Sage Therapeutics®

2024 ANNUAL REPORT

Sahar, Ashley, Katlyn: Experienced Postpartum Depression (PPD)

To our shareholders

Sage remains dedicated to our mission to pioneer solutions to deliver life-changing brain health medications so every person can thrive. Neurological diseases are the leading cause of disability worldwide, placing enormous burden on patients, their families, and healthcare systems. Our mission has never been more important, and we are acting with a sense of urgency to deliver innovative medicines to patients and better serve the needs of providers.

Executed Launch Strategy to Build Commercial Momentum for ZURZUVAE in PPD

2024 marked the first full year following the commercial launch of ZURZUVAE® (zuranolone), the first and only oral treatment approved by the FDA for adults with postpartum depression (PPD). We are energized by the impact we are already having on women with PPD with approximately 6,600 ZURZUVAE prescriptions shipped in 2024. We believe this reflects the medical need and growing demand for new treatments for women with PPD.

Importantly, we are beginning to see a broader paradigm shift in practice patterns among OBGYNs who are at the forefront of peripartum care and continue to be the primary prescribers of ZURZUVAE. With the availability of ZURZUVAE, among OBGYNs that have prescribed, we have seen an increase in their rate of diagnosis and treatment of women with PPD.

We have also made meaningful progress with payors to secure coverage for 95% of commercial and Medicaid patients as well as to reduce step edits or complex prior authorization requirements.

We are encouraged by the strength of ZURZUVAE's launch momentum as a treatment for women with PPD and remain focused on establishing ZURZUVAE as the standard of care for this devastating medical condition.

Restructured our Business and Refocused our Pipeline

Turning to our pipeline, in response to clinical setbacks, we have recalibrated our R&D efforts to focus on neuropsychiatry and neurodevelopmental disorders — areas we believe have the greatest potential for value creation.

SAGE-319, our wholly-owned extrasynaptic-preferring $GABA_A$ receptor positive allosteric modulator (PAM), is currently being investigated as a potential treatment for behavioral symptoms associated with certain neurodevelopmental disorders. Our goal is to alleviate the high burden caused by behavioral symptoms associated with these disorders. We expect to share data from a Phase 1 multiple ascending dose (MAD) study by late 2025.

Our preclinical stage work is centered on our NMDA receptor negative allosteric modulator (NAM) platform, including SAGE-817 and SAGE-039, focusing on potential treatments for neurodevelopmental disorders.

We are also evaluating SAGE-324, a $GABA_A$ receptor PAM, for potential indications, including seizures in developmental and epileptic encephalopathies.

With our commercial focus, prioritized pipeline and balance sheet as of December 31, 2024, we have a cash runway expected to support our operations to mid-2027.

Looking Ahead to 2025

Looking ahead, we are focused on executing our core priorities and evaluating alternatives to create value for shareholders and advance care in brain health. Our achievements would not be possible without the tremendous efforts of our Sage colleagues and collaborators. There is significant opportunity for Sage to make critical progress for patients around the world suffering from brain health disorders, and we look forward to continuing the great work underway, including accelerating progress in maternal mental health and helping many more women with PPD receive treatment with ZURZUVAE. Thank you for your ongoing support as we strive to introduce a new era of brain health medicines.

Barry Greene
Chief Executive Officer
Sage Therapeutics
April 24, 2025

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, 2024

OR

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

For the transition period from _____ to

Commission file number: 001-36544

Sage Therapeutics, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware **(State or Other Jurisdiction of Incorporation or Organization)**	**27-4486580** **(I.R.S. Employer Identification No.)**
55 Cambridge Parkway **Cambridge, Massachusetts** **(Address of Principal Executive Offices)**	**02142** **(Zip Code)**

(617) 299-8380

(Registrant's Telephone Number, Including Area Code)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	SAGE	The Nasdaq Global 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 Exchange Act. Yes ☐ No ☒

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

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

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

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

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

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

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

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

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

The aggregate market value of the registrant's voting and non-voting common stock held by non-affiliates of the registrant as of June 28, 2024 was approximately $590,463,402, computed by reference to the closing price of the registrant's common stock on the Nasdaq Global Market reported for such date.

As of February 4, 2025, there were 61,480,947 shares of common stock, $0.0001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report on Form 10-K incorporates by reference certain information from the registrant's definitive Proxy Statement for its 2025 annual meeting of shareholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year end of December 31, 2024. Except with respect to information specifically incorporated by reference in this Form 10-K, the Proxy Statement is not deemed to be filed as part of this Form 10-K.

