponsors who adhere in good faith with earlier guidance documents have no assurance or recourse against enforcement actions if the guidance documents are later replaced with conflicting guidance. We have relied heavily on current FDA guidance and meetings with the FDA to advance simufilam through the drug development process. Any future changes to existing FDA Guidance for Industry for Alzheimer's disease may have a material adverse effect on our business, may add significant time, cost or complexity to our drug development program for simufilam, or could cause us to cease or delay development of some or all our product candidates.

In addition, changes in FDA regulations, statutes or the interpretation of existing regulations and statutes could impact our business by requiring, for example: (i) changes to our manufacturing arrangements for simufilam; (ii) additions or modifications to product labeling, if and when our product candidates are approved for sale; (iii) the recall or discontinuation of our product candidates from investigational clinical sites; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they may have a material adverse effect on our business, may add significant time, cost or complexity to our drug development program for simufilam, or could cause us to cease or delay development of some or all our product candidates.

Our reliance on third parties for both the supply and manufacture of materials for our product candidates carries the risk that we will not have sufficient quality or quantities of such materials or product candidates, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.

We do not have any manufacturing facilities. We currently rely on CDMOs for all of the manufacture of our materials for preclinical studies and clinical studies and expect to continue to do so for preclinical studies, clinical studies, and for commercial supply of any product candidates that we may develop. We currently have established relationships with several CDMOs for the manufacturing of our product candidates. We may be unable to establish any further agreements with CDMOs or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on CDMOs entails additional risks, including:

- the possible breach of the manufacturing agreement by the third party;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- reliance on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting; and
- the inability to produce required volume in a timely manner and to quality standards.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the U.S. Our failure, or the failure of our CDMOs, to comply with applicable regulations could result in clinical holds on our studies, sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, seizures, or recalls of product candidates or product candidates, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates and harm our business, financial condition, results of operations, and growth prospects.

Any product candidates that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future third-party manufacturers could delay clinical development or marketing approval. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer and may incur added costs and delays in identifying and qualifying any such replacement. Furthermore, securing and reserving production capacity with contract manufacturers may result in significant costs.

We also rely on third-parties for the supply of the raw materials required for the production of our product candidates, and we expect to continue to rely on third party manufacturers for the commercial supply of any of our product candidates for which we obtain marketing approval. Our current and anticipated future dependence upon others for the manufacture of any product candidates we may develop may adversely affect our future profit margins and our ability to commercialize any medicines that receive marketing approval on a timely and competitive basis.

Our employees, principal investigators, consultants and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and vendors. Misconduct by these parties could include intentional failures, reckless and/or negligent conduct or unauthorized activities that violate (i) the laws and regulations of FDA and other regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities, (ii) manufacturing standards, (iii) federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the United States and abroad and (iv) laws that require the true, complete and accurate reporting of financial information or data. In particular, clinical and business arrangements in the biotechnology and healthcare industries are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of financial arrangements, incentive programs and other business arrangements. Such misconduct also could involve the improper use of individually identifiable information, including, without limitation, information obtained in the conduct of clinical trials, creating fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations.

Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could result in significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in government-funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of noncompliance with these laws, contractual damages, reputational harm and the curtailment or restructuring of our operations, any of which could have a negative impact on our business, financial condition, results of operations and prospects.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or furnish under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple mistake or human error. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

Failure to comply with laws regarding data privacy could expose us to risk of enforcement actions and penalties under such laws.

We may be subject to privacy and security laws in the various jurisdictions in which we operate, obtain or store personally identifiable information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. Our ongoing efforts to comply with evolving laws and regulations may be costly and require ongoing modifications to our policies, procedures and systems. Failure to comply with laws regarding data protection by us or our partners or service providers would expose us to risk of enforcement actions and penalties under such laws. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects.

Within the U.S., there are numerous federal and state laws and regulations related to the privacy and security of personal information. For example, at the federal level, the Health Insurance Portability and Accountability Act of 1996, as amended ("HIPAA"), and its implementing regulations establish privacy and security standards that limit the use and disclosure of personally identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information. While we have determined that we are neither a "covered entity" nor a "business associate" directly subject to HIPAA, many of the U.S. health care providers with which we interact are subject to HIPAA, and we may have assumed obligations related to protecting the privacy of personal information. States are increasingly regulating the privacy and security of personal information. For example, the California Consumer Privacy Act ("CCPA"), which took effect in 2020, gives California consumers (defined to include all California residents) certain rights, including the right to ask covered companies to disclose the types of personal information collected, the categories of sources from which such information was collected, the business purpose for collecting or selling the consumer's personal information, the categories of third parties with whom a covered company shares personal information, and specific pieces of information collected by a covered company. The CCPA imposes several obligations on covered companies to provide notice to California consumers regarding their data processing activities. The CCPA also gives California consumers the right to ask covered companies to delete a consumer's personal information and it places limitations on a covered company's ability to sell personal information, including providing consumers a right to opt out of sales of their personal information. Additionally, the California Privacy Rights Act ("CPRA"), which became operational in 2023, significantly modifies the CCPA, including expanding consumers' rights with respect to certain sensitive personal information, and creates a new state agency vested with authority to implement and enforce the CCPA and CPRA. The Virginia Consumer Data Protection Act ("CDPA") went into effect on January 1, 2023. The CDPA provides consumers with new rights to access, correct, delete and obtain a copy of the personal information a covered business holds about them, and to opt out of certain data processing activities.

Because we are developing our lead product candidate for the treatment of Alzheimer's disease, a condition for which there are few recent examples of new drug molecules that have received full FDA approval, and all Phase 3 trials in Alzheimer's disease employ cognitive and functional efficacy endpoints or methodologies that may be considered subjective, there is a heightened risk that the FDA or other regulatory authorities may not consider our Phase 3 clinical trials, or the endpoints of our clinical trials, as evidence of clinically meaningful results or that our clinical results may be difficult to analyze.

If our product candidates advance to the FDA review process, we will need to demonstrate the achievement of success criteria and endpoints such that the FDA will be able to determine the clinical efficacy and safety profile of our product candidates. Because we are developing a novel treatment for Alzheimer's disease, a condition in which there are very few examples of new drug approvals, and our trials employ endpoints or methodologies that may be considered subjective, there is heightened risk that the FDA or other regulatory bodies may not consider our clinical trials, or the endpoints of our clinical trials, as evidence of clinically meaningful results to patients. In addition, the resulting clinical data and results may be difficult to analyze. Even if the FDA does find our success criteria to be sufficiently validated and clinically meaningful, we may not achieve the pre-specified endpoints to a threshold of statistical significance (i.e., p-value <0.05). Even if we believe the data collected from clinical trials of our lead product candidates are promising, these data may not be sufficient to support approval by the FDA or foreign regulatory authorities. Pre-clinical and clinical data can be interpreted in different ways. Accordingly, the FDA or foreign regulatory authorities could interpret these data in different ways from us, which could delay, limit or prevent regulatory approval.

If data from one or both of our Phase 3 trials do not adequately demonstrate the safety or efficacy of our lead product candidate, the regulatory approval for such product candidate could be significantly delayed as we work to meet approval requirements, or, if we are not able to meet these requirements, such approvals could be denied.

We are evaluating two doses (50 mg and 100 mg) of simufilam in on-going Phase 3 trials. If data from one dose in our Phase 3 trials does not adequately demonstrate safety or efficacy, the regulatory approval for the other dose could be significantly delayed as we work to meet approval requirements, or, if we are not able to meet these requirements, such approval could be denied.

We expect to significantly grow the size and capabilities of our organization and we may experience difficulties in effectively managing this growth.

As our development plans and strategies develop, we expect to add a significant number of additional managerial, operational, financial, and other personnel. Future growth will impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, retaining, and motivating additional employees;

- increasing employee headcount;
- managing our internal development efforts effectively, including the clinical and FDA review process for our current and future product candidates, while complying with our contractual obligations to contractors and other third parties;
- expanding our operational, financial and management controls, reporting systems, and procedures; and
- managing increasing operational and managerial complexity.

Our future financial performance and our ability to continue to develop and, if approved, commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth. Our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to manage these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors, and consultants to provide certain services. There can be no assurance that the services of these independent organizations, advisors, and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical studies may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, if at all.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop our product candidates and, accordingly, may not achieve our research, development, and commercialization goals.

Ownership of our corporate headquarters and property leasing are subject to numerous risks and uncertainties.

In 2021, we made an all-cash purchase of an office complex in Austin, Texas, a portion of which serves as our corporate headquarters. Title to this property is held by Austin Innovation Park, LLC, a Texas limited liability company wholly owned by Cassava Sciences. The purchase required a substantial upfront cash investment and may require further commitments of our resources in the future. We have assumed or entered into lessor commitments with independent third parties for portions of our office complex and expect to continue to do so in the future. Commercial property ownership and related leasing activity are subject to many factors that pose substantial financial risks and uncertainties, including tenant default or non-payment of lease obligations by tenants. Macro-economic or other factors outside of our control could have an adverse effect on the demand for leased office space in our locale or may cause a decline in the market value of our corporate headquarters.

At December 31, 2023, we occupied approximately 25% of the property with the remainder either leased or available for lease to third parties. Virtually all existing tenant leases will expire in 2024. We believe tenant leases that expire in 2024 will likely not be extended, renewed or re-leased beyond their expiry date, in which case we will no longer receive rental payments or reimbursement for shared expense for such office space. If we fail to lease unoccupied office space at favorable rates, or if we incur excessive expenses in this effort or incur excessive leasehold improvements or property ownership expenses, our business, operations, future prospects, cash flows, and financial position may be adversely affected. In addition, our property is located in a semi-rural, wooded area of Austin, Texas that is subject to natural disasters such as extreme weather conditions, including but not limited to floods, tornadoes, wildfires, winter storms, lighting, heat waves and drought. Such natural disasters could damage, destroy or impair the value of our property or reduce the number of tenants who are willing or able to continue to lease office space in our property. We may incur substantial expenses as a result of our property's exposure to natural disasters, which could have a material adverse effect on our business and prospects.

Our internal computer systems, or those used by third parties on whom we rely, may fail or suffer other breakdowns, cyberattacks, or information security breaches that could compromise the confidentiality, integrity, and availability of such systems and data, result in material disruptions of our development programs and business operations, risk disclosure of confidential, financial, or proprietary information, and affect our reputation.

In the ordinary course of our business, we collect and store sensitive data, including legally protected patient health information, personally identifiable information about our employees, intellectual property, and proprietary business information. We manage and maintain our applications and data utilizing on-site systems, as well as extensive cloud-based applications and data storage. These applications and data encompass a wide variety of business-critical information including research and development information, commercial information and business and financial information. Despite the implementation of security measures, our internal computer systems and those of our current or future CROs and other contractors and consultants may be vulnerable to damage from computer viruses and unauthorized access. As the cyber-threat landscape evolves, these cyberattacks are growing in frequency, sophistication, and intensity, and are becoming increasingly difficult to detect. Such attacks could include the use of key loggers or other harmful and virulent malware, including ransomware or other denials of service, and can be deployed through malicious websites, the use of social engineering, and/or other means. If a breakdown, cyberattack, or other information security breach were to occur and cause interruptions in our operations, it could result in a misappropriation of confidential information, including our intellectual property or financial information, and a material disruption of our development programs and our business operations. For example, the loss of clinical study data from completed, ongoing, or future clinical studies could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on our third-party research institution collaborators for research and development of our product candidates and other third parties for the manufacture of our product candidates, to conduct clinical studies, and to analyze our clinical study data and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or systems, or inappropriate disclosure of confidential, financial, or proprietary information, including data related to our personnel, we could incur liability or risk disclosure of confidential, financial, or proprietary information, and the further development and commercialization of our product candidates could be delayed. There can be no assurance that we and our business counterparties will be successful in efforts to detect, prevent, or fully recover systems or data from all breakdowns, service interruptions, attacks, or breaches of systems that could adversely affect our business and operations and/or result in the loss of critical or sensitive data, which could result in financial, legal, business, or reputational harm to us.

Our reliance on third parties requires us to share our proprietary information, which increases the possibility that a competitor will discover this information or that our proprietary information will be misappropriated or inadvertently disclosed.

Our reliance on third-party vendors requires us to disclose our proprietary information to these parties, which could increase the risk that a competitor will discover this information or that our proprietary information will be misappropriated or disclosed without our intent to do so. If any of these events were to occur, then our ability to obtain patent protection or other intellectual property rights could be irrevocably jeopardized, and costly, distracting litigation could ensue. Furthermore, if these third-party vendors cease to continue operations and we are not able to quickly find a replacement provider or we lose information or items associated with our products or product candidates, our development programs may be delayed. Although we carefully manage our relationships with our third-party collaborators and CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, clinical operations, financial condition and prospects.

Our business involves environmental risks that may result in liability for us.

In connection with our research and development activities, we, and our collaborators and vendors, are subject to federal, state and local laws, rules, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials, biological specimens, chemicals and wastes. Although we believe that we comply with such applicable laws, regulations and policies in all material respects and have not been required to correct any material noncompliance, we may incur significant costs to comply with environmental and health and safety regulations in the future. Although we believe that our safety procedures for handling and disposing of controlled materials comply with the standards prescribed by state and federal regulations, accidental contamination or injury from these materials may occur. In the event of such an occurrence, we could be held liable for any damages that result and any such liability could exceed our resources.

Business disruptions and lack of appropriate levels of commercial insurance could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of our third-party research institution collaborators, CROs, CDMOs, suppliers, and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, disease epidemics or pandemics, such as COVID-19, and other natural or man-made disasters or business interruptions, for which we are partly or entirely uninsured. In addition, we rely on third parties for conducting certain research and development activities relating to our product candidates, and they may be affected by government shutdowns or withdrawn funding. The occurrence of any such 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 product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

Our day-to-day operations are located in a single office facility in Austin, Texas. Damage or extended periods of interruption to our corporate, development, or research facilities could cause us to cease or delay development of some or all our product candidates. Our insurance might not cover losses under such circumstances and our business may be seriously harmed by such delays and interruption.

Social media platforms have significantly altered the dynamics of corporate communications and present risks and challenges, some of which are and may continue to be unknown to us.

As social media continues to expand, it also presents us with new challenges. The inappropriate or unauthorized use of our confidential information on media platforms could cause brand damage or information leakage, which would cause legal or regulatory issues for us. In addition, negative, inappropriate or inaccurate posts or comments about us or our product candidates on social media internet sites could quickly and irreversibly damage our reputation, image and goodwill. Further, the accidental or intentional disclosure of non-public sensitive information by our workforce or others through media channels could lead to information loss or could lead to legal or regulatory issues for us. In addition, there is a risk of a fraudulent third-party hijacking our information technology systems without our knowledge to access our confidential documents or to use our company name, logo or brand without authorization. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face restrictive regulatory actions or incur other harm and costs to our business.

We also rely on other third parties to label, store and distribute drug supplies for our clinical studies. Any performance failure on the part of our distributors, including with the shipment of any drug supplies, could delay clinical development or marketing approval of any product candidates we may develop or commercialization of our product candidates, producing additional losses and depriving us of potential product revenue.

We are a small company with a limited number of employees. We are highly dependent on our key personnel, and if we are not successful in attracting, motivating, and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract, motivate, and retain highly qualified managerial, scientific, and medical personnel. We are highly dependent on our management, particularly our President and Chief Executive Officer, Remi Barbier, and our scientific and technical personnel. The loss of the services provided by any of our executive officers, other key employees, and other scientific and medical advisors, and our inability to find suitable replacements, could result in delays in the development of our product candidates and harm our business.

Competition for skilled personnel is intense and the turnover rate can be high, which may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. We expect that we may need to recruit talent from outside of our region in Austin, Texas, and doing so may be costly and difficult.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided equity option grants that vest over time and/or a cash bonus plan. The value to employees of these equity grants that vest over time or cash bonus plans may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Although we have employment agreements with our key employees, these employment agreements provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. If we are unable to attract and incentivize quality personnel on acceptable terms, or at all, it may cause our business and operating results to suffer.

We may need to cease our operations if we are unable to attract and retain key personnel.

We are engaged in developing early- and clinical-stage technologies and will continue to do so for the foreseeable future. Unlike larger organizations, we rely on a very small number of highly skilled, and highly sought after, employees to continue the advancement of our development stage technologies. The knowledge and skills contributed by our key employees may be irreplaceable and the loss of a key employee may cause substantial negative financial, operational and scientific consequences for our business. As an example, in the past, we have received research grant awards from NIH, which depended in part on the continued participation of certain key employees, known as Principal Investigators. When such NIH grant awards are in place, the loss of a Principal Investigator may result in the loss of one or more of such research grant awards. Likewise, the intellectual property that is intended to protect our development stage technologies is still evolving and its evolution remains highly dependent on a small number of employees with specific expertise. The loss of a key employee may jeopardize our existing or pending intellectual property or may prevent us from accessing the technical information and knowledge necessary to extend our portfolio of intellectual property. Furthermore, we believe the adverse effects that may result from losing a key employee's participation cannot be compensated with any specific insurance policies, such as "key person" or "business life" insurance. If we are not successful in retaining key employees, our business and financial condition will suffer, and we may need to cease our operations.

If our current research collaborators or scientific advisors terminate their relationships with us or develop relationships with a competitor, our ability to continue our business operations could be adversely affected.

We have relationships with unaffiliated research collaborators at academic and other institutions who conduct research at our request. These research collaborators are not our employees. As a result, we have limited control over their activities and, except as otherwise required by our collaboration agreements, can expect only limited amounts of their time to be dedicated to our activities. Our ability to discover drugs and biomarkers involved in human disease and validate and commercialize diagnostic tests may depend in part on the continuation of these collaborations. If any of these collaborations are terminated, we may not be able to enter into other acceptable collaborations. In addition, our existing collaborations may not be successful. Our research collaborators and scientific advisors may have relationships with other commercial entities, some of which could compete with us. Our research collaborators and scientific advisors sign agreements which provide for the confidentiality of our proprietary information and the results of studies conducted at our request. We may not, however, be able to maintain the confidentiality of our technology and other confidential information related to all collaborations. The dissemination of our confidential information could have a material adverse effect on our business.

Our business may be impacted by political events, war, terrorism, business interruptions and other geopolitical events and uncertainties beyond our control.

War, terrorism, geopolitical uncertainties and other business interruptions could cause damage to, disrupt or cancel the conduct of our clinical studies on a global or regional basis, which could have a material adverse effect on our business, clinical sites or vendors with which we do business. Such events could also decrease patient demand to enroll in our clinical studies or make it difficult or impossible for us to deliver products and services to our clinical investigational sites. In addition, territorial invasions can lead to cybersecurity attacks on technology companies, such as ours, located far outside of the conflict zone. In the event of prolonged business interruptions due to geopolitical events, we could incur significant losses, require substantial recovery time and experience significant expenditures in order to resume our business or clinical operations. We have no operations in Israel, Russia or the Ukraine, but we do not and cannot know if the current uncertainties in these geopolitical areas may escalate and result in broad economic and security conditions or rationing of medical supplies, which could limit our ability to conduct clinical trials outside the U.S. or result in material implications for our business. In addition, our insurance policies typically contain a war exclusion of some description and we do not know how our insurers are likely to respond in the event of a loss alleged to have been caused by geopolitical uncertainties.

Our efforts to minimize the likelihood and impact of a cybersecurity incident may not be successful and our business could be negatively affected by a data breach or other cybersecurity threat or other disruption to our operations, which could result in legal claims against us or could give rise to substantial financial costs to redress any such cybersecurity incident and could harm our relationship with vendors, clinical study participants or regulators.

Our business operation is data-intensive and relies extensively on the use of information technology. In addition, biopharmaceutical firms have been subject to an increasing number of cyberattacks in recent years, particularly cyberattacks targeting the theft of intellectual property and unauthorized access to proprietary clinical research data or sensitive patient information. Given the nature of our business, we are subject to a variety of evolving cybersecurity threats to our information technology infrastructure, including ransomware, unauthorized attempts to gain access to our operations or to sensitive patient information, denial-of-service attacks or various other methods of attacks. As discussed below, similar security threats may be faced by our vendors, consultants, suppliers, subcontractors, clinical investigational sites and non-clinical research labs.

Such cybersecurity 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, nation states and rogue nation-state actors. We could also be impacted by the improper cyber conduct of our employees or others working on behalf of us who have access to our proprietary information or sensitive patient information, which could adversely affect our business and reputation. The occurrence of any material cybersecurity incident could cause substantial disruptions to our business operations. In addition to cyber threats, we may face threats to the security of our facilities or executives, which could materially disrupt our business if carried out.

We also work cooperatively with numerous vendors, consultants, suppliers, subcontractors, clinical investigational sites and non-clinical research labs, which have access to our proprietary or sensitive information. These third parties, which are typically outside our control, may have varying levels of cybersecurity expertise and safeguards and our ability to monitor their cybersecurity practices is limited. These third parties may not have adequate cybersecurity measures in place, and incidents or other interruptions suffered by them could cause us to experience adverse consequences. In particular, cybersecurity incidents in our drug supply chain could have an adverse impact on our ability to timely deliver product candidates to patients and physicians participating in our clinical studies, which could cause us to delay or cancel the completion of our ongoing clinical and non-clinical studies.