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Cautionary Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this Annual Report are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "may", "will", "should", "expects", "intends", "plans", "anticipates", "believes", "estimates", "predicts", "potential", "continue" or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our expectations and goals for commercialization of ZURZUVAE® in the U.S. as a treatment for women with postpartum depression, or PPD, including our beliefs in the potential benefit and profile of ZURZUVAE for the treatment of women with PPD; our estimates as to the number of women with PPD; the potential market opportunity for ZURZUVAE for the treatment of women with PPD; our market access, sales and marketing, customer support, investment, and distribution strategies for ZURZUVAE and related expectations, goals, and assumptions, including our goals to establish ZURZUVAE as the standard of care for women with PPD, expand market growth in PPD, accelerate topline revenue growth, and ultimately help more women with PPD; our market access goal of helping all women with PPD who are prescribed ZURZUVAE gain access to ZURZUVAE as quickly as possible with minimal restrictions; and the potential future results of our commercialization efforts and investment in the U.S.;
- our expectations and estimates regarding: the level of expenses we may incur in connection with our activities, including the cost savings we may realize as a result of our October 2024 corporate reorganization and pipeline prioritization efforts; use of cash, cash runway and projected cash balance at any given time; timing of future cash needs; capital requirements; funding from potential revenue; anticipated funding from ongoing collaborations; sources of future financing; and our ability to obtain additional financing, including on acceptable terms, when needed to fund future operations;
- our plans for the development of our product candidates for the treatment of brain health diseases and disorders, and potentially for other indications, including for SAGE-319 as a potential treatment for behavioral symptoms associated with certain neurodevelopmental disorders; our plans to announce data from a Phase 1 multiple ascending dose study of SAGE-319 by late 2025 and to evaluate next steps, if any, based on these data; our plans to evaluate other potential indications for SAGE-324, including seizures in developmental and epileptic encephalopathies and to provide an update on next steps, if any, in mid-2025; our plans with respect to other research and development activities, including continuing to explore targeted work within our NMDA receptor negative allosteric modulator platform with SAGE-817 and SAGE-039; and expected timelines for our planned activities;
- our expectations regarding our plans to explore strategic alternatives;
- our ability, within the expected time frames, to initiate clinical trials and non-clinical studies of existing or future product candidates, including pivotal clinical trials, and to successfully enroll, complete and announce the results of ongoing or future clinical trials;
- our belief as to potential outcomes of our clinical development and commercialization activities;
- our plans and potential outcomes with respect to interactions with regulatory authorities;
- our plans for and the potential costs, benefits and outcomes of our existing collaborations with Biogen MA Inc., or BIMA, and Biogen International GmbH, or, together with BIMA, Biogen, and Shionogi & Co., Ltd., or Shionogi, and our plans for and potential outcomes of any additional business development efforts;
- our plans and expectations with respect to the potential development of any product or product candidate for markets outside the U.S.;
- our expectations with respect to the availability of supplies of ZURZUVAE and our product candidates, and the expected performance of our third-party manufacturers, including conformity with applicable regulatory requirements;
- our ability to obtain and maintain intellectual property protection for our proprietary assets and other forms of exclusivity relevant to our business;

- the estimated number of patients with diseases or disorders of interest to us and the potential size of the market for our products and product candidates in the indications we are pursuing or plan to study;
- the potential for our current products and current or future product candidates, if successfully developed and approved, for the indications and in the markets for which they are approved and our ability to serve those markets;
- the potential for success of competing products that are or become available for the treatment of PPD or any of the other indications that we are pursuing or may pursue in the future with our products and our product candidates;
- the impact of changes to the macroeconomic environment and geopolitical events on our activities, business and results of operations, and the potential success of our efforts to address or mitigate such impact; and
- other risks and uncertainties, including those listed under Part I, Item 1A, Risk Factors.

Any forward-looking statements in this Annual Report reflect our current views with respect to future events and with respect to our business and future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those described under Part I, Item 1A, Risk Factors and elsewhere in this Annual Report. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

We may from time to time provide estimates, projections and other information concerning, among other things, our industry, the general business environment, and the markets for certain diseases, including estimates regarding the potential size of those markets and the estimated incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events, circumstances or numbers, including actual disease prevalence rates and market size, may differ materially from the information we provide in this Annual Report. Unless otherwise expressly stated, we obtained this industry and business information, market data, prevalence information and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties; industry, medical and general publications; government data; and similar sources, in some cases applying our own assumptions and analysis that may, in the future, prove not to have been accurate.