If cybersecurity threats materialize and we or third-parties that we rely upon are unable to defend against them or to protect sensitive information, including through complying with evolving information security and data protection/privacy regulations, this could cause vendors, clinical study participants, clinical study investigation sites, patients, or governmental authorities to question the adequacy of the threat mitigation and detection processes and procedures that we and our vendors employ. Moreover, depending on the severity of an incident, our proprietary clinical research data, sensitive patient information, intellectual property, including trade secrets and research, development and technical know-how, could be compromised.

Nearly all of our operations carry cybersecurity risks, including risks that they could be breached or that we could fail to detect, prevent or combat attacks, which could result in financial losses and claims against us, and could harm our relationships with our vendors or clinical study participants. The costs and expenses to respond to a material cybersecurity incident or other security threat or disruption may be substantial for a company of our size. Further, we do not carry a separate cybersecurity commercial insurance policy covering the potential financial losses that may occur in the event we experience a cybersecurity incident.

Risks Related to Financial Condition and Capital Requirements

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

We have incurred net losses in each reporting period since our inception, including a net loss of $97.2 million for the year ended December 31, 2023. As of December 31, 2023, we had an accumulated deficit of $380.8 million.

We have invested significant financial resources in research and development activities for product candidates. We do not expect to generate revenue from product sales for several years, if at all. The amount of our future net losses will depend, in part, on the level of our future expenditures and revenue. Moreover, our net losses may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indicator of our future performance.

We expect to continue to incur significant expenses and higher operating losses for the foreseeable future. We anticipate our expenses will remain substantial as we:

- continue our research and discovery activities;
- advance our current and any future product candidates through preclinical and clinical development;
- initiate and conduct additional preclinical, clinical, or other studies for our product candidates;
- work with our CDMO's to scale up the manufacturing processes for our product candidates;
- seek regulatory approvals and marketing authorizations for our product candidates;
- obtain, maintain, protect, defend and enforce our intellectual property portfolio;
- attract, hire, and retain qualified personnel;
- provide additional internal infrastructure to support our continued research and development operations and any planned commercialization efforts in the future;
- experience any delays or encounter other issues related to our operations;
- meet the requirements and demands of being a public company; and
- defend against litigation, claims or other uncertainties that may arise from allegations made against us or our collaborators.

Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. In any quarter, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

We have broad discretion in the use of our capital resources, including the net proceeds from any of our financing transactions, and we may not use them effectively.

We have broad discretion in the application of our capital resources, including the net proceeds from our financing transactions, and investors will not have the opportunity to opine on whether such resources are being used appropriately. We could spend such capital resources in ways that vary substantially from their initially communicated intended use, do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest available capital resources, including net proceeds from our financing transactions, in a manner that does not produce income or that loses value

We have no product revenues and may never achieve revenues or profitability based on product revenues.

We have no products approved for commercial sale. To obtain revenues from the sales of our product candidates that are significant or large enough to achieve profitability, we must succeed, either alone or with third parties, in developing, obtaining regulatory approval for, manufacturing, and marketing product candidates with significant commercial value. This is a significant endeavor that few early-stage biopharmaceutical companies can successfully achieve. Our ability to generate revenue and achieve profitability depends on many factors, including:

- completing research and preclinical and clinical development of our product candidates;
- obtaining regulatory approvals and marketing authorizations for product candidates for which we successfully complete clinical development;
- developing a sustainable and scalable manufacturing process for our product candidates, as well as establishing and maintaining commercially viable supply relationships with third parties that can provide adequate products and services to support clinical activities and commercial demand for our product candidates;
- identifying, assessing, acquiring, and/or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter;
- addressing any competing technological and market developments;
- maintaining, protecting, expanding, and enforcing our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and
- attracting, hiring, and retaining qualified personnel.

Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of our expenses, or when we will be able to generate any meaningful revenue or achieve or maintain profitability, if ever. In addition, our expenses could increase beyond our current expectations if we are required by FDA or foreign regulatory agencies to perform studies in addition to those that we currently anticipate, or if there are any delays in any of our clinical studies or the development of any of our product candidates.

We may require additional capital to fund our operations and to complete the development of our product candidates. A failure to obtain this necessary capital on acceptable terms, or at all, could force us to delay, limit, reduce, or terminate our commercialization efforts, product development, or other operations.

Our operations have required substantial amounts of cash since inception, and we expect our expenses to remain substantial for the foreseeable future. To date, we have financed our operations primarily through the sale of equity securities, research grants and payments received from prior third-party collaborations. Developing our product candidates and conducting clinical studies for the treatment of neurodegenerative diseases, including Alzheimer's disease, will require substantial amounts of capital. We will also require a significant amount of capital to commercialize any approved products.

As of December 31, 2023, we had cash and cash equivalents of $121.1 million. In addition, from January 3, 2024 to February 26, 2024, we received gross proceeds of approximately $21.8 million from the exercise of outstanding warrants. See Note 13 to the consolidated financial statements for more information.

Based on our current operating plan, we believe that our existing cash and cash equivalents will be sufficient to fund our projected operations for at least the next 12 months. Our estimate as to how long we expect our existing cash and cash equivalents to be available to fund our operations is a forward-looking statement, based on assumptions that may prove inaccurate, and we could use our available capital resources sooner than we currently expect. In addition, 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 currently unanticipated circumstances, which may be 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.

We may require additional capital for the further development of our product candidates. Additional capital may not be available when we need it, or on terms acceptable to us or at all. We have no committed source of additional capital. If adequate capital is not available to us on a timely basis, we may be required to significantly delay, limit, reduce or terminate our research and development programs or the commercialization of product candidates, if approved, or be unable to continue or expand our operations, or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition, results of operations, and growth prospects and cause the price of our common stock to decline.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends. If we raise additional funds through collaborations, strategic alliances, or licensing arrangements with pharmaceutical partners, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, or product candidates, or grant licenses on terms that may not be favorable to us.

Global credit and financial market conditions and inflation could negatively impact the value of our portfolio of cash equivalents and our ability to meet our financing objectives.

Our cash and cash equivalents are generally maintained in highly liquid investments with original maturities of three months or less at the time of purchase. While, as of the date of this filing, we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents since December 31, 2023, no assurance can be given that deterioration in conditions of the global credit and financial markets, including inflationary pressure, would not negatively impact our current portfolio of cash equivalents or our ability to meet our financing objectives.

Our operations are subject to the effects of rising inflation.

The United States has experienced historically high levels of inflation over the last three years. According to the U.S. Department of Labor, the annual inflation rate for the United States was approximately 3.4% for the 12 months ended December 31, 2023, after being between 6.5% - 7.0% in each of 2022 and 2021. If the inflation rates continue at historically high levels, for example due to increases in the costs of labor and supplies, it may affect our expenses, such as employee compensation and research and development charges. Research and development expenses account for a significant portion of our operating expenses. Additionally, the U.S. is experiencing a continuing workforce shortage, which in turn has created a very competitive wage environment that may increase our operating costs. To the extent inflation results in further interest rate increases and has other adverse effects on the market, inflation may adversely affect our consolidated financial condition and results of operations or business prospects.

Risks Related to the Ownership of Our Common Stock and Warrants

We do not know whether a sufficient market will continue to develop for our securities or what the market price of our securities will be, and, as a result, it may be difficult for investors to sell shares of our common stock or outstanding warrants.

If a market for our common stock is not sustained, it may be difficult to sell shares of our common stock at an attractive price or at all. Similarly, if an active and stable market for our outstanding warrants is not sustained, it may be difficult to sell such warrants at an attractive price or at all. The trading market for our securities may lack adequate size, liquidity or price transparency. We cannot predict the prices at which our common stock or warrants will trade. Moreover, features of our warrants, such as our redemption right or the 9.9% ownership limitation on exercisability, may affect the trading price of such warrants.

It is possible that in one or more future periods our results of operations and progression of our 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 trading securities may fall.

The market price of our common stock has historically been highly volatile, and we expect it to continue to be volatile, which could result in substantial losses for investors who purchase our shares.

The market price of our common stock has historically been highly volatile. For example, the closing price of our common stock has fluctuated from a low of $12.64 to a high of $30.11 over the 12 months preceding the filing date of this Annual Report on Form 10-K. Some of the factors that may cause the market price of our common stock to fluctuate include:

- the success of existing or new competitive products or technologies;
- the timing and results of clinical studies for our current product candidates and any future product candidates that we may develop;
- failure or discontinuation of any of our product development and research programs;
- results of preclinical studies, clinical studies, or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- 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;
- the level of expenses related to any of our research programs, clinical development programs, or product candidates that we may develop;
- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results or development timelines;
- announcement or expectation of additional financing efforts;
- 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;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry, and market conditions; and
- securities litigation, regardless of merit.

In recent years, the stock market in general, Nasdaq, and the markets for early-stage companies and pharmaceutical and biotechnology companies have 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 are currently and 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.

Hedging arrangements relating to our warrants may affect the value and volatility of our common stock.

In order to hedge their financial positions, certain warrant holders may enter into hedging transactions with respect to our common stock, may unwind or adjust hedging transactions and/or may purchase or sell large blocks of our common stock in one or more market transactions. The effect, if any, of these activities on the trading price of our common stock will depend in part on market conditions and cannot be known in advance, but any of these activities could adversely affect the value and price volatility of our common stock.

The trading price for our warrants may bear little or no relationship to traditional valuation methods, or to the market price of our common stock, and therefore the trading price of the warrants may fluctuate significantly.

The trading price of our warrants may have little or no relationship to, and may be significantly lower, or at times higher, than the price that would otherwise be established using traditional indicators of value, such as our future prospects and those of our industry in general; future potential revenues, earnings, cash flows, and other financial and operating information, or multiples thereof; market prices of securities and other financial and operating information of companies engaged in drug development activities similar to ours; and the views of research analysts. Potential investors should not buy warrants in the open market unless they are willing to take the risk that the trading price of the warrants could fluctuate and decline significantly. In order for warrant holders to recover the value of an investment in the shares of common stock received upon exercise of a warrant (after taking into account the bonus share fraction during any bonus share period) at the exercise price, the value of such shares of common stock must be more than the exercise price of the warrants.

In addition, we may redeem all unexercised warrants at our sole option at any time on or after April 15, 2024, and upon meeting certain other conditions. If we redeem unexercised warrants, they will cease to be outstanding after the redemption date, they will cease to trade, and they will have no value.

If securities analysts do not publish research or reports about our business, or we are the subject of negative publicity, the price of our stock could decline.

The trading market for our securities depends, in part, on the research and reports that securities or industry analysts publish about us or our business. We do not control these analysts. If one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable evaluations of our company or our stock, the price of our securities could decline. If one or more of these analysts cease coverage of our company or fail to publish reports covering our company regularly, our stock may lose visibility in the market, which in turn could cause the price of our securities to decline. In addition, if we are the subject of negative publicity, whether from an analyst, academic, social media, industry group or the general or financial press, the price of our securities may decline.

Short sellers of our stock may be manipulative and may drive down the market price of our common stock.

Short selling—also known as “shorting,” “selling short” or “going short”—refers to the sale of a security or financial instrument that the seller has borrowed from a third party. A short seller hopes to profit from a decline in the value of the securities they are shorting. As it is in the short seller’s financial interest for the price of our stock to decline, some short sellers may publish misrepresentations, falsehoods or mischaracterizations regarding our business operations, including our pre-clinical or clinical results, that are intended to create and spread negative publicity about us. Since negative information can travel fast in the media, short seller activity can lead to a sudden, sharp decline in the market value of the market price of our securities, which is sometimes known as a “short attack.” Issuers, like us, with securities that have historically had limited trading volumes and relatively high volatility, together with the challenges of engaging in new and complex scientific endeavors, can make us particularly vulnerable to such short seller attacks. Short selling may also lead to fluctuations of our stock price, particularly if other investors holding “long” positions in our common stock seek to counter short selling activity by purchasing additional shares, thus making it more difficult and more expensive for short sellers to profit. No assurances can be made that declines in the market price of our common stock will not occur in the future in connection with such activity.

General Risk Factors

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 Section 404(a) of the Sarbanes-Oxley Act ("SOX"), which require annual management assessments of the effectiveness of our internal control over financial reporting. Section 404(b) of SOX also requires our independent auditors to attest to, and report on, the effectiveness of our internal control over financial reporting.

The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by SOX. 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 consolidated financial statements for external purposes in accordance with accounting principles generally accepted in the U.S. Any failure to maintain effective internal controls, or if our independent registered public accounting firm is unable to attest to the effectiveness of our internal control over financial reporting, could have an adverse effect on our business, financial position, and results of operations.

Anti-takeover provisions in our charter documents and Delaware law may prevent or delay removal of incumbent management or a change of control.

Anti-takeover provisions of our amended and restated certificate of incorporation and amended and restated bylaws and Delaware law may have the effect of deterring or delaying attempts by our stockholders to remove or replace management, engage in proxy contests and effect changes in control. The provisions of our charter documents include:

- a classified board so that only one of the three classes of directors on our Board of Directors (the "Board") is elected each year;
- elimination of cumulative voting in the election of directors;
- procedures for advance notification of stockholder nominations and proposals;
- the ability of the Board to amend our bylaws without stockholder approval; and
- the ability of the Board to issue up to 10,000,000 shares of preferred stock without stockholder approval upon the terms and conditions and with the rights, privileges and preferences as the Board may determine.

In addition, as a Delaware corporation, we are subject to Delaware law, including Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years following the date that the stockholder became an interested stockholder unless certain specific requirements are met as set forth in Section 203.

These provisions, alone or together, could have the effect of deterring or delaying changes in incumbent management, proxy contests or changes in control.

Our amended and restated bylaws provide that the federal district courts of the United States of America shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Laws of 1933, 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 federal district courts of the United States of America shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933.

While the Delaware courts have determined that such choice of forum provisions are valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated bylaws. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

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 these types of lawsuits. Furthermore, the enforceability of similar choice of forum provisions in other companies' certificates of incorporation or bylaws has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable. If a court were to find the exclusive-forum provision contained 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 harm our business.

Changes in our ownership could limit our ability to utilize net operating loss carryforwards.

As of December 31, 2023, we had aggregate federal net operating loss carryforwards of approximately $158.7 million, which begin to expire in 2029. Under Section 382 of the Internal Revenue Code of 1986, as amended, changes in our ownership may limit the amount of our net operating loss carryforwards that could be utilized annually to offset our future taxable income, if any. This limitation would generally apply in the event of a cumulative change in ownership of our company of more than 50% within a rolling three-year period. Any such limitation may significantly reduce our ability to utilize our net operating loss carryforwards and tax credit carryforwards. Any such limitation, whether as the result of past offerings, sales of our common stock by our existing stockholders, the issuance of shares of common stock as a result of the exercise of warrants or additional sales of our common stock by us in the future could have a material adverse effect on our results of operations in future years. We have not completed a study to assess whether an ownership change for purposes of Section 382 has occurred.

We may sell additional equity or debt securities to fund our operations, and have outstanding securities exercisable for our common stock, which may result in dilution to our stockholders and impose restrictions on our business.

In order to raise additional capital to support our operations, we may sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock which could result in dilution our stockholders.

We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in prior offerings, and investors purchasing our shares or other securities in the future could have rights superior to existing shareholders. The price per share at which we sell additional shares of our common stock or securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share in prior offerings. You may also be diluted upon the exercise of outstanding stock options as of December 31, 2023 to purchase approximately 3.0 million shares of our common stock at a weighted average price of $15.13 per share, the future issuance of up to approximately 2.9 million compensatory equity awards authorized under our 2018 Omnibus Incentive Plan, and the potential issuance of up to 25.3 million shares of our common stock from exercises of our outstanding warrants, initially issued in January 2024. The issuance of such additional shares of common stock or the perception that issuances could occur, could result in significant downward pressure on our stock price.

The estimates and judgments we make, or the assumptions on which we rely, in preparing our consolidated financial statements could prove inaccurate.

Our consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the U.S. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities and expenses, the amounts of charges accrued by us and related disclosure of contingent assets and liabilities. Such estimates and judgments include development expenses, valuation of stock-based awards and income tax. We base our estimates on historical experience, facts and circumstances known to us and on various other assumptions that we believe to be reasonable under the circumstances. We cannot provide assurances, however, that our estimates, or the assumptions underlying them, will not change over time or otherwise prove inaccurate. If this is the case, we may be required to restate our consolidated financial statements, which could, in turn, subject us to securities class action litigation. Defending against such potential litigation relating to a restatement of our consolidated financial statements would be expensive and would require significant attention and resources of our management. Moreover, our insurance to cover our obligations with respect to the ultimate resolution of any such litigation may be inadequate. As a result of these factors, any such potential litigation could have a material adverse effect on our financial results and cause our stock price to decline, which could in turn subject us to securities class action litigation.

Item 1B. ***Unresolved Staff Comments***

None.

Item 1C. ***Cybersecurity***

In the normal course of business, we collect and store sensitive information, including proprietary and confidential business information, intellectual property, information regarding clinical and non-clinical trials, sensitive third-party information and employee information.

We have processes designed to protect our information systems, data, assets, infrastructure, and computing environments from cybersecurity threats and risks. Our cybersecurity strategy includes the use of managed detection and response services to monitor our network infrastructure and associated endpoints for possible cybersecurity threats. In addition, we use multi-factor authentication, perform periodical penetration testing and other logical, physical and technical controls designed to deter, prevent, mitigate and respond to cybersecurity threats. Further, our information systems include continuous alert plans, and we provide periodical cybersecurity reminders to our employees to emphasizes the importance of adherence to our security policies.

We conduct organizational risk assessment, which help management in identifying data assets and recognizing and assessing potential threats, and investigating potential vulnerabilities. We are in the process of reviewing and implementing incremental information technology strategies to mitigate cybersecurity risks and their possible impacts. Risk assessments enable management to make risk management decisions and assign resources to mitigate risk. We also periodicly engage third parties to assess the effectiveness of our cybersecurity practices.

As of the date of this Annual Report, we do not believe that any past cybersecurity incidents that have been detected have materially affected, or are reasonably likely to materially affect, our business strategy, results of operations, or financial condition. We do not carry a separate cybersecurity commercial insurance policy covering the potential financial losses that may occur in the event we experience a cybersecurity incident.

See “Risk Factors - Risks Related to Our Business and Operations” for additional information about the risks to our business associated with cybersecurity or a breach or compromise to our information security systems.

Item 2. ***Properties***

We own an office complex in Austin, Texas, a portion of which serves as our corporate headquarters. This property is intended to accommodate our anticipated growth and expansion of our operations in the coming years. Maintenance, physical facilities, leasing, property management and other key responsibilities related to property ownership are outsourced to professional real-estate managers. The office complex measures approximately 90,000 rentable square feet. We occupied approximately 25% of the property as of December 31, 2023.

Item 3. ***Legal Proceedings***

We are and, from time to time, we may become, involved in litigation or other legal proceedings and claims, including U.S. government inquiries, investigations and Citizen Petitions submitted to FDA. In addition, we have received, and from time to time, we may receive inquiries from government authorities relating to matters arising from the ordinary course of business. The outcome of these proceedings is inherently uncertain. Regardless of outcome, legal proceedings can have an adverse impact on us because of defense and settlement costs, diversion of management resources, and other factors. At this time, no assessment can be made as to their likely outcome or whether the outcome will be material to us. We believe that our total provision for legal matters are adequate based upon currently available information.

Government Investigations

On November 15, 2021, we disclosed that certain government agencies had asked us to provide corporate information and documents. These were confidential requests. We have been voluntarily cooperating and intend to continue to cooperate with these inquiries. No government agency has informed us that it has found evidence of research misconduct or wrongdoing by the Company or its officers, employees or directors. No government agency has filed any claims or charges relating to these inquiries. We cannot predict the outcome or impact of these ongoing matters, including whether a government agency may pursue an enforcement action against us or others.

Securities Class Actions and Shareholder Derivative Actions

Between August 27, 2021 and October 26, 2021, four putative class action lawsuits were filed alleging violations of the federal securities laws by us and certain named officers. The complaints rely on allegations contained in Citizen Petitions submitted to FDA and allege that various statements made by the defendants regarding simufilam were rendered materially false and misleading. The Citizen Petitions were all subsequently denied by FDA. These actions were filed in the U.S. District Court for the Western District of Texas. The complaints seek unspecified compensatory damages and other relief on behalf of a purported class of purchasers.

On June 30, 2022, a federal judge consolidated the four class action lawsuits into one case and appointed a lead plaintiff and a lead counsel. Lead plaintiff filed a consolidated amended complaint on August 18, 2022 on behalf of a putative class of purchasers of our securities between September 14, 2020 and July 26, 2022. On May 11, 2023, the court dismissed with prejudice plaintiffs' claims against defendant Nadav Friedmann, PhD, MD, our former Chief Medical Officer and a Company director, who is now deceased, but otherwise denied defendants' motion to dismiss. Defendants filed an answer to the consolidated amended complaint on July 3, 2023. On February 22, 2024, plaintiffs filed a motion to supplement their complaint to extend the putative class period through October 12, 2023.