This Annual Report on Form 10-K contains references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this Annual Report and the documents incorporated by reference herein may appear without the ® or ™ 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 companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

Summary of Risks Related to our Business

Our business, prospects, financial condition, and operating results are subject to numerous risks and uncertainties that you should be aware of before making an investment decision, as more fully described under Part I, Item 1A, Risk Factors and elsewhere in this Annual Report. These risks may include, but are not limited to, the following:

- Our future business prospects depend heavily on our ability, with our collaborator Biogen, to successfully continue to commercialize ZURZUVAE for the treatment of women with PPD. We and Biogen may not be successful in our commercialization efforts for ZURZUVAE for the treatment of women with PPD. ZURZUVAE may not achieve, or, even if achieved, maintain, broad market acceptance. We may also encounter other limitations or issues related to the commercialization of ZURZUVAE, including as a result of its price or competition in the market. ZURZUVAE may not achieve brand awareness and adoption among healthcare professionals, including OBGYNs, and our beliefs about the potential for OBGYNs to utilize ZURZUAVE at the forefront of postpartum care may prove to be incorrect. As a result, we may not generate revenues at the levels or on the timing we expect. The number of women with PPD, the unmet need for additional treatment options, and the potential market for ZURZUVAE in this indication may be significantly smaller than we expect. Any setback or delay in our ability to market ZURZUVAE for the treatment of women with PPD may have a material adverse effect on our business and prospects.
- Our plans to explore strategic alternatives and our rejection of an unsolicited, non-binding acquisition proposal from Biogen to acquire all of our outstanding shares not owned by Biogen may have a material adverse effect on our business. Our rejection of the unsolicited, nonbinding acquisition proposal from Biogen, our efforts to enforce the terms of the stock purchase agreement we entered into with Biogen, and our strategic review process may adversely impact our relationship with Biogen, including our efforts to commercialize ZURZUVAE for the treatment of women with PPD. We cannot be certain that our efforts to date with Biogen, including regarding sales force coordination, engagement with payors, and education efforts related to PPD, will not be adversely impacted or that Biogen will continue to make investments related to ZURZUVAE. Any disruption of our relationship with Biogen under the Biogen collaboration agreement may have an adverse impact on sales of ZURZUVAE and may in turn materially adversely affect our business, results of operations, financial condition and prospects. We have not set a timetable for the strategic review process, nor have we made any decisions related to any potential strategic alternatives at this time. There can be no assurance that our strategic review process will result in any transaction or other strategic outcome.
- Our future business prospects also depend heavily on our ability to successfully develop and gain regulatory approval of our product candidates. We cannot be certain that the results of our development programs will be positive or sufficient to file for regulatory approval. Any setback or delay in obtaining regulatory approval for any of our product candidates or in our ability to commence marketing of our products, if approved, may have a material adverse effect on our business and prospects.
- If the affected populations for indications our products and product candidates are targeting, including the addressable markets within such populations, or the number of patients within such markets who are actually treated with our products, are smaller than we anticipate, or our other assumptions with respect to the potential markets for our products and product candidates are incorrect, our ability to achieve profits from the commercialization of such products, if approved, at the levels or on the timing we expect could be materially adversely impacted.
- If serious adverse events or other undesirable side effects are identified during the use of any of our marketed products or product candidates, such events may adversely affect market acceptance or result in other significant negative consequences for an approved product; delay or prevent further development or regulatory approval with respect to product candidates; or cause regulatory authorities to require labeling statements, such as boxed warnings, or a Risk Evaluation and Mitigation Strategy, on approved products.
- We, or our collaboration partners, may not achieve positive results in clinical trials and non-clinical studies of our product candidates. The results of non-clinical studies or clinical trials of our product candidates at any stage may not support further development or may not be sufficient to file for and obtain regulatory approval.
- We may not generate revenues from our existing products, or any of our product candidates if successfully developed, at the levels we expect. We may not achieve events tied to cash milestone payments or other payments from our collaboration partners on the timelines we expect or at all. Our expenses may also be higher than we expect, including as a result of unexpected events or changes in plans. Also, we may not achieve

anticipated cost savings from our October 2024 corporate reorganization at the levels we expect. As a result, our expectations as to our cash runway and the sufficiency of cash to fund our future operations may prove to be incorrect. We will need to raise additional funding, which may not be available on acceptable terms, or at all.

- Any impairment of the ability of our third-party suppliers to supply product or to meet applicable regulatory standards may significantly negatively impact our ability to achieve our goals and plans and to meet the expectations for our business.
- Competing therapies may exist or could be approved that adversely affect the amount of revenue we are able to generate from the sale of ZURZUVAE for the treatment of women with PPD or any of our other current or future product candidates, if successfully developed and approved.
- Our existing collaborations with Biogen and Shionogi, and any future collaborations, may not lead to the successful development or regulatory approval of product candidates or commercialization of products in the territories covered by the applicable collaboration. Our collaborators may have competing priorities, conflicting incentives, or different views than us on key decisions, that may hamper or delay our development and commercialization efforts or increase our costs. Our business may be adversely affected and we may be subject to delays, disputes, or litigation if we disagree significantly with any of our collaborators, or any of our collaborators fails to perform its obligations or terminates our collaboration.
- If we are unable to adequately protect our proprietary technology or obtain and maintain issued patents sufficient to protect our products or product candidates, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.
- If we were to lose our rights to certain licensed intellectual property, or if we are not able to obtain licenses to intellectual property we may determine we need in the future, we may not be able to continue developing or commercializing certain of our products or product candidates, if approved.
- Existing or future laws, regulations, executive orders or policies aimed at reducing healthcare costs may have a material adverse effect on our business or results of operations. Existing, pending or future federal and state reforms aimed at reducing healthcare costs, including pricing and reimbursement of pharmaceutical products, may in the future result in reduced reimbursement and access for our products or cause us to curtail certain development plans due to concerns about commercial viability, any of which could adversely affect our ability to generate revenue and negatively impact our business, results of operations and financial condition.
- We are subject to healthcare laws and regulations, which could expose us to the risk of criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings if we or our employees are alleged or determined not to have complied with such laws and regulations.
- Our stock price may fluctuate in response to a number of factors.

PART I

All brand names or trademarks appearing in this report are the property of their respective owners. Unless the context requires otherwise, references in this report to "Sage," the "Company," "we," "us," and "our" refer to Sage Therapeutics, Inc. and its subsidiaries.

Item 1. Business

Overview

We are a biopharmaceutical company with a mission to pioneer solutions to deliver life-changing brain health medicines, so every person can thrive. Alongside our commercial product for the treatment of postpartum depression, or PPD, we are advancing a portfolio of internally discovered novel chemical entities with the potential to become differentiated treatments designed to improve brain health by primarily targeting two critical central nervous system, or CNS, receptor systems, GABA and NMDA. The GABA receptor family, which is recognized as the major inhibitory neurotransmitter in the CNS, mediates downstream neurologic and bodily function via activation of $GABA_A$ receptors. The NMDA-type receptors of the glutamate receptor system are a major excitatory receptor system in the CNS. Dysfunction in these systems is thought to be at the core of numerous neuropsychiatric and neurodevelopmental disorders.

Our product ZURZUVAE® (zuranolone) was approved by the U.S. Food and Drug Administration, or FDA, in August 2023 for the treatment of PPD in adults. ZURZUVAE is a neuroactive steroid that is a positive allosteric modulator of $GABA_A$ receptors, targeting both synaptic and extrasynaptic $GABA_A$ receptors, and is the first oral, once-daily, 14-day treatment specifically indicated for adults with PPD. ZURZUVAE became commercially available in the U.S. in December 2023 as a treatment option for women with PPD. We and our collaboration partner, Biogen MA Inc., or BIMA, and Biogen International GmbH, or, together with BIMA, Biogen, are jointly commercializing ZURZUVAE in the U.S. under our collaboration and license agreement, or the Biogen Collaboration Agreement, that became effective in December 2020. We and Biogen equally share in all operating profits and losses arising from sales of ZURZUVAE in the U.S., with Biogen recording such product sales.

We jointly commercialize ZURZUVAE with Biogen in the U.S. and have the right to jointly commercialize any additional products containing zuranolone, which, along with ZURZUVAE, we refer to as Licensed 217 Products, if our ongoing and any future development efforts are successful. In addition, we have granted Biogen sole rights to develop and commercialize the Licensed 217 Products outside the U.S., other than in Japan, Taiwan and South Korea, or the Shionogi Territory, with respect to zuranolone, where we have granted such rights to Shionogi & Co., Ltd., or Shionogi. We refer to the territories outside the U.S. to which Biogen has rights under the Biogen Collaboration Agreement with respect to the Licensed 217 Products as the Biogen Territory.

We also have a collaboration agreement with Shionogi for the development of zuranolone in the Shionogi Territory. Shionogi is currently developing zuranolone for the treatment of patients with major depressive disorder, or MDD, in Japan. In the third quarter of 2024, Shionogi reported that it submitted a new drug application, or NDA, in Japan for zuranolone for the treatment of MDD.

We also previously commercialized ZULRESSO® (brexanolone) CIV injection for the treatment of PPD. ZULRESSO is approved in the U.S. for the treatment of PPD in individuals 15 years old and older. We launched ZULRESSO commercially in the U.S. in June 2019. ZULRESSO was administered as a continuous intravenous infusion for two and a half days and could only be administered in qualified medically-supervised healthcare settings. Given the complexities and challenges associated with administration of ZULRESSO, use of the product was limited and further reduced as a result of the availability of ZURZUVAE for the treatment of women with PPD. For that reason, we discontinued commercial availability of ZULRESSO in the U.S. as of December 31, 2024.

We are also evaluating potential indications for SAGE-324, a novel $GABA_A$ receptor positive allosteric modulator intended for chronic oral dosing, including seizures in developmental and epileptic encephalopathies, or DEEs, and expect to provide an update on next steps, if any, in mid-2025.