On November 4, 2021, a related shareholder derivative action was filed, purportedly on behalf of the Company, in the U.S. District Court for the Western District of Texas, asserting claims under the U.S. securities laws and state fiduciary duty laws against certain named officers and the members of the Company's Board. This complaint relies on the allegations made in Citizen Petitions that were submitted to (and subsequently denied by) FDA. The complaint alleges, among other things, that the individual defendants exposed the Company to unspecified damages and securities law liability by causing it to make materially false and misleading statements, in violation of the U.S. securities laws and in breach of their fiduciary duties to the Company. The derivative case seeks, among other things, to recover unspecified compensatory damages on behalf of the Company arising out of the individual defendant's alleged wrongful conduct. Although the plaintiff in this derivative case does not seek relief against the Company, the Company has certain indemnification obligations to the individual defendants. Between November 4, 2021 and June 20, 2023, four additional shareholder derivative actions were filed alleging substantially similar claims, two in the U.S. District Court for the Western District of Texas, one in Texas state court (Travis County District Court) and one in the Delaware Court of Chancery. On July 5, 2022, the three federal court actions were consolidated into a single action. All of the foregoing actions are currently stayed pending further developments in the consolidated securities action described above. On November 9, 2023, another shareholder derivative action alleging substantially similar claims was filed in the U.S. District Court for the Western District of Texas. The parties to that case expect that it will be consolidated into the existing consolidated federal court shareholder derivative action.

On February 2, 2024, a putative class action lawsuit was filed alleging violations of the federal securities law by the Company and certain named officers. The complaint relies on an October 12, 2023 journal article that describes a purported leaked report of alleged scientific misconduct by a scientific collaborator of the Company at City University of New York. The complaint alleges that various statements made by the defendants regarding simufilam were rendered materially false and misleading by this article. The action was filed in the U.S. District Court for the Northern District of Illinois. The complaint seeks unspecified compensatory damages and other relief on behalf of a purported class of purchasers of the Company's securities between August 18, 2022 and October 12, 2023.

We believe the foregoing claims are without merit and intend to defend against these lawsuits vigorously. We are unable to estimate the possible loss or range of loss, if any, associated with these lawsuits.

On August 19, 2022, a shareholder derivative action was filed, purportedly on behalf of the Company, in the Delaware Court of Chancery, asserting claims under state fiduciary duty laws against certain named officers and members of the Company's Board. The complaint alleges, among other things, that the individual defendants breached their fiduciary duties by approving the 2020 Cash Incentive Bonus Plan in August 2020. The complaints seek unspecified compensatory damages and other relief. On January 6, 2023, the plaintiffs filed an amended complaint. Defendants filed a partial answer to the amended complaint on March 10, 2023, and moved to partially dismiss the amended complaint on March 14, 2023. On January 25, 2024, the parties entered into a binding settlement term sheet with respect to this action. The settlement is subject to certain conditions, including the filing of a Stipulation of Settlement and final court approval. The proposed settlement resolves the claims asserted against the Company and the individual defendants and would contain provisions that the settlement does not constitute an admission, concession, or finding of any fault, liability, or wrongdoing of any kind by any defendant. There can be no assurance that the final settlement agreement will be executed or that such agreement will be approved by the court.

Item 4. ***Mine Safety Disclosures***

Not applicable.

PART II

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

Market Information

Our common stock is quoted on Nasdaq, under the symbol "SAVA."

Holders

As of February 20, 2024, there were approximately 28 registered holders of record of our common stock. We believe the actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees.

Sales of Non-Registered Securities

None.

Purchases of Equity Securities by the Issuer

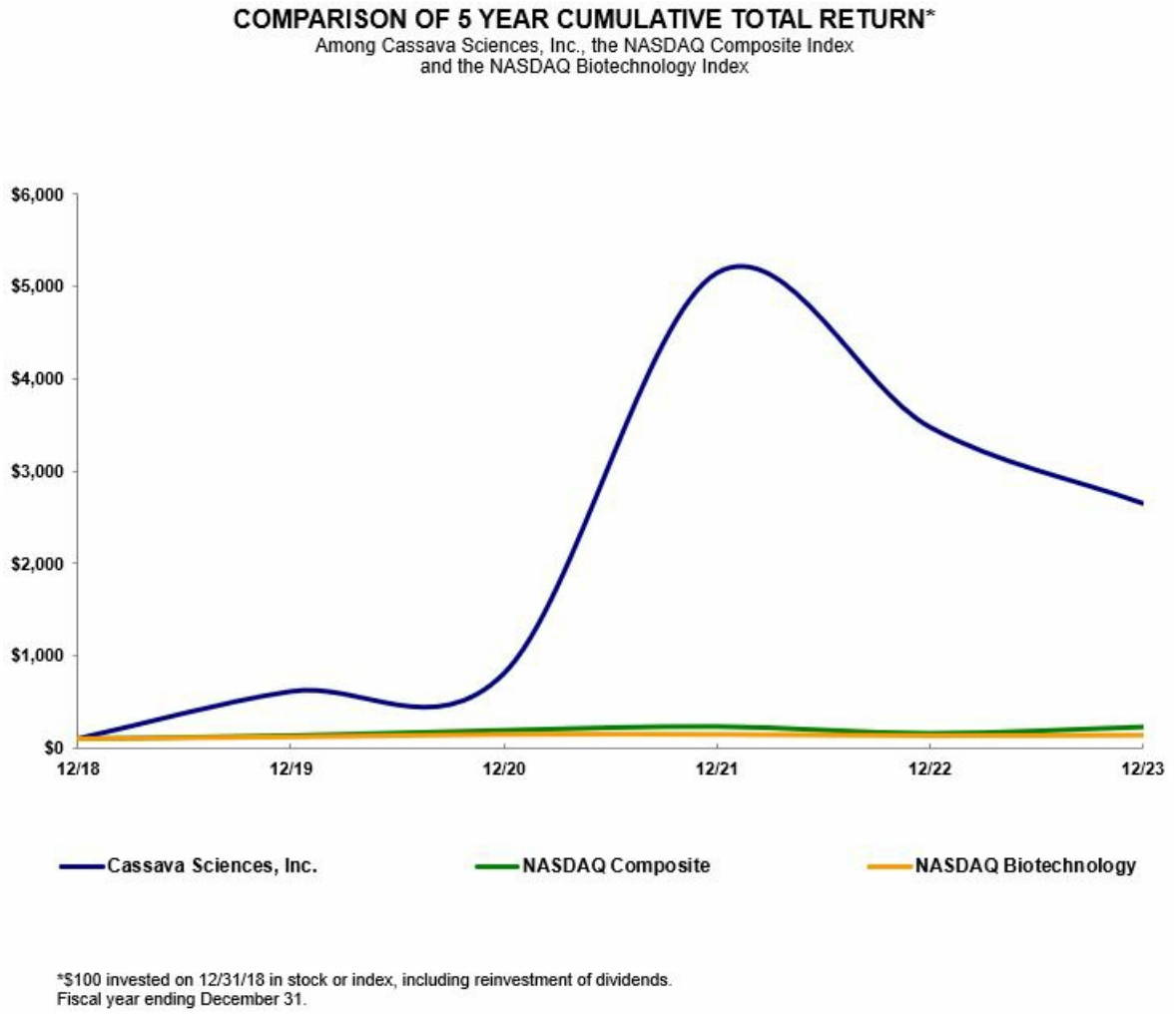
None.

Dividend Policy

We currently expect to retain future earnings, if any, for use in the operation and expansion of our business and, notwithstanding our special non-dividend distributions in December 2012 (of $0.75 per share of common stock totaling $34.0 million) and December 2010 (of $2.00 per share of common stock totaling $85.7 million), we do not anticipate paying any cash dividends in the foreseeable future.

Stock Performance Graph

The following graph compares the cumulative total return to stockholder return on our common stock relative to the cumulative total returns of the NASDAQ Composite Index and the NASDAQ Biotechnology Index. An investment of $100 is assumed to have been made in our common stock and each index on January 1, 2019 and its relative performance is tracked through December 31, 2023. Pursuant to applicable Securities and Exchange Commission rules, all values assume reinvestment of the full amount of all dividends, however no cash dividends have been declared on our common stock to date. The stockholder returns shown on the graph below are based on historical results and are not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.



This performance graph shall not be deemed soliciting material or to be filed with the SEC for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of the Company's filings under the Securities Act or the Exchange Act.

Item 6. ***[Reserved]***

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

This discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and accompanying notes included elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations, and intentions, that are based on the beliefs of our management. Operating results are not necessarily indicative of results that may occur in future periods. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the "Risk Factors" section of this Annual Report on Form 10-K.

Overview

We are a clinical-stage biotechnology company based in Austin, Texas. Our mission is to detect and treat neurodegenerative diseases, such as Alzheimer's disease. Our novel science is based on stabilizing – but not removing – a critical protein in the brain. Our lead therapeutic drug candidate, simufilam, is being evaluated for the proposed treatment of Alzheimer's disease dementia in fully-enrolled, on-going Phase 3 clinical studies.

Over the past 12 years, we have combined state-of-the-art technology with new insights in neurobiology to develop novel solutions for Alzheimer's disease and other neurodegenerative diseases. Our strategy is to leverage our unique scientific/clinical platform to develop a first-in-class program for treating neurodegenerative diseases, such as Alzheimer's.

We currently have two biopharmaceutical assets under development:

- our lead therapeutic product candidate, called simufilam, is a novel oral treatment for Alzheimer's disease dementia; and
- our lead investigational diagnostic product candidate, called SavaDx, is a novel way to detect the presence of Alzheimer's disease from a small sample of blood.

Our scientific approach for the treatment of Alzheimer's disease seeks to simultaneously suppress *both* neurodegeneration and neuroinflammation. We believe our ability to improve multiple vital functions in the brain represents a new, different and crucial approach to address Alzheimer's disease.

We believe simufilam improves brain health by reverting altered FLNA back to its native, healthy conformation, thus countering the downstream toxic effects of altered FLNA. We have generated and published experimental or clinical evidence of improved brain health with simufilam. Importantly, simufilam is not dependent on clearing amyloid from the brain. Since simufilam has a unique drug mechanism of action, we believe its potential therapeutic effects may be additive or synergistic with those of other therapeutic candidates aiming to treat neurodegeneration.

We are currently conducting two randomized placebo-controlled Phase 3 clinical trials of oral simufilam in patients with Alzheimer's disease dementia. Both trials are fully enrolled. The trials have randomized a total of approximately 1,900 patients with mild to moderate Alzheimer's disease at baseline. All efficacy data from our Phase 3 program remain blinded. There are no interim analyses on efficacy outcomes.

Our first Phase 3 study, called RETHINK-ALZ, is designed to evaluate the safety and efficacy of simufilam 100 mg tablets versus placebo over 52 weeks (NCT04994483). Top-line results of our 52-week Phase 3 study are anticipated approximately year-end 2024.

Our second Phase 3 study, called REFOCUS-ALZ, is designed to evaluate the safety and efficacy of oral simufilam 100 mg and 50 mg tablets versus placebo over 76 weeks (NCT05026177). Top-line results of our 76-week Phase 3 study are anticipated approximately mid-year 2025.

Our investigational diagnostic product candidate, called SavaDx, is an early-stage program focused on detecting the presence of Alzheimer's disease from a small sample of blood. The goal is to make the detection of Alzheimer's disease as simple as getting a blood test.

Financial Overview

We have yet to generate any revenues from product sales. We have an accumulated deficit of $380.8 million at December 31, 2023. These losses have resulted principally from costs incurred in connection with research and development activities, salaries and other personnel-related costs and general corporate expenses. Research and development activities include costs of preclinical and clinical studies as well as clinical supplies associated with our product candidates. Salaries and other personnel-related costs include stock-based compensation associated with options and other equity awards granted to employees and non-employees. Our operating results may fluctuate substantially from period to period as a result of the timing of preclinical activities, enrollment rates of clinical studies for our product candidates and our need for clinical supplies.

We believe that our cash and cash equivalents at December 31, 2023, will enable us to fund our operating expenses for at least the next 12 months. In addition, we may seek in the future to fund our operations through additional public or private equity or debt financings or other sources. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. If we are unable to obtain financing or reach profitability, the related lack of liquidity will have a material adverse effect on our operations and future prospects, and we may have to significantly delay, scale back or discontinue the development and commercialization of simufilam, our lead drug candidate, or delay our efforts to expand our product pipeline.

We expect to continue to use significant cash resources in our operations for the next several years. Our cash requirements for operating activities and capital expenditures may increase in the future as we:

- continue our ongoing Phase 3 program with simufilam;
- manufacture large-scale supplies for simufilam;
- conduct other preclinical and clinical studies for our product candidates;
- seek regulatory approvals for our product candidates;
- develop, formulate, manufacture and commercialize our product candidates;
- implement additional internal systems and develop new infrastructure;
- acquire or in-license additional products or technologies, or expand the use of our technology;
- maintain, defend and expand the scope of our intellectual property;
- expend resources related to legal proceedings and claims, including U.S. government inquiries; and
- hire additional personnel.

Product revenue will depend on our ability to receive regulatory approvals for, and successfully market, our product candidates. If our development efforts result in regulatory approval and successful commercialization of our product candidates, we expect to generate revenue from direct sales of our drugs and/or, if we license our drugs to future collaborators, from the receipt of license fees and royalties from sales of licensed products. We conduct our research and development programs through a combination of internal and collaborative programs. We rely on arrangements with universities, certain collaborators, CDMOs, CROs and clinical research sites for a significant portion of our product development efforts.

Components of Operating Results

Operating Expenses

Research and Development Expenses

We focus substantially all of our research and development efforts in the development of simufilam. Research and development expenses for our investigational diagnostic product candidate, SavaDx, represented less than 1% of total research and development expenses for the periods presented. The following table summarizes expenses by category for research and development efforts (in thousands):

	Years ended December 31,		
	2023	2022	2021
Phase 2 and Phase 3 clinical trials	$ 71,087	$ 54,149	$ 12,322
Pre-clinical and Phase 1 studies	6,425	2,966	927
Chemical, Manufacturing and Controls costs (“CMC costs”)	2,910	2,573	4,606
Personnel related	5,723	5,631	4,633
Stock-based compensation	2,050	1,631	1,302
Other	1,228	1,082	1,023
	$ 89,423	$ 68,032	$ 24,813

Clinical trial costs include the costs of our CRO. CMC costs include costs related to our contract development and manufacturing organizations. Research and development expenses include compensation, contractor fees and supplies as well as allocated common costs such as facilities.

During the year ended December 31, 2023, we did not receive reimbursement from NIH research grants. During the years ended December 31, 2022 and 2021, we received $0.9 million and $3.9 million in research grants from the NIH, respectively. When applicable, the proceeds from grants are recorded as reductions to our research and development expenses.

Our technology has been applied across certain of our portfolio of product candidates. Data, know-how, personnel, clinical results, research results and other matters related to the research and development of any one of our product candidates also relate to, and further the development of, our other product candidates. As a result, costs allocated to a specific product candidate may not necessarily reflect the actual costs surrounding research and development of such product candidate due to cross application of the foregoing.

Estimating the dates of completion of clinical development, and the costs to complete development, of our product candidates would be highly speculative and subjective. Pharmaceutical products take a significant amount of time to research, develop and commercialize. The clinical study portion of the development of a new drug alone usually spans several years. We expect our research and development expenses to decrease modestly in 2024 as a result of decreased spending for our Phase 3 program, as patient screening and enrollment are now complete for the Phase 3 clinical studies. The decrease in Phase 3 program costs is expected to be partially offset by increased enrollment in the open-label study as well as higher stock-based compensation expense. We expect to reassess our future research and development plans based on our review of data we receive from our current research and development activities. The cost and pace of our future research and development activities are linked and subject to change.

Critical Accounting Estimates

The preparation of our consolidated financial statements in accordance with U.S. generally accepted accounting principles requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues, expenses and interest income in our consolidated financial statements and accompanying notes. We evaluate our estimates on an ongoing basis, including those estimates related to agreements and research collaborations. We base our estimates on historical experience and various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Our significant accounting policies are described in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, and we believe that the accounting policies discussed below involve the greatest degree of complexity and exercise of significant judgments and estimates by our management. The methods, estimates and judgments that we use in applying our accounting policies have a significant impact on our results of operations and, accordingly, we believe the policies described below are the most critical for understanding and evaluating our financial condition and results of operations.

- Research Contracts, Prepaids and Accruals. We have entered into various research and development contracts with research institutions and other third-party vendors. These agreements are generally cancelable. Related payments are recorded as research and development expenses as incurred. We record prepaids and accruals for estimated ongoing research costs. When evaluating the adequacy of prepaid expenses and accrued liabilities, we analyze progress of the studies including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the prepaid and accrued balances at the end of any reporting period. Actual results could differ from our estimates. Our historical prepaid and accrual estimates have not been materially different from actual costs.

- Legal and other contingencies. The Company is subject to lawsuits, claims, allegations and investigations regarding simufilam and SavaDx. The Company believes the claims are without merit and intends to defend against these lawsuits vigorously. The Company is unable to estimate the possible loss or range of loss, if any, associated with these lawsuits. However, litigation is subject to inherent uncertainties, and unfavorable rulings could occur. If an unfavorable ruling were to occur, it may cause a material adverse impact on the results of operations, cash flows, or financial condition for the period in which the ruling occurs, or future periods. Refer to Note 12 to the Consolidated Financial Statements for further information on contingencies.

- 2020 Cash Incentive Bonus Plan. In 2020, we established the 2020 Cash Incentive Bonus Plan (the “Plan”) to incentivize Plan participants. Awards under the Plan are accounted for as liability awards under Accounting Standards Codification (ASC) 718, “Stock-based Compensation”. The fair value of each potential Plan award will be determined once a grant date occurs and will be remeasured each reporting period. Compensation expense associated with the Plan will be recognized over the expected achievement period for each Plan award, when a Performance Condition is considered probable of being met.

  The Plan was established to promote the long-term success of the Company by creating an “at-risk” cash bonus program that rewards Plan participants with additional cash compensation in lockstep with significant increases in our market capitalization. The Plan is considered “at-risk” because Plan participants will not receive a cash bonus unless our market capitalization increases significantly and (1) we complete a merger or acquisition transaction that constitutes a sale of ownership of the Company or its assets (a Merger Transaction) or (2) the Compensation Committee of the Board (the Compensation Committee) determines the Company has sufficient cash on hand, as defined in the Plan, to render payment (each, a “Performance Condition”), neither of which may ever occur. Because of the inherent discretion and uncertainty regarding these requirements, we have concluded that a Plan grant date has not occurred as of December 31, 2023. No actual cash payments were authorized or made to participants under the Plan through December 31, 2023.

- Stock-based Compensation. We recognize non-cash expense for the fair value of all stock options and other share-based awards. We use the Black-Scholes option valuation model to calculate the fair value of stock options, using the single-option award approach and straight-line attribution method. Significant judgments and estimates are made in determining inputs to the Black-Scholes option valuation model. See Note 7 to our Consolidated Financial Statements for significant assumptions regarding stock-based compensation.

Recent Accounting Pronouncements

See Note 2. Summary of Significant Accounting Policies, in Notes to the Consolidated Financial Statements in Item 8 of Part II of this Annual Report on Form 10-K.

Results of Operations – Comparison of years ended December 31, 2023 and 2022

Research and Development Expense

Research and development expenses consist primarily of costs of drug development work associated with our product candidates, including:

- clinical studies,
- preclinical testing,
- clinical supplies and related formulation and design costs, and
- compensation and other personnel-related expenses.

Research and development expenses increased to $89.4 million in 2023 from $68.0 million in 2022, representing a 31% increase. This increase was due primarily to costs related to conducting the ongoing Phase 3 clinical program of simufilam, costs of a cognition maintenance study and an ongoing open-label study in simufilam compared to the prior year. Higher pre-clinical study costs also contributed to the increase.

We expect research and development expense to decrease modestly in future periods as patient screening and enrollment is complete for our Phase 3 clinical program. The decrease in Phase 3 program costs is expected to be partially offset by increased enrollment in the open-label study as well as higher stock-based compensation expense due to new grant awards in 2023.

General and Administrative Expense

General and administrative expenses consist of personnel costs, allocated expenses and other expenses for outside professional services, including legal, human resources, audit and accounting services. Personnel costs consist of salaries, bonus, benefits and stock-based compensation. Allocated expenses consist primarily of existing facility costs. We incur insurance, audit, investor relations, SOX compliance and other administrative and professional services expenses associated with operating as a public company, including expenses related to compliance with the rules and regulations of the SEC and Nasdaq. General and administrative expense increased to $16.5 million in 2023 from $12.0 million in 2022. The 38% increase was due primarily to higher legal fees, stock-based compensation due to new grant awards and personnel costs compared to the prior year.

Interest Income

Interest and other income, net, was $7.8 million in 2023 compared to $2.8 million in 2022. The increase in interest income was due to increases in interest rates in 2023 compared to the prior year.

We expect interest income to decrease in 2024 compared to 2023 as we use cash balances in operations.