Our other area of focus is SAGE-319, an extrasynaptic-preferring $GABA_A$ receptor positive allosteric modulator, or $GABA_A$ PAM, designed to have a novel pharmacology and a differentiated clinical profile from other $GABA_A$ PAMs in our portfolio. We are currently investigating SAGE-319 as a potential treatment for behavioral symptoms associated with certain neurodevelopmental disorders. We expect to announce data from a Phase 1 multiple ascending dose study by late 2025, and will evaluate next steps, if any, based on these data.

We expect to continue to focus on the development of product candidates for the treatment of both acute and chronic brain health disorders, including work on allosteric modulation of the $GABA_A$ and NMDA receptor systems in the brain, and are continuing to explore targeted work within our NMDA receptor negative allosteric modulator, or NMDAR NAMs, platform, focusing on potential treatments for neurodevelopmental disorders, with SAGE-817 and SAGE-039. The $GABA_A$ and NMDA receptor systems are broadly accepted as impacting many neuropsychiatric and neurodevelopmental disorders, spanning disorders of mood, seizure, cognition, anxiety, sleep, pain, and movement, among others. We believe that we may have the opportunity to develop molecules from our internal portfolio with the goal of addressing a number of these disorders in the future, and also believe that we may have opportunity to use our scientific approach to explore targets beyond the $GABA_A$ and NMDA receptor systems and to develop compounds in areas of unmet need outside of brain health.

Our Strategy

Our goal is to build a top-tier biopharmaceutical company that is the leader in developing and commercializing life-changing brain health medicines. Key elements of our strategy are to:

- successfully commercialize ZURZUVAE, along with our collaboration partner, Biogen, for the treatment of women with PPD in the U.S., including our goals to establish ZURZUVAE as the standard of care for women with PPD, expand market growth in PPD, accelerate topline revenue growth, and ultimately help more women with PPD;
- investigate SAGE-319 as a potential treatment for behavioral symptoms associated with certain neurodevelopmental disorders;
- evaluate potential further indications for SAGE-324;
- support our collaboration with Biogen with respect to zuranolone in the U.S., and support Biogen's development of zuranolone in the Biogen Territory and Shionogi's development of zuranolone in the Shionogi Territory;
- continue work on our prioritized pipeline focused on neurodevelopmental disorders and neuropsychiatry, including to explore targeted work within our NMDAR NAMs platform with SAGE-817 and SAGE-039;
- focus on maintaining a strong balance sheet while reducing operating expenses;
- continue to explore business development opportunities, including opportunities to establish licenses, collaborations, or other agreements or alliances with other biotechnology and pharmaceutical companies, at the appropriate time, where we believe a collaboration may add significant value to our efforts, including through capabilities, infrastructure, speed or financial contributions, or to acquire new compounds, product candidates or products if we believe such opportunities will help us achieve our goals or meet other strategic objectives;
- prepare and file NDAs with the FDA, and conduct permitted pre-launch activities with respect to any of our product candidates that we believe have been successfully developed;
- commercialize any product candidates for which we obtain regulatory approval, including the manufacture of commercial supplies;
- evaluate the market potential and regulatory pathways for our product candidates beyond zuranolone in the European Union, or EU, and other jurisdictions outside the U.S., and determine how best to move forward where and when it may make business and strategic sense; and

- continue to build, maintain, defend, leverage, and expand our intellectual property portfolio, including by utilizing the strengths of our proprietary chemistry platform and scientific know-how to expand our portfolio of new chemical entities with the goals of lessening our long-term reliance on the success of any one program and facilitating long-term growth.

Understanding the Foundations of Our Approach

The CNS is composed of a vast and complex network of different structures and cell types, most of which serve, directly or indirectly, to provide a means for the nervous system to signal or communicate with other nerve cells to regulate brain function. The cell type responsible for this signaling is called a neuron. One way chemical or electrical signals exert their effects on neurons is by traveling across a physical gap located between two neurons, called a synapse. Presynaptic neurons transmit signals whereas postsynaptic neurons react to the signals. The human brain contains approximately 86 billion neurons, each having hundreds to tens of thousands of synapses to allow for this communication. This process is essential to all things, from organ function to movement, memory and all behavioral processes. Neurotransmission is the process by which signaling molecules, called neurotransmitters, are released by a presynaptic neuron, travel over the synaptic space and bind to and interact with receptors on a postsynaptic neuron. Depending on the nature of the neurotransmitter and receptor, this interaction results in excitation, inhibition or modulation of the receiving neuron's behavior.

We are currently focused on developing drugs based on selective allosteric modulation of neurotransmitter receptors in the CNS. Allosteric modulators are a class of small molecules that interact at a site different from the site where neurotransmitters bind, and allow the potential for fine-tuning of neuronal signals. We believe that nowhere in the body is it more important to maintain normal rhythms than in the brain, and accordingly we believe that allosteric modulation approaches are well-suited for the treatment of diseases and disorders of the brain.

We utilize our proprietary chemistry capabilities to design and identify drug candidates that target critical CNS proteins and have properties aligned to the indications of interest. Our goal is to select for development compounds that we believe are capable of varying degrees of desired activity rather than complete activation or inhibition.

Our focus as a company is on brain health, and we are currently primarily targeting two critical CNS receptor systems: GABA and NMDA. The GABA receptor family, which is recognized as the major inhibitory neurotransmitter in the CNS, mediates downstream neurologic and bodily function in part via activation of $GABA_A$ receptors. $GABA_A$ receptors play a key role in regulating neuron excitability. The NMDA-type receptors of the glutamate receptor system are a major excitatory receptor system in the CNS. NMDA receptors serve a critical role in CNS-related activities. Dysfunction in these systems is implicated in a broad range of brain disorders.

Our proprietary chemistry platform is currently centered on our knowledge of the chemical scaffolds of endogenous neuroactive steroids. We have leveraged this platform to assemble a chemistry portfolio of greater than 15,000 compounds. We believe our proprietary chemistry platform allows us to:

- control important properties such as half-life, brain penetration and the types of receptors our drugs act upon, thereby modulating either inhibition or excitation either acutely or chronically; and
- create drugs that are designed to exert control over the intensity of receptor activation or deactivation, with the potential to hit targets in the brain with more precision, with the goal of increased tolerability and fewer off-target side effects than current CNS therapies or previous therapies that have failed in development.

We target diseases and disorders of the brain where we believe patient populations are easily identified, clinical endpoints are well-defined, and development pathways are feasible.

Our Product Pipeline

The following table summarizes the status of our product and product candidate portfolio as of the filing date of this Annual Report.

*Under a collaboration agreement between Sage and Shionogi & Co., Ltd., Shionogi has the right to develop and commercialize zuranolone in Japan, Taiwan, and South Korea. Please refer to the U.S. Prescribing Information for ZURZUVAE.
**We are evaluating potential indications, including seizures in developmental and epileptic encephalopathies (DEEs), and expect to provide an update on next steps, if any, in mid-2025. Biogen terminated its rights as to the SAGE-324 program in September 2024; the termination will be effective on February 17, 2025. SAGE-324 was previously evaluated in a Phase 2 clinical trial for the treatment of essential tremor, and we anticipate that any future development of SAGE-324 for the treatment of seizures in DEEs would commence with a Phase 2 clinical trial.

ZURZUVAE (zuranolone)

Our product ZURZUVAE (zuranolone) was approved by the FDA in August 2023 for the treatment of PPD in adults. ZURZUVAE is a neuroactive steroid that is a positive allosteric modulator of $GABA_A$ receptors, targeting both synaptic and extrasynaptic $GABA_A$ receptors, and is the first oral, once-daily, 14-day treatment specifically indicated for adults with PPD. ZURZUVAE became commercially available in the U.S. for women with PPD in December 2023. We and our collaboration partner, Biogen, are jointly commercializing ZURZUVAE in the U.S. under the Biogen Collaboration Agreement. We and Biogen equally share in all operating profits and losses arising from sales of ZURZUVAE in the U.S., with Biogen recording such product sales.

ZURZUVAE (zuranolone) received a Schedule IV classification from the Drug Enforcement Administration, or DEA. The approval of ZURZUVAE to treat PPD in adults was based on two pivotal clinical trials in adult women with PPD. ZURZUVAE includes a boxed warning that instructs healthcare professionals to advise patients that ZURZUVAE causes driving impairment due to central nervous system depressant effects, and that people who take ZURZUVAE should not drive a motor vehicle or engage in other potentially hazardous activities requiring complete mental alertness until at least 12 hours after ZURZUVAE administration for the duration of the 14-day treatment course. ZURZUVAE can cause CNS depressant effects. The most common side effects of ZURZUVAE include sleepiness or drowsiness, dizziness, common cold, diarrhea, feeling tired, weak, or having no energy, and urinary tract infection.

PPD symptoms are some of the most common medical complications during and after pregnancy, and PPD is characterized by depressive symptoms that can begin during pregnancy or within the first 4 weeks to 12 months following childbirth. PPD symptoms may include sadness and depressed mood; anxiety or agitation; loss of interest in daily activities; changes in eating and sleeping habits; feeling overwhelmed; fatigue and decreased energy; inability to concentrate; hypervigilance about the baby or lack of interest in the baby; and feelings of worthlessness, shame or guilt. Based on our analysis of available data, we estimate that approximately 500,000 women in the U.S. each year may

experience symptoms of PPD. PPD can lead to devastating consequences for a woman and for her family. In addition, the economic burden associated with perinatal depression can be vast and can impact patients, their families, employers, and healthcare payors.