Other income, net

We record the activities related to leasing office space to third parties in buildings we own as other income, net, as leasing is not core to the Company's operations. Other income, net, was $0.9 million during the year ended December 31, 2023 compared to $1.0 million during 2022. We expect other income, net, to decrease in 2024 as higher vacancy rates are expected to lower rental income.

Depreciation and amortization for the office complex is included in general and administrative and research and development expense, and thus not reflected in other income, net.

Comparison of the years ended December 31, 2022 and 2021

Refer to "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Results of Operations" in our 2022 Annual Report on Form 10-K for a discussion of the results of operations for the year ended December 31, 2022 compared to the year ended December 31, 2021.

Liquidity and Capital Resources

Since inception, we have financed our operations primarily through public and private stock offerings, payments received under collaborative agreements and interest earned on our cash and cash equivalents balances. We intend to continue to use our capital resources to fund research and development activities, capital expenditures, working capital requirements and other general corporate purposes. As of December 31, 2023, cash and cash equivalents totaled $121.1 million.

2024 Common Stock Warrant Distribution and On-going Offering

On January 3, 2024, we completed a distribution of approximately 16.9 million warrants to purchase shares of our common stock to holders of record of our common stock as of the close of business on December 22, 2023.

From January 3, 2024 to February 26, 2024, a total of approximately 659,000 warrants were exercised at an exercise price of $33.00 per warrant resulting in gross proceeds to the Company of approximately $21.8 million and the issuance of approximately 989,000 shares of our common stock, including Bonus Share Fractions. After the first $20 million of gross proceeds, the Company is obligated to pay a commission of 2.5% of the gross proceeds from the sale of shares of common stock in the offering to our financial advisor for the warrant distribution.

Until the Bonus Share Expiration Date (described below), a holder exercising its warrants will receive an additional 0.5 shares of common stock for each warrant exercised, without the payment of any additional exercise price. The right to receive the Bonus Share Fraction will expire upon the earlier of (i) the first business day following the last day of the first 30 consecutive trading day period (commencing on or after January 3, 2024) in which the daily volume weighted average price (the "VWAP") of the shares of common stock has been at the then applicable trigger price, initially $26.40, for at least 20 trading days (whether or not consecutive) (the "Bonus Price Condition") and (ii) the date specified by the Company upon not less than 20 business days' public notice (either condition being the "Bonus Share Expiration Date"). Any warrant exercised with an exercise date after the Bonus Share Expiration Date will not be entitled to the Bonus Share Fraction. The Company will make a public announcement of the Bonus Share Expiration Date (i) at least 20 business days prior to such date, in the case of the Company setting a Bonus Share Expiration Date and (ii) prior to market open on the Bonus Share Expiration Date in the case of a Bonus Price Condition.

Unless earlier redeemed, the warrants will expire and cease to be exercisable on November 15, 2024. The warrants are redeemable at the Company's sole option at any time with a redemption date on or after April 15, 2024. We will provide at least 20 calendar days' notice by press release of the date selected, if any, for a redemption. The warrant offering is ongoing as of the date of filing of this Annual Report on Form 10-K.

2022 Registered Direct Offering

On November 22, 2022, we completed a common stock offering pursuant to which certain investors purchased 1,666,667 shares of common stock at a price of $30.00 per share. Net proceeds of the offering were approximately $47.3 million after deducting offering expenses.

2021 Registered Direct Offering

On February 12, 2021, we completed a common stock offering pursuant to which certain investors purchased 4,081,633 shares of common stock at a price of $49.00 per share. Net proceeds of the offering were approximately $189.7 million after deducting offering expenses.

At the Market (ATM) Common Stock Issuance

On May 1, 2023, we entered into an at-the-market offering program ("ATM") to sell, from time to time, shares of our common stock having an aggregate offering price of up to $200 million in common stock pursuant to a shelf registration statement that was filed with the SEC on May 1, 2023 and became effective immediately upon filing. We are obligated to pay a commission of up to 3% of the gross proceeds from the sale of shares of common stock under the ATM. We are not obligated to sell any shares in the offering.

There were no common stock sales under the ATM during the year ended December 31, 2023.

In March 2020, we entered into an at-the-market offering program ("2020 Program") to sell, from time to time, shares of our common stock having an aggregate offering price of up to $100 million in transactions pursuant to a shelf registration statement that was declared effective by the SEC on May 5, 2020. We gave notice of termination for the 2020 Program effective on April 26, 2023, which was effective May 1, 2023. There were no common stock sales under the 2020 Program through its termination.

NIH Research Grant Awards

Our research has been previously supported by NIH under multiple research grant awards. Strong, historical support from NIH has allowed us to advance our two lead product candidates, simufilam and SavaDx, into clinical development.

In May 2021, we were awarded a new research grant award from NIH of up to $2.7 million to support clinical readiness activities for a Phase 3 program with simufilam. This non-dilutive research grant is intended to strengthen our clinical program of simufilam, our investigational drug to treat Alzheimer's disease. All of our NIH research grant awards are paid out on a reimbursement basis and require milestone-based technical progress. There were no remaining funds for NIH grant awards as of December 31, 2023.

2020 Cash Incentive Bonus Plan Obligations

In August 2020, the Board approved the *2020 Cash Incentive Bonus Plan* (the Plan). The Plan was established to promote the long-term success of the Company by creating an "at-risk" cash bonus program that rewards Plan participants with additional cash compensation in lockstep with significant increases in the Company's market capitalization. The Plan is considered "at-risk" because Plan participants will not receive a cash bonus unless the Company's market capitalization increases significantly and certain other conditions specified in the Plan are met. Specifically, Plan participants will not be paid any cash bonuses unless (1) the Company completes a merger or acquisition transaction that constitutes a sale of ownership of the Company or its assets (a Merger Transaction) or (2) the Compensation Committee determines the Company has sufficient cash on hand, as defined in the Plan. Plan participants will be paid all earned cash bonuses in the event of a Merger Transaction.

As of December 31, 2022, the Company's independent directors were participants in the Plan. However, effective March 16, 2023, the Board amended the Plan to remove all independent directors as participants in the Plan and the independent directors consented to such removal. The independent directors' share of potential benefits under the Plan were completely forfeited to the Company and will not be allocated to any other participant under the Plan. The Company's independent directors have not received, and as a result of such amendment will never receive, any payments under the Plan.

The Company's market capitalization, including all outstanding stock options, was $89.4 million at the inception of the Plan in August 2020. If the Company were to exceed a $5 billion market capitalization for no less than 20 consecutive trading days, and conditions noted above for payment are met, all Plan milestones would be deemed achieved, in which case total cash bonus awards would range from a minimum of $111.4 million up to a hypothetical maximum of $289.7 million. Any warrants outstanding are excluded from the determination of market capitalization.

The Company's potential financial obligation to Plan participants at December 31, 2023 totaled $6.5 million (after the March 2023 Plan amendment), based upon the achievement of one Plan milestone in the Company's market capitalization in 2020. No actual cash bonus payments have been made to any Plan participant, as the Company has not yet satisfied all the conditions necessary for amounts to be paid under the Plan. During the year ended December 31, 2021, the Company's market capitalization increased substantially. These increases triggered the achievement of 11 additional Plan milestones. Collectively, the achievement of such milestones could trigger potential Company obligations to Plan participants ranging from a minimum of $74.9 million up to a hypothetical maximum of $202.3 million, with exact amounts to be determined by the Compensation Committee and contingent upon future satisfaction of a Performance Condition.

No valuation milestones were achieved during the years ended December 31, 2023 or 2022.

No actual cash payments were authorized or made to participants under the Plan as of December 31, 2023, or through the filing date of this Annual Report on Form 10-K.

Use of Cash

The following table sets forth a summary of the primary sources and uses of cash for each of the periods presented below (in thousands):

	Years ended December 31,		
	2023	2022	2021
Net cash used in operating activities	$ (82,025)	$ (77,514)	$ (30,196)
Net cash used in investing activities	(414)	(2,712)	(22,214)
Net cash provided by financing activities	2,560	47,804	192,341
Net (decrease) increase in cash and cash equivalents	$ (79,879)	$ (32,422)	$ 139,931

Net cash used in operating activities was $82.0 million for the year ended December 31, 2023, resulting primarily from the net loss reported of $97.2 million partially offset by an increase in accounts payable of $6.9 million and accrued development expense of $0.8 million, a decrease in in prepaid and other assets of $1.7 million, stock-based compensation expense of $4.6 million and depreciation and amortization of $1.0 million.

Net cash used in operating activities was $77.5 million for the year ended December 31, 2022, resulting primarily from the net loss reported of $76.2 million, a decrease in accounts payable of $3.4 million, accrued compensation and benefits of $1.7 million and a decrease in accrued developmental expenses of $0.5 million, partially offset by a decrease in in prepaid and other assets of $1.2 million, and stock-based compensation expense of $2.1 million.

Net cash used in investing activities during the year ended December 31, 2023 was $0.4 million as final payment was made on renovations and fixtures for our corporate headquarters.

Net cash used in investing activities during the year ended December 31, 2022 was $2.7 million related to renovations and fixtures for our corporate headquarters.

Net cash provided by financing activities during the year ended December 31, 2023 was $2.6 million from the exercise of stock options.

Net cash provided by financing activities during the year ended December 31, 2022 was $47.8 million, consisting of $47.3 million in proceeds from our registered direct offering of common stock in November 2022 and $0.5 million from the exercise of stock options.

Use of Cash – Comparison of the years ended December 31, 2022 and 2021

Refer to “Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations—Results of Operations” in our 2022 Annual Report on Form 10-K for a discussion of use of cash for the year ended December 31, 2022 compared to the year ended December 31, 2021.

Property and Leases

We own an office complex in Austin, Texas, a portion of which serves as our corporate headquarters. This property is intended to accommodate our anticipated growth and expansion of our operations in the coming years. Maintenance, physical facilities, leasing, property management and other key responsibilities related to property ownership are outsourced to professional real-estate managers. The office complex measures approximately 90,000 rentable square feet. At December 31, 2023, we occupied approximately 25% of the property with the remainder either leased or available for lease to third parties. Virtually all existing tenant leases will expire in 2024. We believe tenant leases that expire in 2024 may likely not be extended, renewed or re-leased beyond their expiry date, in which case we will no longer receive rental payments or reimbursement for shared expense for such office space.

We leased approximately 6,000 square feet of office space pursuant to a non-cancelable operating lease in Austin, Texas expiring in April 2024. We terminated this lease on February 22, 2023 with no continuing obligations.

Future Funding Requirements

We have an accumulated deficit of $380.8 million at December 31, 2023. We expect our cash requirements to be significant in the future. The amount and timing of our future cash requirements will depend on regulatory and market acceptance of our product candidates and the resources we devote to researching and developing, formulating, manufacturing, commercializing and supporting our products. We believe that our current resources should be sufficient to fund our operations for at least the next 12 months. We may seek additional future funding through public or private financing in the future, if such funding is available and on terms acceptable to us.

If we raise additional funds by issuing equity or equity-linked securities, our stockholders will experience dilution, which may be substantial. If we raise additional funds through the issuance of preferred equity securities or through debt financing, the terms of such future preferred equity or debt into which we enter may impose upon us additional covenants that restrict our operations, including limitations on our ability to incur liens or additional debt, pay dividends, repurchase our common stock, make certain investments and engage in certain merger, consolidation or asset sale transactions. Any debt financing or additional equity that we raise may contain terms that are not favorable to us or our stockholders. If we are unable to raise additional funds when needed, we may be required to delay, reduce, or terminate some or all of our development programs and clinical trials. We may also be required to sell or license to others rights to our drug candidates in certain territories or indications that we would prefer to develop and commercialize ourselves.

Item 7A. ***Quantitative and Qualitative Disclosures about Market Risk***

We are exposed to market risks in the ordinary course of our business, primarily related to interest rate sensitivities and, to a lesser extent, currency fluctuations related to our clinical operations outside the U.S.

Interest Rate Sensitivity

We are exposed to market risk related to changes in interest rates. We had cash and cash equivalents of $121.1 million as of December 31, 2023, which consisted primarily of U.S. Treasury securities and money market accounts.

The primary objective of our investment activities is to preserve capital to fund our operations. We also seek to maximize income from our investments without assuming significant risk. To achieve our objectives, we maintain investment vehicles with high credit quality and short-term duration, in accordance with our board-approved investment policy. Such interest-earning instruments carry a degree of interest rate risk. However, due to the generally short-term maturities and low risk profile of our cash equivalents, an immediate 100 basis point increase or decrease in interest rates during any of the periods presented would increase or decrease our annual net loss by less than $2 million in our condensed consolidated financial statements.

Item 8. ***Consolidated Financial Statements and Supplementary Data***

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Cassava Sciences, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Cassava Sciences, Inc. (the Company) as of December 31, 2023 and 2022, the related consolidated statements of operations, stockholders' equity and cash flows for each of the three 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 three years in the period ended December 31, 2023, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2023, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 28, 2024 expressed an unqualified opinion thereon.

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 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. 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.

Critical Audit Matters

The critical audit matters communicated below are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Description of the Matter **Prepaid and Accrued Development Expenses Related to CRO Pass Through Costs for Clinical Trials**

As explained in Note 2 to the consolidated financial statements, the Company contracts with a contract research organization (CRO) to assist the Company in conducting clinical trials, the costs for which are recorded as research and development expenses as incurred. A portion of these costs are pass through costs, which are costs incurred by third parties contracted by the CRO to perform certain services for clinical trials. These costs are passed through to the Company by the CRO. Depending on the timing of CRO payments, the Company records these costs as either prepaid or accrued development expenses. These prepaid or accrued development expenses are based on management’s determination of pass through costs incurred by the third parties based on the status of the clinical trials. At December 31, 2023, based on timing of invoicing and costs incurred, prepaid and accrued development expenses for CRO pass through costs were $317 thousand and $182 thousand, respectively.

Auditing the Company’s prepaid and accrued development expenses related to CRO pass through costs for clinical trials was challenging because the recorded amounts involved management’s validation of the completeness and accuracy of costs incurred for services provided but not yet billed by third parties to the CRO.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design, and tested the operating effectiveness of controls over the Company's process of accounting for prepaid and accrued development expenses related to CRO pass through costs for clinical trials, including management's review of the progress of clinical trial activity in comparison to budgets and invoices received from the CRO.

To evaluate the adequacy of the Company's prepaid and accrued development expenses related to CRO pass through costs for clinical trials, our audit procedures included, among others, testing the completeness and accuracy of the underlying data used by management to determine the prepaid and accrued development expenses. To evaluate completeness and accuracy of the data, on a sample basis, we: (i) obtained confirmation directly from the CRO of key clinical trial contract terms and conditions and any amendments thereto, as well as pass through costs incurred to date, (ii) agreed data used in the calculation to the contracts with the CRO, and any amendments thereto, and/or the data obtained from the CRO, (iii) corroborated the progress of clinical trials through inquiry of Company personnel who oversee clinical trials, and (iv) obtained and reviewed subsequent invoices received from the CRO to corroborate the prepaid and accrued development expenses at the end of the reporting period.

Description of the Matter

Loss Contingencies

The Company is subject to lawsuits, claims, allegations, and investigations regarding simufilam and SavaDx. As described in Note 12 to the consolidated financial statements, such allegations and claims could result in adverse consequences. At December 31, 2023, the Company was unable to determine the likelihood of a loss, if any, associated with these lawsuits and investigations and therefore was unable to reasonably estimate a loss or range of loss.

Auditing management's accounting for, and disclosure of, loss contingencies related to the lawsuits and investigations was challenging because management's evaluation of the likelihood of loss required judgment.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design, and tested the operating effectiveness of controls over the Company's process of evaluation of the accounting for and disclosure of these matters. This included controls over management's assessment of the likelihood of incurrence of a loss and whether the loss or range of loss was reasonably estimable, and the development of related disclosures.

Our audit procedures included gaining an understanding of the status of ongoing lawsuits and investigations, reading the meeting minutes of the board of directors and of the committees of the board of directors, reading summaries of the proceedings and related correspondence, requesting letters from internal and external legal counsel, meeting with internal and external legal counsel to discuss developments related to the lawsuits and investigations together with our forensic professionals, and obtaining written representations from the Company on these matters. We also evaluated the Company's disclosures in relation to these matters.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2002.

Austin, Texas
February 28, 2024

CASSAVA SCIENCES, INC.

CONSOLIDATED BALANCE SHEETS
(In thousands, except share and par value data)

	December 31, 2023	December 31, 2022
ASSETS		
Current assets:		
Cash and cash equivalents	$ 121,136	$ 201,015
Prepaid expenses and other current assets	8,497	10,211
Total current assets	129,633	211,226
Operating lease right-of-use assets	—	122
Property and equipment, net	21,854	22,864
Intangible assets, net	176	622
Total assets	$ 151,663	$ 234,834
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable and other accrued expenses	$ 10,573	$ 4,017
Accrued development expense	3,037	2,280
Accrued compensation and benefits	200	170
Operating lease liabilities, current	—	104
Other current liabilities	385	492
Total current liabilities	14,195	7,063
Operating lease liabilities, non-current	—	35
Other non-current liabilities	—	197
Total liabilities	14,195	7,295
Commitments and contingencies (Notes 10, 11 and 12)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized, none issued and outstanding	—	—
Common stock, $0.001 par value; 120,000,000 shares authorized; 42,236,919 and 41,735,557 shares issued and outstanding at December 31, 2023 and December 31, 2022, respectively	42	42
Additional paid-in capital	518,195	511,049
Accumulated deficit	(380,769)	(283,552)
Total stockholders' equity	137,468	227,539
Total liabilities and stockholders' equity	$ 151,663	$ 234,834

See accompanying notes to consolidated financial statements.

CASSAVA SCIENCES, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except per share data)

	Years ended December 31,		
	2023	**2022**	**2021**
Operating expenses:			
Research and development, net of grant reimbursement	$ 89,423	$ 68,032	$ 24,813
General and administrative	16,534	11,988	8,055
Total operating expenses	105,957	80,020	32,868
Operating loss	(105,957)	(80,020)	(32,868)
Interest income	7,833	2,777	49
Other income, net	907	997	434
Net loss	$ (97,217)	$ (76,246)	$ (32,385)
Net loss per share, basic and diluted	$ (2.32)	$ (1.90)	$ (0.82)
Shares used in computing net loss per share, basic and diluted	41,932	40,202	39,405

See accompanying notes to consolidated financial statements.

CASSAVA SCIENCES, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(In thousands, except share data)

	Common stock		Additional paid-in capital	Accumulated deficit	Total stockholders' equity
	Shares	Par value			
Balance at December 31, 2020	35,237,987	35	267,086	(174,921)	92,200
Stock-based compensation for:					
Stock options for employees	—	—	1,706	—	1,706
Stock options for non-employees	—	—	53	—	53
Issuance of common stock pursuant to exercise of stock options	143,153	—	1,824	—	1,824
Issuance of common stock pursuant to exercise of warrants	554,019	1	691	—	692
Common stock issued in conjunction with registered direct offering, net of issuance costs	4,081,633	4	189,821	—	189,825
Net loss	—	—	—	(32,385)	(32,385)
Balance at December 31, 2021	40,016,792	$ 40	$ 461,181	$ (207,306)	$ 253,915
Stock-based compensation for:					
Stock options for employees	—	—	1,972	—	1,972
Stock options for non-employees	—	—	94	—	94
Expiration of restricted stock Performance Awards	(57,143)	—	—	—	—
Issuance of common stock pursuant to exercise of stock options	109,241	—	475	—	475
Common stock issued in conjunction with registered direct offering, net of issuance costs	1,666,667	2	47,327	—	47,329
Net loss	—	—	—	(76,246)	(76,246)
Balance at December 31, 2022	41,735,557	$ 42	$ 511,049	$ (283,552)	$ 227,539
Stock-based compensation for:					
Stock options for employees	—	—	4,493	—	4,493
Stock options for non-employees	—	—	93	—	93
Issuance of common stock pursuant to exercise of stock options	501,362	—	2,560	—	2,560
Net loss	—	—	—	(97,217)	(97,217)
Balance at December 31, 2023	42,236,919	$ 42	$ 518,195	$ (380,769)	$ 137,468

See accompanying notes to consolidated financial statements.

CASSAVA SCIENCES, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Years ended December 31,		
	2023	**2022**	**2021**
Cash flows from operating activities:			
Net loss	$ (97,217)	$ (76,246)	$ (32,385)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	4,586	2,066	1,759
Depreciation	1,084	804	310
Amortization of intangible assets	446	497	224
Changes in operating assets and liabilities:			
Prepaid and other assets	1,714	1,189	(10,956)
Operating lease right-of-use assets and liabilities	(17)	(9)	28
Accounts payable and other accrued expenses	6,896	(3,449)	6,215
Accrued development expense	757	(523)	2,084
Accrued compensation and benefits	30	(1,707)	1,794
Other liabilities	(304)	(136)	731
Net cash used in operating activities	(82,025)	(77,514)	(30,196)
Cash flows from investing activities:			
Purchase of property and equipment	(414)	(2,712)	(22,214)
Net cash used in investing activities	(414)	(2,712)	(22,214)
Cash flows from financing activities:			
Proceeds from issuance of common stock upon exercise of stock options	2,560	475	1,824
Proceeds from issuance of common stock upon exercise of 2018 warrants	—	—	692
Proceeds from common stock offering, net of issuance costs	—	47,329	189,825
Net cash provided by financing activities	2,560	47,804	192,341
Net (decrease) increase in cash and cash equivalents	(79,879)	(32,422)	139,931
Cash and cash equivalents at beginning of period	201,015	233,437	93,506
Cash and cash equivalents at end of period	$ 121,136	$ 201,015	$ 233,437
Supplemental cash flow information:			
Non-cash investing activities			
Purchases of property and equipment included in accounts payable	$ —	$ 340	$ —

See accompanying notes to consolidated financial statements.