ZURZUVAE is the first and only oral product approved by the FDA for women with PPD (and the second approved product for PPD after ZULRESSO). The current standard of care for PPD is comprised of psychotherapy and, in women with moderate or severe PPD, the cautious use of pharmacological therapies such as selective serotonin reuptake inhibitors, or SSRIs, and serotonin and norepinephrine reuptake inhibitors, or SNRIs.

Naturally occurring allopregnanolone is found at its highest levels in women during the third trimester of pregnancy, returning to normal levels generally within 24 hours after giving birth. Levels of allopregnanolone have been found to be lower in women with PPD than in healthy women. It may be that women with PPD are particularly sensitive to the rapid decline in allopregnanolone after birth, potentially causing $GABA_A$-system mediated mood disruption. These data led to our interest in evaluating allosteric modulators of the $GABA_A$ receptor—such as brexanolone and zuranolone—for the treatment of PPD.

On August 4, 2023, the FDA issued a complete response letter, or CRL, related to the NDA for zuranolone for the treatment of MDD. The CRL stated that the NDA did not provide substantial evidence of effectiveness to support the approval of zuranolone for the treatment of MDD and that one or more additional clinical trials will be needed. We and Biogen have agreed not to pursue further development of zuranolone for the treatment of MDD in the U.S. This decision was based on the significant new investment and time we expect would be needed to conduct additional studies to support approval. We and Biogen plan to continue to collaborate on the commercialization of ZURZUVAE in PPD.

We have granted Biogen sole rights to develop and commercialize zuranolone outside the U.S., other than in Japan, Taiwan and South Korea where we have granted rights to Shionogi. Shionogi is currently developing zuranolone for the treatment of patients with MDD in Japan.

SAGE-324

Under the Biogen Collaboration Agreement, we and Biogen also previously agreed to jointly develop and commercialize products containing SAGE-324, which we refer to as the Licensed 324 Products. In July 2024, we and Biogen announced topline results from the KINETIC 2 Study, a Phase 2b dose-ranging clinical trial evaluating SAGE-324, a novel $GABA_A$ receptor positive allosteric modulator intended for chronic oral dosing, in the treatment of patients with essential tremor. The KINETIC 2 Study did not demonstrate a statistically significant dose-response relationship in change from baseline to Day 91 based on the primary endpoint, the TETRAS PS Item 4 (upper limb) total score, in participants with essential tremor. In addition, there were no statistically significant differences demonstrated for any dose of SAGE-324 versus placebo in the change from baseline to Day 91 on the TETRAS PS Item 4 or the TETRAS Activities of Daily Living Composite Score. In the study, 147 participants (129 monotherapy and 18 adjunct therapy who were on a stable dose of propranolol prior to and during the study) were randomized in approximately equal proportions to placebo and each of the three formulations of SAGE-324—15 mg, 30 mg, and 60 mg (with up-titration)—for a three-month treatment period. Overall, there was a dose-relationship observed in the incidence of CNS depressant treatment emergent adverse events, or TEAEs, and in the frequency of TEAEs, leading to study drug discontinuation. The most common TEAEs reported in any treatment group were somnolence, dizziness, fatigue, feeling abnormal, headache, and balance disorder. The majority of reported TEAEs were mild or moderate in intensity. Given these results, we and Biogen decided to close the open-label Phase 2 clinical trial of SAGE-324 designed to evaluate the long-term safety and tolerability of SAGE-324 in patients with essential tremor and we do not plan to conduct further clinical development of SAGE-324 in essential tremor.

In September 2024, Biogen notified us of its termination of the Biogen Collaboration Agreement solely with respect to the Licensed 324 Products on a worldwide basis, effective February 17, 2025, or the SAGE-324 Termination. As a result of the SAGE-324 Termination, as of February 17, 2025, all licenses granted by us to Biogen or by Biogen to us regarding the Licensed 324 Products shall expire with respect to the Licensed 324 Products on a worldwide basis. Biogen shall grant to us an irrevocable, perpetual license for any Biogen background technology, Biogen collaboration technology or joint collaboration technology that exists as of February 17, 2025 with respect to the Licensed 324 Products on a

worldwide basis, in each case in accordance with the terms of the Biogen Collaboration Agreement. We and Biogen continue to be responsible for our respective share of costs for ongoing activities related to the Licensed 324 Products in accordance with the terms of the Biogen Collaboration Agreement until February 17, 2025.

We are evaluating other potential indications for SAGE-324, including seizures in DEEs, and expect to provide an update on next steps, if any, in mid-2025.

SAGE-319

SAGE-319 is an extrasynaptic-preferring $GABA_A$ PAM designed to have a novel pharmacology and a differentiated clinical profile from other $GABA_A$ PAMs in our portfolio. We are currently investigating SAGE-319 as a potential treatment for behavioral symptoms associated with certain neurodevelopmental disorders. We expect to announce data from a Phase 1 multiple ascending dose study by late 2025, and will evaluate next steps, if any, based on these data.