CASSAVA SCIENCES, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. General, Liquidity and Basis of Presentation

Cassava Sciences, Inc. and its wholly-owned subsidiary (collectively referred to as the "Company") discovers and develops proprietary pharmaceutical product candidates that may offer significant improvements to patients and healthcare professionals. The Company generally focuses its product discovery and development efforts on disorders of the nervous system.

Basis of Consolidation

The consolidated financial statements include the accounts of the Company and its wholly-owned subsidiary. All intercompany transactions have been eliminated in consolidation.

Liquidity

The Company has incurred significant net losses and negative cash flows since inception, and as a result has an accumulated deficit of $ 380.8 million at December 31, 2023. The Company expects its cash requirements to be significant in the future. The amount and timing of the Company's future cash requirements will depend on regulatory and market acceptance of its product candidates and the resources it devotes to researching and developing, formulating, manufacturing, commercializing and supporting its products. The Company may seek additional funding through public or private financing in the future, if such funding is available and on terms acceptable to the Company. There are no assurances that additional financing will be available on favorable terms, or at all. However, management believes that the current working capital position will be sufficient to meet the Company's working capital needs for at least the next 12 months.

2. Summary of Significant Accounting Policies

Use of Estimates

The Company makes estimates and assumptions in preparing its consolidated financial statements in conformity with accounting principles generally accepted in the United States. These estimates and assumptions affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amount of revenue earned and expenses incurred during the reporting period. The Company evaluates its estimates on an ongoing basis, including those estimates related to clinical trials and manufacturing agreements. Actual results could differ from these estimates and assumptions.

Proceeds from Grants

During 2023, there were no reimbursements received pursuant to National Institutes of Health ("NIH") research grants. In 2022, and 2021, the Company received $ 0.9 million and $ 3.9 million of reimbursement, respectively, from the NIH and National Institute on Drug Abuse. The Company records the proceeds from these grants as reductions to its research and development expenses.

Cash and Cash Equivalents and Concentration of Credit Risk

The Company invests in cash and cash equivalents. The Company considers highly-liquid financial instruments with original maturities of three months or less to be cash equivalents. Highly liquid investments that are considered cash equivalents include money market accounts and funds, certificates of deposit and U.S. Treasury securities. The Company maintains its cash and cash equivalents at one financial institution.

Fair Value Measurements

The Company recognizes financial instruments in accordance with the authoritative guidance on fair value measurements and disclosures for financial assets and liabilities. This guidance defines fair value, establishes a framework for measuring fair value in accordance with GAAP, and expands disclosures about fair value measurements. The guidance also establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value. These tiers include:

- Level 1 includes quoted prices in active markets.
- Level 2 includes significant observable inputs, such as quoted prices for identical or similar securities, or other inputs that are observable and can be corroborated by observable market data for similar securities. The Company uses market pricing and other observable market inputs obtained from third-party providers. It uses the bid price to establish fair value where a bid price is available. The Company does not have any financial instruments where the fair value is based on Level 2 inputs.
- Level 3 includes unobservable inputs that are supported by little or no market activity. The Company does not have any financial instruments where the fair value is based on Level 3 inputs.

If a financial instrument uses inputs that fall in different levels of the hierarchy, the instrument will be categorized based upon the lowest level of input that is significant to the fair value calculation. The fair value of cash and cash equivalents was based on Level 1 inputs at December 31, 2023 and 2022.

Business Segments

The Company reports segment information based on how it internally evaluates the operating performance of its business units, or segments. The Company's operations are confined to one business segment: the development of novel drugs and diagnostics.

Stock-based Compensation

The Company recognizes non-cash expense for the fair value of all stock options and other share-based awards. The Company uses the Black-Scholes option valuation model ("Black-Scholes") to calculate the fair value of stock options, using the single-option award approach and straight-line attribution method. This model requires the input of subjective assumptions including expected stock price volatility, expected life and estimated forfeitures of each award. These assumptions consist of estimates of future market conditions, which are inherently uncertain, and therefore, are subject to management's judgment. For all options granted, it recognizes the resulting fair value as expense on a straight-line basis over the vesting period of each respective stock option, generally three or four years.

The Company has granted share-based awards that vest upon achievement of certain performance criteria ("Performance Awards"). The Company multiplies the number of Performance Awards by the fair value of its common stock on the date of grant to calculate the fair value of each award. It estimates an implicit service period for achieving performance criteria for each award. The Company recognizes the resulting fair value as expense over the implicit service period when it concludes that achieving the performance criteria is probable. It periodically reviews and updates as appropriate its estimates of implicit service periods and conclusions on achieving the performance criteria. Performance Awards vest and common stock is issued upon achievement of the performance criteria.

Net Loss per Share

The Company computes basic net loss per share on the basis of the weighted-average number of common shares outstanding for the reporting period. Diluted net loss per share is computed on the basis of the weighted-average number of common shares outstanding plus potential dilutive common shares outstanding using the treasury-stock method. Potential dilutive common shares consist of outstanding common stock options and warrants. There is no difference between the Company's net loss and comprehensive loss. The numerators and denominators in the calculation of basic and diluted net loss per share were as follows (in thousands, except net loss per share data):

	Years ended December 31,		
	2023	2022	2021
Numerator:			
Net loss	$ (97,217)	$ (76,246)	$ (32,385)
Denominator:			
Shares used in computing net loss per share, basic and diluted	41,932	40,202	39,405
Net loss per share, basic and diluted	$ (2.32)	$ (1.90)	$ (0.82)
Dilutive common stock options excluded from net loss per share, diluted	2,123	2,055	2,211

The Company excluded common stock options and warrants outstanding, along with 57,143 restricted stock awards, from the calculation of net loss per share, diluted, because the effect of including outstanding options would have been anti-dilutive. The 57,143 restricted stock awards expired during the year ended December 31, 2022.

Fair Value of Financial Instruments

Financial instruments include accounts payable, accrued expenses and other liabilities. The estimated fair value of certain financial instruments may be determined using available market information or other appropriate valuation methodologies. However, considerable judgment is required in interpreting market data to develop estimates of fair value; therefore, the estimates are not necessarily indicative of the amounts that could be realized or would be paid in a current market exchange. The effect of using different market assumptions and/or estimation methodologies may be material to the estimated fair value amounts. The carrying amounts of accounts payable, accrued expenses and other liabilities are at cost, which approximates fair value due to the short maturity of those instruments.

Research Contracts, Prepaids and Accruals

The Company has entered into various research and development contracts with research institutions and other third-party vendors. These agreements are generally cancelable. Related payments are recorded as research and development expenses as incurred. The Company records prepaids and accruals for estimated ongoing research costs. When evaluating the adequacy of the prepaid expenses and accrued liabilities, the Company analyzes progress of the studies including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the prepaid and accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical prepaid and accrual estimates have not been materially different from actual costs.

Incentive Bonus Plan

In 2020, the Company established the 2020 Cash Incentive Bonus Plan (the "Plan") to incentivize Plan participants. Awards under the Plan are accounted for as liability awards under ASC 718 "*Stock-based Compensation*". The fair value of each potential Plan award will be determined once a grant date occurs and will be remeasured each reporting period. Compensation expense associated with the Plan will be recognized over the expected achievement period for each Plan award, when a Performance Condition (as defined below) is considered probable of being met. See Note 11 for further discussion of the Plan.

Leases

The Company recognizes assets and liabilities that arise from leases. For operating leases, the Company is required to recognize a right-of-use asset and a lease liability, initially measured at the present value of the lease payments during the lease term, in the consolidated balance sheets. The Company elected the short-term lease recognition exemption for all leases that qualify. This means, for those leases that qualify, the Company does not recognize right-of-use assets or lease liabilities. As the Company`s leases do not provide an implicit rate, it uses its incremental borrowing rate based on the information available at the commencement date in determining the present value of lease payments. Lease expense for lease payments is recognized on a straight-line basis over the lease term.

Property and equipment

Property and equipment is recorded at cost, net of accumulated depreciation. Depreciation is recorded using the straight-line method over the estimated useful lives of the assets. Owned buildings and related improvements have estimated useful lives of 39 years and approximately 10 years, respectively. Tenant improvements related to leased space are amortized using the straight-line method over the useful lives of the improvements or the remaining term of the corresponding leases, whichever is shorter. The remaining term of the corresponding leases is approximately 0.4 years.

Property and equipment are reviewed for impairment when events or changes in circumstances indicate the carrying amount of an asset may not be recoverable. If property and equipment are considered to be impaired, an impairment loss is recognized.

Intangible assets

Acquired intangible assets are recorded at fair value at the date of acquisition and primarily consist of lease-in-place agreements and leasing commissions. Intangible assets are amortized over the estimated life of the lease-in-place agreements, which approximates 0.3 years at December 31, 2023.

Intangible assets are reviewed for impairment on an annual basis, and when there is reason to believe that their values have been diminished or impaired. If intangible assets are considered to be impaired, an impairment loss is recognized.

Income Taxes

The Company accounts for income taxes under the asset and liability method. Deferred tax assets and liabilities are recognized for the estimated future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases. Deferred tax balances are adjusted to reflect tax rates based on currently enacted tax laws, which will be in effect in the years in which the temporary differences are expected to reverse. The Company has accumulated significant deferred tax assets that reflect the tax effects of net operating loss and tax credit carryovers and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Realization of certain deferred tax assets is dependent upon future earnings. The Company is uncertain about the timing and amount of any future earnings. Accordingly, the Company offsets these deferred tax assets with a valuation allowance.

The Company accounts for uncertain tax positions in accordance with ASC 740, “Income Taxes”, which clarifies the accounting for uncertainty in tax positions. These provisions require recognition of the impact of a tax position in the Company’s financial statements only if that position is more likely than not of being sustained upon examination by taxing authorities, based on the technical merits of the position. Any interest and penalties related to uncertain tax positions will be reflected as a component of income tax expense.

3. Prepaid Expenses and Other Current Assets

Prepaid and other current assets at December 31, 2023 and 2022 consisted of the following (in thousands):

	December 31,	
	2023	2022
Prepaid insurance	$ 759	$ 874
Contract research organization and other deposits	6,489	9,177
Interest receivable	962	—
Other	287	160
Total prepaid expenses and other current assets	$ 8,497	$ 10,211

Contract research organization and other deposits represent cash payments made to vendors in excess of expenses incurred.

4. Real Property and Other Income, Expense

The Company owns a two-building office complex in Austin, Texas, a portion of which serves as its corporate headquarters. This property is intended to accommodate the Company's anticipated growth and expansion of its operations in the coming years. Maintenance, physical facilities, leasing, property management and other key responsibilities related to property ownership are being outsourced to professional real-estate managers. The office complex measures approximately 90,000 rentable square feet. At December 31, 2023, the Company occupied approximately 25 % of the property with the remainder either leased or available for lease to third parties.

The Company records the net income from building operations and leases as other income, net, as leasing is not core to the Company's operations. Building depreciation and amortization for space not occupied by the Company is included in general and administrative expense. Building depreciation and amortization for space occupied by the Company is allocated between general and administrative expense and research and development expense. Components of other income, net, for the periods presented were as follows (in thousands):

	Years ended December 31,		
	2023	2022	2021
Lease revenue	$ 2,283	$ 2,459	$ 911
Property operating expenses	(1,376)	(1,462)	(477)
Other income, net	$ 907	$ 997	$ 434

The Company had accrued property taxes related to the building totaling $ 338,000 and $ 433,000 at December 31, 2023 and 2022, respectively, included in other current liabilities.

5. Property and Equipment

The components of property and equipment, net, as of December 31, 2023 and 2022 were as follows (in thousands):

	December 31,	
	2023	**2022**
Land	$ 3,734	$ 3,734
Buildings	15,980	15,980
Site improvements	494	470
Tenant improvements	3,062	3,016
Furniture and equipment	868	851
Construction in progress	—	13
Gross property and equipment	$ 24,138	$ 24,064
Accumulated depreciation	(2,284)	(1,200)
Property and equipment, net	$ 21,854	$ 22,864

Depreciation expense for property and equipment was $ 1,084,000 , $ 804,000 and $ 310,000 for the years ended December 31, 2023, 2022 and 2021, respectively.

6. Intangible assets

The components of intangible assets, net, as of December 31, 2023 and 2022 were as follows (in thousands):

	December 31,	
	2023	**2022**
Lease-in-place agreements	$ 1,053	$ 1,053
Leasing commissions and other	293	290
Gross intangible assets	$ 1,346	$ 1,343
Accumulated amortization	(1,170)	(721)
Intangible assets, net	$ 176	$ 622

Amortization expense for intangible assets was $ 446,000 , $ 497,000 and $ 224,000 for the years ended December 31, 2023, 2022 and 2021, respectively.

Amortization expense for finite-lived intangible assets is expected to be as follows (in thousands):

For the year ending December 31,	
2024	172
2025	4
Total amortization	$ 176

7. Stockholders' Equity and Stock-Based Compensation

Preferred Stock

The Company's Board of Directors (the "Board") has the authority to issue preferred stock in one or more series and to fix the rights, preferences, privileges, restrictions and the number of shares constituting any series or the designation of the series.

2022 Registered Direct Offering

On November 22, 2022, the Company completed a common stock offering pursuant to which certain investors purchased 1,666,667 shares of common stock at a price of $ 30.00 per share. Net proceeds of the offering were approximately $ 47.3 million after deducting offering expenses.

2021 Registered Direct Offering

On February 12, 2021, the Company completed a common stock offering pursuant to which certain investors purchased 4,081,633 shares of common stock at a price of $ 49.00 per share. Net proceeds of the offering were approximately $ 189.8 million after deducting offering expenses.

At the Market (ATM) Common Stock Issuance

On May 1, 2023, the Company entered into an at-the-market offering program ("ATM") to sell, from time to time, shares of Company common stock having an aggregate offering price of up to $ 200 million in common stock pursuant to a shelf registration statement that was filed with the U.S. Securities and Exchange Commission (the "SEC") on May 1, 2023 and became effective immediately upon filing. The Company is obligated to pay a commission of up to 3 % of the gross proceeds from the sale of shares of common stock under the ATM. The Company is not obligated to sell any shares in the offering.

There were no common stock sales under the ATM during the year ended December 31, 2023.

In March 2020, the Company entered into an at-the-market offering program ("2020 Program") to sell, from time to time, shares of Company common stock having an aggregate offering price of up to $ 100 million in transactions pursuant to a shelf registration statement that was declared effective by the SEC on May 5, 2020. The Company gave notice of termination for the 2020 Program on April 26, 2023, which was effective May 1, 2023. There were no common stock sales under the 2020 Program through its termination.

2008 Equity Incentive Plan

Under the Company's 2008 Equity Incentive Plan, or 2008 Equity Plan, its employees, directors and consultants received share-based awards, including grants of stock options and performance awards. The 2008 Equity Plan expired in December 2017. Share-based awards generally expire ten years from the date of grant.

2018 Equity Incentive Plan

The Company's Board or a designated Committee of the Board is responsible for administration of the Company's 2018 Omnibus Incentive Plan (the 2018 Plan) and determines the terms and conditions of each option granted, consistent with the terms of the 2018 Plan. The Company's employees, directors, and consultants are eligible to receive awards under the 2018 Plan, including grants of stock options and performance awards. Share-based awards generally expire ten years from the date of grant. The 2018 Plan, as amended on May 5, 2022, provides for issuance of up to 5,000,000 shares of common stock, par value $ 0.001 per share, subject to adjustment as provided in the 2018 Plan.

When stock options or performance awards are exercised net of the exercise price and taxes, the number of shares of stock issued is reduced by the number of shares equal to the amount of taxes owed by the award recipient and that number of shares are cancelled. The Company may then use its cash to pay tax authorities the amount of statutory taxes owed by and on behalf of the award recipient.

Stock Options

The following summarizes information about stock option activity during 2023:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term in Years	Aggregate Intrinsic Value in Millions
Outstanding as of December 31, 2022	2,529,448	$ 12.13	3.94	$ 49.60
Options granted	1,162,000	18.91		
Options exercised	(602,420)	8.38		
Options forfeited/canceled	(49,999)	32.59		
Outstanding as of December 31, 2023	3,039,029	—	—	$ —
Vested and expected to vest at December 31, 2023	3,039,029	15.13	6.21	$ 30.28
Exercisable at December 31, 2023	1,836,174	$ 11.09	3.98	$ 26.18

Of the stock options exercised during the year ended December 31, 2023, 101,058 stock options were net settled in satisfaction of the exercise price, with no cash proceeds received.

The following summarizes information about stock options at December 31, 2023 by a range of exercise prices:

		Options outstanding			Options exercisable	
Range of exercise prices		Number of outstanding options	Weighted average remaining contractual life (in years)	Weighted average exercise price	Number of vested options	Weighted average exercise price
From	To					
$ 0.95	$ 3.24	804,834	4.8	$ 2.17	804,834	$ 2.17
$ 4.09	$ 13.02	656,230	2.9	$ 8.33	647,167	$ 8.34
$ 14.21	$ 16.94	62,634	1.9	$ 16.00	62,634	$ 16.00
$ 17.54	$ 17.54	800,000	9.8	$ 17.54	44,442	$ 17.54
$ 21.11	$ 77.00	715,331	7.2	$ 33.20	277,097	$ 41.29
		3,039,029	6.2	$ 15.13	1,836,174	$ 11.09

The Company uses Black-Scholes to estimate the fair value of options granted. Black-Scholes considers a number of factors, including the market price of the Company's common stock. Factors utilized in Black-Scholes to value each stock option granted, and the weighted average fair value of options granted during the years ended December 31, 2023, 2022 and 2021 were as follows:

	2023	2022	2021
Volatility	152 % to 155 %	151 % to 154 %	147 % to 151 %
Risk-free interest rates	3.82 % to 4.37 %	1.98 % to 3.69 %	1.12 % to 1.42 %
Expected life of option (in years)	7	7	7
Dividend yield	zero	zero	zero
Forfeiture rate	zero	zero	zero
Weighted average fair value of stock options granted	$ 18.21	$ 35.16	$ 65.83

Volatility is based on reviews of the historical volatility of the Company's common stock. Risk-free interest rates are based on yields of U.S. treasury notes in effect at the date of grant. Expected life of option is based on actual historical option exercises. Dividend yield is zero because the Company does not anticipate paying cash dividends in the foreseeable future.

As of December 31, 2023, the Company expects to recognize compensation expense of $ 24.2 million related to non-vested options held by equity plan participants over the weighted average remaining recognition period of 2.8 years.

Performance Awards

The following summarizes information about performance award activity during 2023:

	Number of Performance Awards
Outstanding as of December 31, 2022	7,142
Granted	—
Vested	—
Forfeited/canceled	—
Outstanding as of December 31, 2023	7,142

During the year ended December 31, 2022, a total of 57,143 shares of restricted stock awards expired as performance criteria related to these Performance Awards were not attained. These shares of restricted stock were returned to the 2008 Equity Incentive Plan, which expired in December 2017, and thus were retired.

If and when outstanding Performance Awards vest, the Company would recognize $ 101,000 in stock-based compensation expense. These performance awards expire in 2026.

Stock-Based Compensation Expense

The following summarizes information about stock-based compensation expense, in thousands:

	Years ended December 31,		
	2023	2022	2021
Research and development	$ 2,050	$ 1,631	$ 1,302
General and administrative	2,536	435	457
Total stock-based compensation expense	$ 4,586	$ 2,066	$ 1,759

8. Employee 401(k) Benefit Plan

The Company has a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code. The plan covers substantially all employees. Employees are eligible to participate in the plan the first day of the month after hire and may contribute up to the current statutory limits under Internal Revenue Service regulations. The 401(k) plan permits the Company to make additional matching contributions on behalf of all employees. Through December 31, 2023, the Company has not made any matching contributions to the 401(k) plan.

9. Income Taxes

The Company did not provide for income taxes during the periods presented because it had book and federal taxable losses in those years and the tax benefit that would have resulted from the pre-tax losses was fully offset by a change in the valuation allowance.

The reconciliation of the statutory federal income tax rate to the Company's effective tax rate for periods presented was as follows:

	Year ended December 31,		
	2023	**2022**	**2021**
Tax at federal statutory rate	21%	21%	21%
State tax, net of federal benefit	—	—	—
Share-based compensation	0.2	(0.5)	1.2
Research and development credits	5.1	4.9	2.3
Section 162(m) limitation	—	(0.2)	(0.5)
Other	(2.3)	(1.8)	(0.2)
Change in valuation allowance	(24.0)	(23.4)	(23.8)
Effective income tax rate	—%	—%	—%

Deferred tax assets and valuation allowance

Deferred tax assets reflect the tax effects of net operating loss and tax credit carryforwards and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The Company's deferred taxes assets at December 31, 2023 and 2022 were valued at the corporate tax rate of 21 %. The Company offsets its deferred tax assets by a valuation allowance because it is uncertain about the timing and amount of any future profits. Significant components of its deferred tax assets are as follows (in thousands):

	December 31,	
	2023	**2022**
Deferred tax assets:		
Net operating loss carryforwards	$ 33,322	$ 28,017
Share-based compensation	2,561	2,706
Research and development credit carryforwards	12,557	9,681
Capitalized research and development expenses	27,538	12,690
Other	1,371	934
Total deferred tax assets	77,349	54,028
Valuation allowance	(77,349)	(54,002)
Net deferred tax assets	—	26
Deferred tax liabilities:		
Operating lease right-of-use assets	—	(26)
Total deferred tax liabilities	—	(26)
Net deferred tax asset (liability)	$ —	$ —

The valuation allowance increased by $ 23.3 million and $ 17.8 million in 2023 and 2022, respectively, due primarily to continuing operations.

The Company's net operating loss carryforwards of $ 158.7 million are federal, of which $ 74.1 million expires between 2029 and 2037 and $ 84.6 million carries forward indefinitely. As of December 31, 2023, the Company had federal research and development tax credits of approximately $ 21.1 million, which expire in the years 2024 through 2043.

Unrecognized tax benefits

As of December 31, 2023, 2022 and 2021, the Company has unrecognized tax benefits related to tax credits of $ 8.4 million, $ 6.5 million and $ 5.0 million, respectively. None of the unrecognized tax benefits as of December 31, 2023, if recognized, would impact the effective tax rate due to the valuation allowance and no interest or penalties have been recognized. A reconciliation of the beginning and ending balance of unrecognized tax benefits is as follows (in thousands):

	Year ended December 31,		
	2023	2022	2021
Beginning balance	$ 6,496	$ 5,001	$ 4,500
Expired research and development tax credits	$ (50)	$ —	$ —
Additions based on tax positions related to the current year	1,967	1,495	501
Ending balance	$ 8,413	$ 6,496	$ 5,001

As of December 31, 2023, there were no unrecognized tax benefits that we expect would change significantly over the next 12 months.

The Company files U.S. and Texas income tax returns. In the United States, the statute of limitations with respect to the federal income tax returns for tax years after 2019 are open to audit; however, since the Company has net operating losses, the taxing authority has the ability to review tax returns prior to the 2020 tax year and make adjustments to these net operating loss carryforwards. We are not under audit in any taxing jurisdiction at this time.

10. Leases and Commitments

Right-of-use Asset and Liability

The Company had an operating lease for approximately 6,000 square feet of office space in Austin, Texas expiring April 30, 2024. The Company terminated this lease on February 22, 2023 with no continuing obligations.

Cash paid for operating lease liabilities totaled $ 24,000 , $ 155,000 and $ 109,000 during the years ended December 31, 2023, 2022 and 2021, respectively.

Other Commitments

The Company conducts its product research and development programs through a combination of internal and collaborative programs that include, among others, arrangements with universities, contract research organizations and clinical research sites. It has contractual arrangements with these organizations that are generally cancelable. The Company's obligations under these contracts are largely based on services performed.

The Company is dependent on contract development and manufacturing organizations for the manufacture of all our materials for clinical studies.

Note 11. 2020 Cash Incentive Bonus Plan

In August 2020, the Board approved the Plan. The Plan was established to promote the long-term success of the Company by creating an "at-risk" cash bonus program that rewards Plan participants with additional cash compensation in lockstep with significant increases in the Company's market capitalization. The Plan is considered "at-risk" because Plan participants will not receive a cash bonus unless the Company's market capitalization increases significantly and certain other conditions specified in the Plan are met. Specifically, Plan participants will not be paid any cash bonuses unless (1) the Company completes a merger or acquisition transaction that constitutes a sale of ownership of the Company or its assets (a Merger Transaction) or (2) the Compensation Committee of the Board (the Compensation Committee) determines the Company has sufficient cash on hand, as defined in the Plan. Because of the inherent discretion and uncertainty regarding these requirements, the Company has concluded that a Plan grant date has not occurred as of December 31, 2023.

Plan participants will be paid all earned cash bonuses in the event of a Merger Transaction.

As of December 31, 2022, the Company's independent directors were participants in the Plan. However, effective March 16, 2023, the Board amended the Plan to remove all independent directors as participants in the Plan and the independent directors consented to such removal. The independent directors' share of potential benefits under the Plan were completely forfeited to the Company and will not be allocated to any other participant under the Plan. The Company's independent directors have not received, and as a result of such amendment will never receive, any payments under the Plan.

The Company's market capitalization for purposes of the Plan is determined based on either (1) the Company's closing price of one share on the Nasdaq Capital Market multiplied by the total issued and outstanding shares and options to purchase shares of the Company, or (2) the aggregate consideration payable to security holders of the Company in a Merger Transaction. Any warrants outstanding are excluded from the determination of market capitalization. This constitutes a market condition under applicable accounting guidance.

The Plan triggers a potential cash bonus each time the Company's market capitalization increases significantly, up to a maximum $5 billion in market capitalization. The Plan specifies 14 incremental amounts between $200 million and $5 billion (each increment, a "Valuation Milestone"). Each Valuation Milestone triggers a potential cash bonus award in a pre-set amount defined in the Plan. Each Valuation Milestone must be achieved and maintained for no less than 20 consecutive trading days for Plan participants to be eligible for a potential cash bonus award. Approximately 67% of each cash bonus award associated with a Valuation Milestone is subject to adjustment and approval by the Compensation Committee. Any amounts not awarded by the Compensation Committee are no longer available for distribution.

If the Company were to exceed a $5 billion market capitalization for no less than 20 consecutive trading days, all Valuation Milestones would be deemed achieved, in which case cash bonus awards would range from a minimum of $111.4 million up to a hypothetical maximum of $289.7 million. Payment of cash bonuses is deferred until such time as (1) the Company completes a Merger Transaction, or (2) the Compensation Committee determines the Company has sufficient cash on hand to render payment (each, a "Performance Condition"), neither of which may ever occur. Accordingly, there can be no assurance that Plan participants will ever be paid a cash bonus that is awarded under the Plan, even if the Company's market capitalization increases significantly.

The Plan is accounted for as a liability award. The fair value of each Valuation Milestone award will be determined once a grant date occurs and will be remeasured each reporting period. Compensation expense associated with the Plan will be recognized over the expected achievement period for each of the 14 Valuation Milestones, when a Performance Condition is considered probable of being met.

In October 2020, the Company achieved the first Valuation Milestone. Subsequently in 2020, the Compensation Committee approved a potential cash bonus award of $6.5 million in total for all Plan participants (after taking into account the March 2023 Plan amendment), subject to future satisfaction of a Performance Condition.

During the year ended December 31, 2021, the Company achieved 11 additional Valuation Milestones triggering potential Company obligations to all Plan participants from a minimum of $74.9 million up to a hypothetical maximum of $202.3 million (after taking into account the March 2023 Plan amendment), to be determined by the Compensation Committee and contingent upon future satisfaction of a Performance Condition. However, no compensation expense has been recorded since no grant date has occurred and no Performance Conditions are considered probable of being met. There is no continuing service requirement for Plan participants once the Compensation Committee approves a cash bonus award.

No Valuation Milestones were achieved during the years ended December 31, 2023 and 2022.

No actual cash payments were authorized or made to participants under the Plan through December 31, 2023 and the date of filing of this Annual Report on Form 10-K.

12. Contingencies

The Company is, and from time to time, the Company may become, involved in litigation or other legal proceedings and claims, including U.S. government inquiries, investigations and Citizen Petitions submitted to FDA. In addition, the Company has received, and from time to time may receive, inquiries from government authorities relating to matters arising from the ordinary course of business. The outcome of these proceedings is inherently uncertain. Regardless of outcome, legal proceedings can have an adverse impact on the Company because of defense and settlement costs, diversion of management resources, and other factors. At this time, no assessment can be made as to their likely outcome or whether the outcome will be material to the Company. The Company believes that its total provisions for legal matters are adequate based upon currently available information.

Government Investigations

On November 15, 2021, the Company disclosed that certain government agencies had asked the Company to provide corporate information and documents. These were confidential requests. The Company has been voluntarily cooperating and intends to continue to cooperate with these inquiries. No government agency has informed the Company that it has found evidence of research misconduct or wrongdoing by the Company or its officers, employees or directors. No government agency has filed any claims or charges relating to these inquiries. We cannot predict the outcome or impact of these ongoing matters, including whether a government agency may pursue an enforcement action against the Company or others.

Securities Class Actions and Shareholder Derivative Actions

Between August 27, 2021 and October 26, 2021, four putative class action lawsuits were filed alleging violations of the federal securities laws by the Company and certain named officers. The complaints rely on allegations contained in Citizen Petitions submitted to FDA and allege that various statements made by the defendants regarding simufilam were rendered materially false and misleading. The Citizen Petitions were all subsequently denied by FDA. These actions were filed in the U.S. District Court for the Western District of Texas. The complaints seek unspecified compensatory damages and other relief on behalf of a purported class of purchasers.

On June 30, 2022, a federal judge consolidated the four class action lawsuits into one case and appointed a lead plaintiff and a lead counsel. Lead plaintiff filed a consolidated amended complaint on August 18, 2022 on behalf of a putative class of purchasers of the Company's securities between September 14, 2020 and July 26, 2022. On May 11, 2023, the court dismissed with prejudice plaintiffs' claims against defendant Nadav Friedmann, PhD, MD, our former Chief Medical Officer and a Company director, who is now deceased, but otherwise denied defendants' motion to dismiss. Defendants filed an answer to the consolidated amended complaint on July 3, 2023. On February 22, 2024, plaintiffs filed a motion to supplement their complaint to extend the putative class period through October 12, 2023.

On November 4, 2021, a related shareholder derivative action was filed, purportedly on behalf of the Company, in the U.S. District Court for the Western District of Texas, asserting claims under the U.S. securities laws and state fiduciary duty laws against certain named officers and the members of the Company's Board. This complaint relies on the allegations made in Citizen Petitions that were submitted to (and subsequently denied by) FDA. The complaint alleges, among other things, that the individual defendants exposed the Company to unspecified damages and securities law liability by causing it to make materially false and misleading statements, in violation of the U.S. securities laws and in breach of their fiduciary duties to the Company. The derivative case seeks, among other things, to recover unspecified compensatory damages on behalf of the Company arising out of the individual defendant's alleged wrongful conduct. Although the plaintiff in this derivative case does not seek relief against the Company, the Company has certain indemnification obligations to the individual defendants. Between November 4, 2021 and June 20, 2023, four additional shareholder derivative actions were filed alleging substantially similar claims, two in the U.S. District Court for the Western District of Texas, one in Texas state court (Travis County District Court) and one in the Delaware Court of Chancery. On July 5, 2022, the three federal court actions were consolidated into a single action. All of the foregoing actions are currently stayed pending further developments in the consolidated securities action described above. On November 9, 2023, another shareholder derivative action alleging substantially similar claims was filed in the U.S. District Court for the Western District of Texas. The parties to that case expect that it will be consolidated into the existing consolidated federal court shareholder derivative action.

On February 2, 2024, a putative class action lawsuit was filed alleging violations of the federal securities law by the Company and certain named officers. The complaint relies on an October 12, 2023 journal article that describes a purported leaked report of alleged scientific misconduct by a scientific collaborator of the Company at City University of New York. The complaint alleges that various statements made by the defendants regarding simufilam were rendered materially false and misleading by this article. The action was filed in the U.S. District Court for the Northern District of Illinois. The complaint seeks unspecified compensatory damages and other relief on behalf of a purported class of purchasers of the Company's securities between August 18, 2022 and October 12, 2023.

The Company believes the foregoing claims are without merit and intends to defend against these lawsuits vigorously. The Company is unable to estimate the possible loss or range of loss, if any, associated with these lawsuits.

On August 19, 2022, a shareholder derivative action was filed, purportedly on behalf of the Company, in the Delaware Court of Chancery, asserting claims under state fiduciary duty laws against certain named officers and members of the Company's Board. The complaint alleges, among other things, that the individual defendants breached their fiduciary duties by approving the 2020 Cash Incentive Bonus Plan in August 2020. The complaints seek unspecified compensatory damages and other relief. On January 6, 2023, the plaintiffs filed an amended complaint. Defendants filed a partial answer to the amended complaint on March 10, 2023, and moved to partially dismiss the amended complaint on March 14, 2023. On January 25, 2024, the parties entered into a binding settlement term sheet with respect to this action. The settlement is subject to certain conditions, including the filing of a Stipulation of Settlement and final court approval. The proposed settlement resolves the claims asserted against the Company and the individual defendants and would contain provisions that the settlement does not constitute an admission, concession, or finding of any fault, liability, or wrongdoing of any kind by any defendant. There can be no assurance that the final settlement agreement will be executed or that such agreement will be approved by the court.

13. Subsequent Event - Warrant Dividend Distribution

On January 3, 2024, the Company completed a distribution to the holders of record of the Company's shares of common stock in the form of warrants to purchase shares of common stock. Each holder of record of the Company's common stock as of the close of business on December 22, 2023 received four warrants for every ten shares of common stock (rounded down for any fractional warrant) resulting in the issuance of approximately 16.9 million warrants.

Each warrant entitles the holder to purchase, at the holder's sole expense and exclusive election, at an exercise price of $ 33.00 per warrant, one share of common stock plus, to the extent described below, the Bonus Share Fraction. Payment for shares of common stock upon exercise of warrants must be in cash.

A Bonus Share Fraction entitles a holder to receive an additional 0.5 of a share of common stock (rounded down for any fractional share) for each warrant exercised (the "Bonus Share Fraction") without payment of any additional exercise price. The right to receive the Bonus Share Fraction will expire upon the earlier of (i) the first business day following the last day of the first 30 consecutive trading day period (commencing on or after January 3, 2024) in which the daily volume weighted average price (the "VWAP") of the shares of common stock has been at the then applicable trigger price, initially $ 26.40 , for at least 20 trading days (whether or not consecutive) (the "Bonus Price Condition") and (ii) the date specified by the Company upon not less than 20 business days' public notice (either condition being the "Bonus Share Expiration Date"). Any warrant exercised with an exercise date after the Bonus Share Expiration Date will not be entitled to the Bonus Share Fraction. The Company will make a public announcement of the Bonus Share Expiration Date (i) at least 20 business days prior to such date, in the case of the Company setting a Bonus Share Expiration Date and (ii) prior to market open on the Bonus Share Expiration Date in the case of a Bonus Price Condition.

Unless earlier redeemed, the warrants will expire and cease to be exercisable on November 15, 2024 (the “Expiration Date”). The warrants are redeemable at the Company’s sole option at any time with a redemption date on or after April 15, 2024. The Company will provide at least 20 calendar days’ notice by press release of the date selected for redemption (the “Redemption Date”). The redemption price upon any redemption shall equal to 1/10 of $ 0.01 per warrant. The warrants may be exercised at any time starting on January 3, 2024 until the earlier of (1) the Expiration Date and (2) the business day prior to the Redemption Date.

The number of shares of Common Stock issuable upon exercise is subject to certain anti-dilution adjustments, including for share dividends, splits, subdivisions, spin-offs, consolidations, reclassifications, combinations, non-cash distributions and cash dividends. Terms of the warrants prohibit ownership by warrant exercise of 9.9% or more of the Company's common stock by a single or affiliated group of stockholders without the Company's prior written consent.

The right to exercise warrants shall be automatically suspended in a circumstance while there is no effective registration statement registering the shares of common stock issuable upon exercise of the warrants. Such registration statement was declared effective by the SEC on May 1, 2023. The warrant Expiration Date or the Redemption Date, as the case may be, shall be extended by the number of days comprised in the event of a suspension.

The Company may from time to time and in its sole discretion amend warrants for one or more of the following purposes: (i) to cure any ambiguity, omission, defect or inconsistency; (ii) to provide for the assumption by a successor company in any business combination; (iii) to postpone the Expiration Date; (iv) to decrease the warrant exercise price or increase the basic warrant exercise rate or the Bonus Share Fraction; (v) to reinstate a Bonus Share Period after the Bonus Share Expiration Date; (vi) to provide for net share settlement upon exercise of the warrants; (vii) to make any change that does not adversely affect the rights of any warrant holder in any material respect; (viii) to provide for a successor warrant agent or calculation agent; (ix) in connection with any business combination, to provide that the warrants are exercisable for appropriate consideration; or (x) other conforming changes.

The warrants are listed and traded separately from the Company's common stock on the Nasdaq Capital Market under the ticker “SAVAW”.

From January 3, 2024 to February 26, 2024, a total of approximately 659,000 warrants were exercised resulting in gross proceeds to the Company of approximately $ 21.8 million. The Company issued approximately 989,000 shares of common stock, including Bonus Share Fractions, from the exercise of warrants through February 26, 2024. After the first $ 20 million of gross proceeds, the Company is obligated to pay a commission of 2.5 % of the gross proceeds from the sale of shares of common stock in the offering to the Company's financial advisor for the warrant distribution.

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

None.

Item 9A. *Controls and Procedures*

Evaluation of disclosure controls and procedures.

Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this Annual Report on Form 10-K. Based on this evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that our disclosure controls and procedures were effective 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 the Securities and Exchange Commission, or SEC, rules and forms and that such information is accumulated and communicated to management as appropriate to allow timely decisions regarding required disclosures.

Management's annual report on internal control over financial reporting. Our management is responsible for establishing and maintaining adequate internal control over our financial reporting. Our management has assessed the effectiveness of internal control over financial reporting as of December 31, 2023. Our assessment was based on criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, in Internal Control-Integrated Framework (2013 Framework).

Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with generally accepted accounting principles. Our internal control over financial reporting includes those policies and procedures that:

(1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect our transactions and dispositions of our assets;
(2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of consolidated financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and board of directors; and
(3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of our assets that could have a material effect on the consolidated financial statements.

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

Based on it's assessment under the COSO framework, management concluded that our internal control over financial reporting as of December 31, 2023 was effective.

Changes in internal control over financial reporting.

There was no change in our internal control over financial reporting that occurred during the quarter ended December 31, 2023 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

The effectiveness of our internal control over financial reporting as of December 31, 2023 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report which is included herein.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Cassava Sciences, Inc.

Opinion on Internal Control Over Financial Reporting

We have audited Cassava Sciences, Inc.'s internal control over financial reporting as of December 31, 2023, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Cassava Sciences, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2023, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2023 and 2022, the related consolidated statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2023, and the related notes and our report dated February 28, 2024 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's annual report on internal control over financial reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

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

/s/ Ernst & Young LLP

Austin, Texas
February 28, 2024

Item 9B. ***Other Information***

During the quarter ended December 31, 2023, none of our directors or officers (as defined in Rule 16a-1(f) of the Exchange Act) informed us of the adoption or termination of a "Rule 10b5-1 trading arrangement" or "non-Rule 10b5-1 trading arrangement," as those terms are defined in Regulation S-K, Item 408.

Item 9C. ***Disclosure Regarding Foreign Jurisdictions that Prevent Inspection***

None**.**

PART III

Item 10. ***Directors and Executive Officers and Corporate Governance***

The information regarding our directors (other than the biographies below), executive officers, director nomination process and the audit committee of the Board is incorporated by reference from "Directors and Executive Officers" in our Proxy Statement for our 2024 Annual Meeting of Stockholders.

Biographies of Directors and Executive Officers

Remi Barbier, the Company's founder, has served as President, Chief Executive Officer and Chairman of the Board of Directors since the Company's inception in 1998. Prior to that time, Mr. Barbier helped in the growth or founding of Exelixis Inc., a publicly-traded drug development company, ArQule, Inc., a drug development company acquired by Merck & Co., and EnzyMed, Inc., a chemistry company acquired by Albany Molecular Research, Inc. Mr. Barbier is a trustee emeritus of the Carnegie Institute of Washington, the Santa Fe Institute, the Advisory Board of the University of California Institute for Quantitative Biosciences and a life science incubator at the University of Arkansas for Medical Sciences. Mr. Barbier received his B.A. from Oberlin College and his M.B.A. from the University of Chicago.

R. Christopher Cook has served as Senior Vice President and General Counsel since October 2022. He previously served, since 2017, as the Global Head of Litigation and Government Investigations for Alcon, a publicly traded medical device and pharmaceutical company, as well as the Vice President and division General Counsel for Walmart Central America in San Jose, Costa Rica. Mr. Cook also spent seventeen years at Jones Day, where he was a litigation partner in the firm's Washington, DC and Chicago offices. He served as an Assistant United States Attorney in Chicago and graduated from Harvard Law School.

James W. Kupiec, M.D. joined the Company in January 2021 as Chief Clinical Development Officer and has served as our Chief Medical Officer since December 2022. Dr. Kupiec joined the Company after three decades of drug development experience at Pfizer, Sanofi and Ciba-Geigy. Dr. Kupiec previously served as Vice President, Global Clinical Leader for Parkinson's Disease and Clinical Head of the Neuroscience Research Unit for Pfizer, Inc., in Cambridge, MA. He joined Pfizer in 2000 after seven years with Sanofi, and two years with Ciba-Geigy Pharmaceuticals. During his 17-year career at Pfizer, Dr. Kupiec had extensive governance, business development, alliance and leadership responsibilities. Dr. Kupiec earned his BS with Honors in Biochemistry at Stony Brook University and his MD from the Albert Einstein College of Medicine. He completed his residency training at the Strong Memorial Hospital, University of Rochester School of Medicine, and is certified by the American Board of Internal Medicine. He served as an investigator on many clinical trials before transitioning to the pharmaceutical industry.

Eric Schoen has served as Chief Financial Officer since 2018. Prior to joining the Company, Mr. Schoen served in numerous financial leadership roles. Most recently, he served as Vice President, Senior Vice President, Finance and Chief Accounting Officer of Aspira Women's Health Inc. (formerly Vermillion, Inc.), a publicly-held women's health company, from 2011 to 2017. Mr. Schoen also began his career and spent nine years with PricewaterhouseCoopers in the audit and assurance, transaction services and global capital markets practices. Mr. Schoen received his B.S. in Finance from Santa Clara University.

Robert Anderson, Jr. has served as a director since December 2023. Mr. Anderson has decades of operational experience in cybersecurity, counterintelligence, economic espionage and critical incident response and management. Mr. Anderson previously led more than 20,000 FBI employees as the bureau's Executive Assistant Director of the Criminal, Cyber, Response and Services Branch— the No. 3 position in the organization. Mr. Anderson is currently Chairman of the Board and Chief Executive Officer of Cyber Defense Labs, an advisory firm focused on cybersecurity, where he has served as CEO since March 2019 and Chairman since January 2022. Mr. Anderson holds a Bachelor of Science and a Master in Public Administration from Wilmington University.

Richard J. Barry has served as a director since June 2021. Since June 2015, Mr. Barry has also served as a director of Sarepta Therapeutics, Inc., (Nasdaq: SRPT). Mr. Barry has extensive experience in the investment management business. He was a founding member of Eastbourne Capital Management LLC, and served as a Managing General Partner and Portfolio Manager from 1999 to its close in 2010. Prior to Eastbourne, Mr. Barry was a Portfolio Manager and Managing Director of Robertson Stephens Investment Management. Mr. Barry holds a Bachelor of Arts from Pennsylvania State University.

Pierre Gravier has served as a director since December 2023. Since July 2023, Mr. Gravier has been the Chief Financial Officer of PTC Therapeutics, Inc., a publicly traded biotechnology company. From 2013 to July 2023, Mr. Gravier was previously Managing Director in the healthcare group of Perella Weinberg Partners, a leading global independent advisory firm that provides strategic, financial, and tactical advice in connection with executing mergers, acquisitions and other corporate strategies. Mr. Gravier holds a Master's Degree in Finance from ESCP Business School and a Master of Science in Bioengineering from the University of Technology of Compiègne.

Robert Z. Gussin, Ph.D. has served as a director since 2003. Dr. Gussin worked at Johnson & Johnson for 26 years, most recently as Chief Scientific Officer and Corporate Vice President, Science and Technology from 1986 through his retirement in 2000. Dr. Gussin served on the board of directors of Duquesne University and the advisory boards of the Duquesne University Pharmacy School and the University of Michigan Medical School Department of Pharmacology. Dr. Gussin received his B.S. and M.S. degrees and D.Sc. with honors from Duquesne University and his Ph.D. in Pharmacology from the University of Michigan, Ann Arbor.

Claude Nicaise, M.D. has served as a director since December 2023. Since June 2015, Dr. Nicaise has also served as a director of Sarepta Therapeutics, Inc., (Nasdaq: SRPT). Since January 2021, Dr. Nicaise has served as a member of the board of directors of Gain Therapeutics. Since March 2021, Dr. Nicaise has served as a member of the board of directors of Chemomab Therapeutics Ltd. Dr. Nicaise has held clinical/regulatory leadership roles that have resulted in 14 new drug approvals in various diseases areas, including neuroscience. Dr. Nicaise is the founder of Clinical Regulatory Services, a company providing advice on clinical and regulatory matters to biotechnology companies. Dr. Nicaise served as Executive Vice President, Regulatory at Ovid Therapeutics Inc., a company that develops medicines for orphan diseases of the brain, from 2015 to March 2023. Dr. Nicaise was a Senior Vice President of Strategic Development and Global Regulatory Affairs at Alexion Pharmaceuticals from 2008 to 2014. From 1983 to 2008, Dr. Nicaise served in various positions of increasing responsibility at Bristol-Myers Squibb, including senior positions such as Vice President of Global Development and Vice-President of Worldwide Regulatory Science and Strategy. Dr. Nicaise received his M.D. from the Université Libre de Bruxelles in Belgium.

Michael J. O'Donnell, Esq. has served as a director since 1998. Mr. O'Donnell has been a partner in the law firm of Orrick, Herrington & Sutcliffe LLP since June 2021. Orrick, Herrington & Sutcliffe LLP provides legal services to the Company. Previously, Mr. O'Donnell was a member of Morrison & Foerster LLP from 2011 to 2021. Mr. O'Donnell serves as corporate counsel to numerous public and private biopharmaceutical and life sciences companies. Previously, Mr. O'Donnell was a member of Wilson Sonsini Goodrich & Rosati. Mr. O'Donnell received his J.D., cum laude, from Harvard University and his B.A. from Bucknell University, summa cum laude.

Sanford R. Robertson has served as a director since 1998. Mr. Robertson has been a partner of Francisco Partners, a technology buyout fund, since 1999. Prior to founding Francisco Partners, Mr. Robertson was the founder and chairman of Robertson, Stephens & Company, a technology investment bank sold to BankBoston in 1998. Mr. Robertson was previously the lead director of Salesforce.com, a publicly-held provider of enterprise cloud computing applications. Mr. Robertson received his B.A. and M.B.A. degrees with distinction from the University of Michigan.

Patrick J. Scannon, M.D., Ph.D. has served as a director since 2007. Dr. Scannon is one of the founders of XOMA. From 2006 to 2016, Dr. Scannon was Executive Vice President, Chief Biotechnology Officer of XOMA. From 1993 to 2006, Dr. Scannon served as Chief Scientific and Medical Officer of XOMA. Dr. Scannon retired from XOMA and resigned from XOMA's board of directors in 2016. Dr. Scannon received his Ph.D. in organic chemistry from the University of California, Berkeley and his M.D. from the Medical College of Georgia.

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16(a) of the Exchange Act requires our executive officers and directors and persons who own more than ten percent (10%) of a registered class of our equity securities to file reports of ownership and changes in ownership with the SEC. Executive officers, directors and greater than ten percent (10%) stockholders are required to furnish us with copies of all Section 16(a) forms they file. We believe all of our executive officers and directors complied with all applicable filing requirements during 2023.

Code of Ethics

We have adopted a Code of Ethics that applies to all of our directors, officers and employees, including our principal executive officer and principal financial officer. We publicize the Code of Ethics through posting the policy on our website, http://www.cassavasciences.com. We will disclose on our website any waivers of, or amendments to, our Code of Ethics.

Item 11. *Executive Compensation*

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the heading "Executive Compensation and Other Matters."

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

The information required by this Item regarding security ownership of certain beneficial owners and management is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the heading "Security Ownership of Certain Beneficial Owners and Management."

The following table summarizes the securities authorized for issuance under our equity compensation plans as of December 31, 2023:

	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights		Weighted Average Exercise Price of Outstanding Options, Warrants and Rights		Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans	
Equity compensation plans approved by stockholders	3,046,171	(1)	$ 15.10	(2)	2,966,705	(3)
Equity compensation plans not approved by stockholders	—		—		—	
	3,046,171		$ 15.10		2,966,705	

(1) Includes outstanding stock options and awards for 1,131,382 shares of our common stock under the 2008 Plan and 1,914,793 shares of our common stock under the 2018 Plan.

(2) Includes the weighted average stock price for outstanding stock options of $11.18 under the 2008 Plan and $17.45 for the 2018 Plan.

(3) Represents 2,908,688 shares of our common stock for the 2018 Plan and 58,017 for the Employee Stock Purchase Plan. No future awards shall occur under the 2008 Plan.

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

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the heading "Certain Relationships and Related Transactions."

Item 14. ***Principal Accountant Fees and Services***

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the heading “Principal Accountant Fees and Services.”

PART IV

Item 15. ***Exhibits and Financial Statement Schedules***

(a) The following documents are filed as part of this Form 10-K:

(1) *Consolidated Financial Statements (included in Part II of this report):*

Report of Independent Registered Public Accounting Firm

Consolidated Balance Sheets

Consolidated Statements of Operations

Consolidated Statements of Stockholders' Equity

Consolidated Statements of Cash Flows

Notes to Consolidated Financial Statements

(2) *Consolidated Financial Statement Schedules:*

All consolidated financial statement schedules are omitted because the information is inapplicable or presented in the notes to the consolidated financial statements.

(3) *Management Contracts, Compensatory Plans and Arrangements*.

Management contracts, compensatory plans and arrangements are indicated by the symbol “*” in the applicable exhibits listed in Item 15(b), below.

(b) *Exhibits*

The exhibits listed below are filed as part of this Form 10-K other than Exhibit 32.1, which shall be deemed furnished.

Exhibit No.		Description	Incorporated by Reference			Filed Herewith
			Form	Filing Date	Exhibit No.	
3.1		Amended and Restated Certificate of Incorporation.	10-Q	7/29/2005	3.1	
3.2		Certificate of Amendment of Restated Certificate of Incorporation.	8-K	5/8/2017	3.1	
3.3		Certificate of Amendment of Restated Certificate of Incorporation.	10-K	3/29/2019	3.3	
3.4		Amended and Restated Bylaws of Cassava Sciences, Inc.	8-K	9/13/23	3.4	
4.1		Specimen Common Stock Certificate.	10-Q	8/12/2019	4.1	
4.2		Description of Registrant's Securities.				X
4.3		Warrant Agreement (including Form of Warrant), dated January 3, 2024, between the Company, Computershare Inc., a Delaware corporation, and Computershare Trust Company, N.A., as Warrant Agent.	8-K	1/3/24	4.1	
10.1		Form of Indemnification Agreement between Registrant and each of its directors and officers.	10-K	3/1/2022	10.1	
10.5*	*	Employment Agreement, dated July 1, 1998 and amended December 17, 2008, between Registrant and Remi Barbier.	10-K	2/13/2009	10.12	
10.6	*	2000 Employee Stock Purchase Plan, as amended and restated.	10-Q	7/29/2010	10.1	
10.7	*	2008 Equity Incentive Plan.	8-K	5/29/2008	10.1	
10.8	*	Amendment Number 1 to the 2008 Equity Incentive Plan.	10-Q	8/1/2013	10.1	
10.9	*	Amendment No. 2 to Employment Agreement between Registrant and Remi Barbier.	10-Q	8/1/2013	10.2	
10.10	*	2018 Omnibus Incentive Plan.	8-K	5/11/2018	10.1	
10.11		Capital On Demand™ Sales Agreement, dated as of May 1, 2023, between Cassava Sciences, Inc. and JonesTrading Institutional Services LLC	8-K	5/1/2023	1.1	
10.12	*	Cassava Sciences, Inc. 2020 Cash Incentive Bonus Plan (As Amended March 16, 2023).	10-Q	8/3/2023	10.2	
10.13	*	Employment Agreement, executed on October 9, 2018, by and between Registrant and Eric Schoen.	8-K	10/11/2018	10.1	
10.14	*	Employment Agreement, executed on January 1, 2021, by and between Registrant and Dr. James Kupiec.	8-K	1/6/2021	10.1	
10.15+		Master Services Agreement between Cassava Sciences, Inc. and Evonik Corporation, dated February 22, 2021.	8-K	3/11/2021	10.1	
10.16+		Master Services Agreement between Cassava Sciences, Inc. and Premier Research International LLC, dated June 11, 2021	10-Q	8/4/2021	10.3	

10.17+	Agreement of Sale and Purchase Between DWF IV Lakewood, LP and Cassava Sciences, Inc. dated July 2, 2021	10-Q	11/15/2021	10.4	
10.18*	Amendment 1 to 2018 Omnibus Incentive Plan	10-Q	8/4/2022	10.1	
10.19*	Employment Agreement, executed on October 13, 2022, by and between Registrant and R. Christopher Cook	8-K	10/27/2022	10.1	
10.19*	Cassava Sciences Non-Employee Director Compensation Plan	10-Q	8/3/2023	10.3	
21.1	Subsidiaries of the Registrant.				X
23.1	Consent of Independent Registered Public Accounting Firm.				X
31.1	Certification of Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
31.2	Certification of Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
32.1	Certifications of the Chief Executive Officer and the Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
97	Policy Regarding Recovery of Erroneously Awarded Compensation				X
101.INS	Inline XBRL Instance Document.				X
101.SCH	Inline XBRL Taxonomy Extension Schema Document.				X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.				X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.				X
101.LAB	Inline XBRL Taxonomy Extension Labels Linkbase Document.				X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.				X
104	The cover page from the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2023, formatted in Inline XBRL (included in Exhibit 101).				X

* Management contract, compensatory plan or arrangement.
+ Confidential portions of this document have been redacted as permitted by applicable regulations.

(c) *Consolidated Financial Statement Schedules*

All consolidated financial statement schedules are omitted because the information is inapplicable or presented in the notes to the consolidated financial statements.

Item 16. ***Form 10-K Summary***

The Company has elected not to include summary information.

SIGNATURES

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

(Principal Executive

Cassava Sciences, Inc.
(Registrant)

/s/ REMI BARBIER
Remi Barbier,
Chairman of the Board of Directors,
President and Chief Executive Officer

Dated: February 28, 2024

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ REMI BARBIER Remi Barbier	President, Chief Executive Officer and Chairman of the Board of Directors (Principal Executive Officer)	February 28, 2024
/s/ ERIC J. SCHOEN Eric J. Schoen	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	February 28, 2024
/s/ ROBERT ANDERSON, JR. Robert Anderson, Jr.	Director	February 28, 2024
/s/ RICHARD J. BARRY Richard J. Barry	Director	February 28, 2024
/s/ PIERRE GRAVIER Pierre Gravier	Director	February 28, 2024
/s/ ROBERT Z. GUSSIN, PH.D. Robert Z. Gussin, Ph.D.	Director	February 28, 2024
/s/ CLAUDE NICAISE, M.D. Claude Nicaise, M.D.	Director	February 28, 2024
/s/ MICHAEL J. O'DONNELL, ESQ. Michael J. O'Donnell, Esq.	Director	February 28, 2024
/s/ SANFORD R. ROBERTSON Sanford R. Robertson	Director	February 28, 2024
/s/ PATRICK SCANNON, M.D., PH.D. Patrick Scannon, M.D., Ph.D.	Director	February 28, 2024

Exhibit 4.2

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

The following is a brief description of (i) the common stock, $0.001 par value per share ("Common Stock"), of Cassava Sciences, Inc. (the "Company") and (ii) the warrants, each whole warrant exercisable for shares of Common Stock ("Warrants"), of the Company, each of which is registered pursuant to Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act").

Description of Common Stock

General

The following summary of the material features of our Common Stock and certain provisions of Delaware law do not purport to be complete and is subject to, and qualified in its entirety by, the provisions of our amended and restated certificate of incorporation, our bylaws, the Delaware General Corporation Law ("DGCL") and other applicable law. For additional detail about our capital stock, please refer to our amended and restated certificate of incorporation and bylaws, each as amended, copies of which are included as exhibits to our Annual Report on Form 10-K for the year ended December 31, 2023.

As of the date of this Exhibit to the Form 10-K, our authorized capital stock consists of 130,000,000 shares. The Company is authorized to issue two classes of shares to be designated, respectively, Common Stock and Preferred Stock. The total number of shares of Common Stock which this Company is authorized to issue is 120,000,000, with a par value of $0.001, and the total number of shares of Preferred Stock which we is authorized to issue is 10,000,000, with a par value of $0.001. As of December 31, 2023, there were 42,236,919 shares of Common Stock issued and outstanding. Our Common Stock is listed on the Nasdaq Capital Market under the symbol "SAVA."

Liquidation Rights

In the event of our liquidation, dissolution or winding up, the holders of Common Stock are entitled to share ratably in all assets remaining after payment of liabilities, subject to prior distribution rights of preferred stock then outstanding. The Common Stock has no preemptive or conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to the Common Stock.

Voting Right

The holders of Common Stock are entitled to one vote per share on all matters to be voted upon by the stockholders.

Dividends

Subject to preferences that may be applicable to any outstanding preferred stock, the holders of Common Stock are entitled to receive ratably any dividends that may be declared from time to time by the board of directors out of funds legally available for that purpose. However, the Company is not currently paying any dividends.

No Preemptive or Similar Rights

The Common Stock has no preemptive or conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to the Common Stock.

Limitation on Rights of Holders of Common Stock – Preferred Stock

We currently have no shares of preferred stock outstanding. Our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions granted to or imposed upon the preferred stock. Any or all of these rights may be greater than the rights of the Common Stock.

The board of directors, without stockholder approval, can issue preferred stock with voting, conversion or other rights that could negatively affect the voting power and other rights of the holders of Common Stock. Preferred stock could thus be issued quickly with terms calculated to delay or prevent a change in control of us or make it more difficult to remove our management. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of the Common Stock.

Certain Anti-Takeover Matters

Our amended and restated certificate of incorporation requires that certain amendments of the amended and restated certificate of incorporation and certain amendments by the stockholders of our bylaws require the approval of at least 66 2/3% of the voting power of all outstanding stock. These provisions could discourage a potential acquirer from making a tender offer or otherwise attempting to obtain control of our company and could delay changes in our management.

Our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to the board of directors. At an annual meeting, stockholders may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors. Stockholders may also consider a proposal or nomination by a person who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given to our Secretary timely written notice, in proper form, of his or her intention to bring that business before the meeting. The bylaws do not give the board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting of the stockholders. However, our bylaws may have the effect of precluding the conduct of business at a meeting if the proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

Our bylaws provide that only our board of directors, the chairman of the board, the president or the chief executive officer may call a special meeting of stockholders. Because our stockholders do not have the right to call a special meeting, a stockholder could not force stockholder consideration of a proposal over the opposition of the board of directors by calling a special meeting of stockholders prior to such time as a majority of the board of directors believed or the chief executive officer believed the matter should be considered or until the next annual meeting provided that the requestor met the notice requirements. The restriction on the ability of stockholders to call a special meeting means that a proposal to replace the board also could be delayed until the next annual meeting.

Director Classification

Our amended and restated certificate of incorporation provides for our board of directors to be divided into three classes serving staggered terms. Approximately one-third of the board of directors will be elected each year. The provision for a classified board could prevent a party who acquires control of a majority of the outstanding voting stock from obtaining control of the board of directors until the second annual stockholders meeting following the date the acquirer obtains the controlling stock interest. The classified board provision could discourage a potential acquirer from making a tender offer or otherwise attempting to obtain control of our company and could increase the likelihood that incumbent directors will retain their positions. Our amended and restated certificate of incorporation provides that directors may be removed with cause by the affirmative vote of the holders of the outstanding shares of Common Stock.

Limitation of Liability and Indemnification Matters

Our amended and restated certificate of incorporation provides that to the fullest extent permitted by the DGCL as the same exists or as may hereafter be amended, a director of the Company or any subsidiary of the Company will not be held personally liable to the Company or its stockholders and will otherwise be indemnified by the Company for monetary damages for breach of fiduciary duty as a director of the Company, any predecessor of the Company or any subsidiary of the Company.

The Company, under the amended and restated certificate of incorporation, also indemnifies to the fullest extent permitted by law any person made or threatened to be made a party to an action or proceeding, whether criminal, civil, administrative or investigative, by reason of the fact that he, his testator or intestate is or was a director or officer of the Company, any predecessor of the Company or any subsidiary of the Company or serves or served at any other enterprise as a director or officer at the request of the Company, any predecessor to the Company or any subsidiary of the Company.

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the DGCL. Under Section 203, we would generally be prohibited from engaging in any business combination with any interested stockholder for a period of three years following the time that this stockholder became an interested stockholder unless:

- prior to this time, the board of directors of the Company approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction that resulted in the stockholder's becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the Company outstanding at the time the transaction commenced, excluding shares owned by persons who are directors and also officers, and by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- at or subsequent to such time, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2⁄3% of the outstanding voting stock that is not owned by the interested stockholder.

Under Section 203, a "business combination" includes:

- any merger or consolidation involving the Company and the interested stockholder;
- any merger or consolidation involving the Company and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the assets of the Company involving the interested stockholder;
- any transaction that results in the issuance or transfer by the Company of any stock of the Company to the interested stockholder, subject to limited exceptions;
- any transaction involving the Company that has the effect of increasing the proportionate share of the stock of any class or series of the Company beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the Company

In general, Section 203 defines an interested stockholder as an entity or person beneficially owning 15% or more of the outstanding voting stock of the Company and any entity or person affiliated with or controlling or controlled by such entity or person.

Description of the Warrants

General

The following summary of the material features of our Warrants and certain provisions of Delaware law do not purport to be complete and is subject to, and qualified in its entirety by, the provisions of our amended and restated certificate of incorporation, our bylaws, the warrant agreement, dated as of January 3, 2024 (the "Warrant Agreement"), between the Company and Computershare Inc. and Computershare Trust Company, N.A., as warrant agents, the DGCL and other applicable law. For additional detail about our Warrants, please refer to our amended and restated certificate of incorporation and bylaws, each as amended from time to time, copies of which are included as exhibits to our Annual Report on Form 10-K for the year ended December 31, 2023.

As of the date of distribution of the Warrants, January 3, 2024 , there were 16,894,704 Warrants issued and outstanding. Our Warrants are listed on the Nasdaq Capital Market under the symbol "SAVAW."

Warrant Exercise Rate

Each Warrant represents the right to purchase from the Company one share of Common Stock (the "Basic Warrant Exercise Rate") plus the Bonus Share Fraction (as defined below), if any as described below, for the applicable exercise date for cash at an initial exercise price of $33.00 (the "Exercise Price") per Warrant, payable in U.S. dollars.

Until the Bonus Share Fraction Expiration Date (as defined below), a holder exercising its Warrants will receive, in addition to the Basic Warrant Exercise Rate, initially, an additional 0.5 of a Common Share for each Warrant exercised (subject to adjustment as described herein, the "Bonus Share Fraction") without payment of any additional Exercise Price.

The right to receive the Bonus Share Fraction will expire at 5:00 p.m. New York City time (the "Bonus Share Expiration Date") upon the earlier of (i) the first business day following the last day of the first 30 consecutive trading day period commencing on or after the distribution date in which the daily VWAPs (as defined in the Warrant Agreement) of the shares of Common Stock has been at least equal to the then applicable Bonus Share Expiration Trigger Price (as defined in the Warrant Agreement) for at least 20 trading days (whether or not consecutive) (the "Bonus Price Condition") and (ii) the date specified by the Company upon not less than 20 business days' notice. Any Warrant exercised with an exercise date after the Bonus Share Expiration Date will not be entitled to any Bonus Share Fraction.

The "Bonus Share Expiration Trigger Price" is initially $26.40, subject to certain adjustments described in the Warrant Agreement.

The Basic Warrant Exercise Rate plus any Bonus Share Fraction is referred to as the Warrant Exercise Rate. The Basic Warrant Exercise Rate, the Bonus Share Fraction and the Bonus Share Expiration Trigger Price are each subject to certain adjustments described in the "Anti-Dilution Adjustments" section below.

The Company will make a public announcement of the Bonus Share Expiration Date (i) prior to market open on the Bonus Share Expiration Date in the case of a Bonus Price Condition and (ii) at least 20 Business Days prior to such date, in the case of the Company setting a Bonus Share Expiration Date.

Expiration

Except as described below, the Warrants will expire and cease to be exercisable at 5:00 p.m. New York City time on November 15, 2024 (the "Expiration Date").

Redemption

The Warrants are redeemable at the Company's sole option at any time with a redemption date on or after April 15, 2024.

By public announcement only, the Company will provide at least 20 calendar days' notice (the "Redemption Notice") of the date selected for redemption (the "Redemption Date"). The redemption price upon any redemption shall equal to 1/10 of $0.01 per Warrant.

In the event of a redemption of the Warrants, Warrants will be exercisable until 5:00 p.m. New York City time on the business day immediately preceding the Redemption Date. The Warrants will not be exercisable after 5:00 p.m. New York City time on the business day immediately preceding the Redemption Date and will cease to be outstanding after the Redemption Date.

Exercise

All or any part of the Warrants may be exercised prior to the earlier of (x) 5:00 p.m. New York City time on the Expiration Date and (y) 5:00 p.m. New York City time on the Business Day prior to the Redemption Date by delivering a completed form of election to purchase shares of Common Stock, which contains certain representations by the holder of the Warrants, and payment of the Exercise Price in cash. Any such delivery that occurs on a day that is not a Business Day or is received after 5:00 p.m., New York City time, on any given Business Day will be deemed received and exercised on the next succeeding Business Day. Record owners of Warrants may exercise Warrants through the process established by the Warrant Agent. Indirect, "street name" holders of Warrants should contact their broker, bank or other intermediary for information on how to exercise Warrants.

If a registration statement is not effective at any time or from time to time, the right to exercise Warrants shall be automatically suspended until such registration statement becomes effective as described under “Registration and Suspension” below.

Upon delivery of Warrant Shares upon exercise of Warrants, the Company will issue such whole number of Warrant Shares as the exercising Warrant holder is entitled to receive.

Without the prior written consent of the Company (which consent may be withheld in the Company’s sole discretion), a holder will not be permitted to exercise Warrants for any shares of Common Stock, and the Company shall not be obligated to effect such exercise if, following such exercise, the holder (together with such holder’s affiliates, and any other persons acting as a group with such holder and its affiliates) would beneficially own 9.9% or more of the shares of Common Stock outstanding, including without limitation, through synthetic or derivative financial instruments that give effect to a direct or indirect ownership in the common stock of the Company (the “Ownership Limitation”). No consideration or repayment will be made to any holder as a result of an inability to exercise a Warrant in whole or in part because of such ownership limitations. The terms “beneficial ownership” and “group” shall be determined in accordance with Section 13(d) of the Exchange Act and the rules and regulations promulgated thereunder. For purposes of determining whether the Ownership Limitation has been reached, a holder may rely on the number of outstanding shares of Common Stock reflected in (x) the Company’s most recent periodic or annual report filed with the SEC or (y) any more recent notice published on the Company’s website.

Registration and Suspension

The Company has agreed in the Warrant Agreement to use commercially reasonable efforts to cause a shelf registration statement (including, at the Company’s election, an existing registration statement), to be filed pursuant to Rule 415 (or any successor provision) of the Securities Act, covering the issuance of shares of Common Stock to the Warrant holders upon exercise of the Warrants to remain effective until the earlier of (i) such time as all Warrants have been exercised and (ii) the earlier of the Expiration Date and the Redemption Date.

Anti-Dilution Adjustments

The Basic Warrant Exercise Rate shall be subject to adjustment, without duplication, upon the occurrence of certain events, including, among others, stock dividends payable in shares of Common Stock, stock splits, reclassifications and combinations, certain rights offerings to holders of shares of Common Stock, other distributions and spin-offs of securities to holders of shares of Common Stock, and cash dividends on shares of Common Stock, each as more fully described in the Warrant Agreement, except that the Company shall not make any such adjustments if each holder has the opportunity to participate, at the same time and upon the same terms as holders of the shares of Common Stock and solely as a result of holding the Warrants in any of the transactions described below, without having to exercise such holder’s Warrants, as if such holder held a number of shares of Common Stock equal to the product (rounded down to the nearest whole multiple of a share of Common Stock) of (i) the Warrant Exercise Rate in effect on the record date for such transaction and (ii) the number of Warrants held by it on such record date. The Bonus Share Fraction and the Bonus Share Expiration Trigger Price will be proportionately adjusted for any adjustment to the Basic Warrant Exercise Rate.

All adjustments to the Basic Warrant Exercise Rate shall be made by the Calculation Agent to the nearest whole multiple of 0.00001 (with 0.000005 being rounded upwards) share of Common Stock. Any adjustments described above shall be made successively whenever an event referred to therein shall occur.

Business Combinations and Reorganizations

In the event of a merger, consolidation, amalgamation, statutory share exchange or similar transaction that requires the approval of the Company's shareholders (a "Business Combination") or reclassification of Common Stock, other than a reclassification of Common Stock referred to in "Anti-Dilution Adjustments" above, the right of a Warrant holder to receive Common Stock upon exercise of a Warrant will be converted into the right to exercise a Warrant to acquire, per each Warrant, the number of shares or other securities or property (including cash) that a number of shares of Common Stock equal to the Warrant Exercise Rate (in effect at the time of such Business Combination or reclassification) immediately prior to such Business Combination or reclassification would have been entitled to receive upon consummation of such Business Combination or reclassification (the amount of such shares, other securities or property in respect of a share of Common Stock being herein referred to as a "Unit of Reference Property"). If the Business Combination causes the Common Stock to be converted into, or exchanged for, the right to receive more than a single type of consideration (determined based in part upon any form of shareholder election), then the composition of the Unit of Reference Property into which the Warrants will be exercisable will be deemed to be the weighted average of the types and amounts of consideration actually received by the holders of Common Stock.

Exhibit 21.1

Cassava Sciences, Inc. Subsidiaries

Subsidiary	State/Country of Incorporation/Formation
Austin Innovation Park, LLC	Texas

EXHIBIT 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

1) Registration Statement (Form S-8 No. 333-265540) pertaining to the 2018 Omnibus Incentive Plan of Registrant,

2) Registration Statement (Form S-3 No. 333-271542) and related Prospectus of Cassava Sciences, Inc.,

3) Registration Statement (Form S-8 No. 333-168390) pertaining to the 2000 Employee Stock Purchase Plan of Registrant,

4) Registration Statement (Form S-8 No. 333-225708) pertaining to the 2018 Omnibus Incentive Plan of Registrant,

5) Registration Statement (Form S-8 No. 333-147336) pertaining to the 2000 Employee Stock Purchase Plan of Registrant, and

6) Registration Statement (Form S-3 No. 333-152676) pertaining to the 2008 Equity Incentive Plan of Registrant;

of our reports dated February 28, 2024, with respect to the consolidated financial statements of Cassava Sciences, Inc. and the effectiveness of internal control over financial reporting of Cassava Sciences, Inc. included in this Annual Report (Form 10-K) of Cassava Sciences, Inc. for the year ended December 31, 2023.

/s/ Ernst &Young LLP

Austin, Texas
February 28, 2024

EXHIBIT 31.1

PRINCIPAL EXECUTIVE OFFICER CERTIFICATION PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Remi Barbier, certify that:

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

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

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

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

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

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

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

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

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

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

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

/s/ REMI BARBIER
Remi Barbier,
Chairman of the Board of Directors,
President and Chief Executive Officer
(Principal Executive Officer)

Date: February 28, 2024

EXHIBIT 31.2

PRINCIPAL FINANCIAL OFFICER CERTIFICATION PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Eric J. Schoen, certify that:

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

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

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

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

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

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

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

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

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

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

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

/s/ ERIC J. SCHOEN
Eric J. Schoen,
Chief Financial Officer
(Principal Financial Officer)

Date: February 28, 2024

EXHIBIT 32.1

CERTIFICATIONS OF THE CHIEF EXECUTIVE OFFICER AND THE
CHIEF FINANCIAL OFFICER PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, each of the undersigned officers of Cassava Sciences, Inc. (the "Company"), hereby certifies that to the best of such officer's knowledge:

1. The Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2023, and to which this certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and

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

Date: February 28, 2024

/s/ REMI BARBIER
Remi Barbier,
Chairman of the Board of Directors,
President and Chief Executive Officer

/s/ ERIC J. SCHOEN
Eric J. Schoen,
Chief Financial Officer

Exhibit 97.

POLICY REGARDING RECOVERY OF ERRONEOUSLY AWARDED COMPENSATION
EFFECTIVE OCTOBER 2, 2023

This Policy Regarding Recovery of Erroneously Awarded Compensation (the " ***Policy***") is established by Cassava Sciences, Inc. (the "***Company***"), a Delaware corporation, effective as of October 2, 2023 (the " ***Effective Date***").

1. Purpose. The Company is committed to promoting high standards of honest and ethical business conduct and compliance with applicable laws, rules, and regulations. In accordance with the applicable rules of The Nasdaq Stock Market (the "***Nasdaq Rules***") and Section 10D and Rule 10D-1 of the Securities Exchange Act of 1934, as amended (the "***Exchange Act***") ("***Rule 10D-1***"), this Policy explains when the Company will be required to seek recovery of Incentive Compensation erroneously awarded to a Covered Person. All capitalized terms used and not otherwise defined herein shall have the meanings set forth in Section 11, below.

2. Miscalculation of Financial Reporting Measure Results. In the event of a Restatement, the Company will seek to recover, reasonably promptly, all Recoverable Incentive Compensation from a Covered Person in accordance with this Policy, the Nasdaq Rules, and Rule 10D-1. Such recovery, in the case of a Restatement, will be made without regard to any individual knowledge or responsibility related to the Restatement. Notwithstanding the foregoing, if the Company is required to undertake a Restatement, the Company will not be required to recover the Recoverable Incentive Compensation if the Compensation Committee determines it Impracticable to do so, in the reasonable exercise of its business judgment after reviewing all the relevant facts and circumstances.

If such Recoverable Incentive Compensation was not awarded or paid on a formulaic basis, the Company will seek to recover the amount of Recoverable Incentive Compensation that the Compensation Committee determines in good faith should be recouped pursuant to this Policy.

3. Other Actions. The Compensation Committee may, subject to applicable law, seek recovery in the manner it chooses, including by seeking reimbursement from the Covered Person of all or part of the compensation awarded or paid, by electing to withhold unpaid compensation, by set-off, or by rescinding or canceling unvested stock.

In the reasonable exercise of its business judgment under this Policy, the Compensation Committee may in its sole discretion determine whether and to what extent additional action is appropriate to address the circumstances surrounding a Restatement to minimize the likelihood of any recurrence and to impose such other discipline as it deems appropriate.

4. No Indemnification or Reimbursement. Notwithstanding the terms of any other policy, program, agreement, or arrangement, in no event will the Company or any of its affiliates indemnify or reimburse a Covered Person for any loss under this Policy and in no event will the Company or any of its affiliates pay premiums on any insurance policy that would cover a Covered Person's potential obligations with respect to Recoverable Incentive Compensation under this Policy.

5. Administration and Interpretation of Policy. The Compensation Committee shall have the sole and exclusive authority to administer this Policy in accordance with and subject to the Nasdaq Rules and Rule 10D-1. The Compensation Committee is authorized to make such determinations and interpretations and to take such actions as it deems necessary, appropriate, or advisable for the administration of this Policy and for the Company's continued compliance with Nasdaq Rules, Section 10D, Rule 10D-1, and any other applicable law, regulation, rule, or interpretation of the U.S. Securities and Exchange Commission ("***SEC***") or Nasdaq promulgated or issued therewith.

6. Other Claims and Rights. The remedies under this Policy are in addition to, and not in lieu of, any legal and equitable claims the Company or any of its affiliates may have or any actions that may be imposed by law enforcement agencies, regulators, administrative bodies, or other authorities. Further, the exercise by the Compensation Committee of any rights pursuant to this Policy will not impact any other rights that the Company or any of its affiliates may have with respect to any Covered Person subject to this Policy.

This Policy has been established for the exclusive benefit of the Company. This Policy does not confer any rights, remedies, or authority upon, nor shall this Policy be enforced by, any person or entity other than the Company, the Board, and the Compensation Committee as set forth in this Policy.

7. Acknowledgement by Covered Persons; Condition to Eligibility for Incentive Compensation. The Company will provide notice to and seek acknowledgement of this Policy from each Covered Person, provided that the failure to provide such notice or obtain such acknowledgement will have no impact on the applicability or enforceability of this Policy. After the Effective Date, the Company must be in receipt of a Covered Person's acknowledgement as a condition to such Covered Person's eligibility to receive Incentive Compensation.

8. Amendment; Termination. The Board or the Compensation Committee may in its discretion amend or terminate this Policy at any time as it deems necessary. Notwithstanding anything in this Section 8 to the contrary, no amendment or termination of this Policy shall be effective if such amendment or termination would (after taking into account any actions taken by the Company contemporaneously with such amendment or termination) cause the Company to violate any federal securities laws, SEC rule, or Nasdaq Rule.

9. Effectiveness. Except as otherwise determined in writing by the Compensation Committee, this Policy will apply to any Incentive Compensation that is Received by a Covered Person on or after the Effective Date.

10. Disclosure Requirements. The Company shall file all disclosures with respect to this Policy required by applicable SEC filings and rulings.

11. Definitions. For purposes of this Policy, the following capitalized terms shall have the meanings set forth below.

11.1 "***Applicable Period***" means the three completed fiscal years of the Company immediately preceding the earlier of (i) the date the Board, a committee of the Board, or the officer or officers of the Company authorized to take such action if Board action is not required, concludes (or reasonably should have concluded) that a Restatement is required or (ii) the date a court, regulator, or other legally authorized body directs the Company to prepare a Restatement. The "Applicable Period" also includes any transition period (that results from a change in the Company's fiscal year) within or

immediately following the three completed fiscal years identified in the preceding sentence.

11.2 "***Board***" means the Board of Directors of the Company.

11.3 "***Company***" shall refer solely and exclusively to Cassava Sciences, Inc. and shall not include any other person or entity, including any successor company or acquiror.

11.4 "***Compensation Committee***" means the Company's committee of independent directors responsible for executive compensation decisions, or in the absence of such a committee, a majority of the independent directors serving on the Board of the Company.

11.5 "***Covered Person***" means any person who is, or was at any time, during the Applicable Period, an Executive Officer of the Company.

11.6 "***Executive Officer***" means each individual who is currently or was previously designated as an "officer" of the Company as defined in Rule 16a-1(f) under the Exchange Act. For the avoidance of doubt, the identification of an executive officer for purposes of this Policy shall include each executive officer who is or was identified pursuant to Item 401(b) of Regulation S-K or Item 6.A of Form 20-F, as applicable, as well as the principal financial officer and principal accounting officer (or, if there is no principal accounting officer, the controller).

11.7 "***Financial Reporting Measure***" means a measure that is determined and presented in accordance with the accounting principles used in preparing the Company's financial statements (including but not limited to "non-GAAP" financial measures, such as those appearing in the Company's earnings releases or Management Discussion and Analysis), and any measure that is derived wholly or in part from such measure. Stock price and total shareholder return (and any measures derived wholly or in part therefrom) shall be considered Financial Reporting Measures.

11.8 "***Impracticable.***" The Compensation Committee may determine in good faith that recovery of Recoverable Incentive Compensation is "Impracticable" if: (i) pursuing such recovery would violate home country law of the jurisdiction of incorporation of the Company where that law was adopted prior to November 28, 2022 and the Company provides an opinion of home country counsel to that effect acceptable to the Company's applicable listing exchange; (ii) the direct expense paid to a third party to assist in enforcing this Policy would exceed the Recoverable Incentive Compensation and the Company has (A) made a reasonable attempt to recover such amounts and (B) provided documentation of such attempts to recover to the Company's applicable listing exchange; or (iii) recovery would likely cause an otherwise tax-qualified retirement plan, under which benefits are broadly available to employees of the Company, to fail to meet the requirements of Section 401(a)(13) or Section 411(a) of the Internal Revenue Code of 1986, as amended.

11.9 "***Incentive Compensation***" means any compensation that is granted, earned, or vested based wholly or in part upon the attainment of a Financial Reporting Measure. Incentive Compensation does not include any base salaries (except with respect to any salary increases earned wholly or in part based on the attainment of a Financial Reporting Measure performance goal); bonuses paid solely at the discretion of the Compensation Committee or Board that are not paid from a "bonus pool" that is determined by satisfying a Financial Reporting Measure performance goal; bonuses paid solely upon satisfying one or more subjective standards and/or completion of a specified employment period; non-equity incentive plan awards earned solely upon satisfying one or more strategic measures or operational measures; and equity awards that vest solely based on the passage of time and/or attaining one or more non-Financial Reporting Measures.

11.10 "***Received.***" Incentive Compensation is deemed "Received" in the Company's fiscal period during which the Financial Reporting Measure specified in the Incentive Compensation award is attained, even if the payment or grant of the Incentive Compensation occurs after the end of that period.

11.11 "***Recoverable Incentive Compensation***" means the amount of any erroneously awarded Incentive Compensation (calculated on a pre-tax basis) Received by a Covered Person during the Applicable Period that is in excess of the amount that otherwise would have been Received if the calculation were based on the Restatement. For the avoidance of doubt Recoverable Incentive Compensation does not include any Incentive Compensation Received by a person (i) before such person began service in a position or capacity meeting the definition of an Executive Officer, (ii) who did not serve as an Executive Officer at any time during the performance period for that Incentive Compensation, or (iii) during any period the Company did not have a class of its securities listed on a national securities exchange or a national securities association. For Incentive Compensation based on (or derived from) stock price or total shareholder return where the amount of Recoverable Incentive Compensation is not subject to mathematical recalculation directly from the information in the applicable Restatement, the amount will be determined by the Compensation Committee based on a reasonable estimate of the effect of the Restatement on the stock price or total shareholder return upon which the Incentive Compensation was Received (in which case, the Company will maintain documentation of such determination of that reasonable estimate and provide such documentation to the Company's applicable listing exchange).

11.12 "***Restatement***" means an accounting restatement of any of the Company's financial statements filed with the Securities and Exchange Commission under the Exchange Act, or the Securities Act of 1933, as amended, due to the Company's material noncompliance with any financial reporting requirement under U.S. securities laws, including any required accounting restatement to correct an error in previously issued financial statements that is material to the previously issued financial statements (commonly referred to as "Big R" restatements), or that would result in a material misstatement if the error were corrected in the current period or left uncorrected in the current period (commonly referred to as "little r" restatements).