Dalzanemdor (SAGE-718)

We previously evaluated dalzanemdor in certain cognitive disorders associated with NMDA receptor dysfunction. In November 2024, we announced that the DIMENSION Study, a Phase 2 clinical trial evaluating dalzanemdor for the treatment of patients with cognitive impairment associated with Huntington's disease, did not demonstrate a statistically significant difference versus placebo on the primary endpoint, and analyses of secondary endpoints did not demonstrate statistically significant or clinically meaningful differences in participants treated with dalzanemdor compared to placebo. In addition, in October 2024, we announced that the LIGHTWAVE Study, a Phase 2 clinical trial evaluating dalzanemdor for the treatment of patients with mild cognitive impairment and mild dementia due to Alzheimer's disease, did not meet its primary endpoint, and analyses did not demonstrate any meaningful differences versus placebo in the other exploratory endpoints. Previously, in April 2024, we announced that the PRECEDENT Study, a Phase 2 clinical trial evaluating dalzanemdor as a treatment for cognitive impairment due to Parkinson's disease, did not meet its primary endpoint, and analyses did not suggest any meaningful differences versus placebo in the other exploratory endpoints. Based on these results, we do not plan to pursue further development of dalzanemdor.

Further Exploration of $GABA_A$ and NMDA Receptors and New Areas of Interest

We expect to continue to focus our research and development efforts on allosteric modulation of the $GABA_A$ and NMDA receptor systems in the brain, including targeted work within our NMDAR NAMs platform, focusing on potential treatments for neurodevelopmental disorders, with SAGE-817 and SAGE-039. The $GABA_A$ and NMDA receptor systems are broadly accepted as impacting many neuropsychiatric and neurodevelopmental disorders, spanning disorders of mood, seizure, cognition, anxiety, sleep, pain, and movement among others. We believe that we may have opportunities to develop molecules from our internal portfolio to address a number of these disorders in the future. Our ability to identify and develop such novel brain health therapies is enabled by our proprietary chemistry platform that is centered, as a starting point, on knowledge of the chemical scaffolds of certain endogenous neuroactive steroid compounds. We believe our knowledge of the chemistry and activity of allosteric modulators allows us to efficiently design molecules with different characteristics. This diversity enables us to regulate important properties such as half-life, brain penetration and receptor pharmacology to develop product candidates that have the potential for better selectivity, increased tolerability, and fewer off-target side effects than either current therapies or previous therapies which have failed in development.

We believe our ability to design and develop novel molecules with distinct profiles and receptor subtype selectivity may also provide us with the option, if we choose, to potentially partner certain assets with third parties who possess the development and commercialization capabilities to pursue these programs. We may also evaluate opportunities to acquire new compounds, product candidates or products from other companies or from academic institutions if we believe such opportunities will help us achieve our goals or meet other strategic objectives.

Manufacturing and Supply

We neither own nor operate, and currently have no plans to own or operate, any manufacturing facilities. We currently source all of our clinical and non-clinical material supply through third-party contract manufacturing organizations, or CMOs. We rely on our contract manufacturers to manufacture sufficient quantities of ZURZUVAE active drug substance, finished drug product and packaged and labeled product. We also previously relied on our contract manufacturers for commercial supplies of active drug substance, finished drug product and packaged and labeled product with respect to ZULRESSO until we discontinued ZULRESSO commercial availability in the U.S. as of December 31, 2024. We intend to source all of our future commercial supplies of ZURZUVAE and our product candidates, if approved by the FDA, from CMOs.

We have a long-term supply agreement with our contract manufacturer for ZURZUVAE drug product. We have an inventory of ZURZUVAE drug substance and drug product in place to help mitigate any potential supply risks. All commercial supplies are intended to be manufactured applying current Good Manufacturing Practices, or cGMP.

We have established relationships with CMOs under which the CMOs manufacture clinical and non-clinical supplies of drug substance and drug product for our product candidates on a purchase order basis under master service and quality agreements. All clinical supplies of drug substance and drug product are intended to be manufactured under cGMP. Starting materials and key intermediates to support the production of these product candidates are manufactured by other CMOs. We do not currently have arrangements in place for either long-term supply or redundant supply of drug substance or drug product for any of our product candidates. We intend to put long-term supply agreements in place at the appropriate time for drug substance and drug product for our product candidates, if development continues. We plan to mitigate potential commercial supply risks for any products that are approved in the future through inventory management and through exploring additional manufacturers to provide drug substance or drug product. We also intend to improve the manufacturing process for our product candidates and manufacture clinical supplies as development progresses.

ZURZUVAE, SAGE-319, and SAGE-324 are small molecules isolated as stable crystalline solids. We believe the syntheses of ZURZUVAE, SAGE-319, and SAGE-324 are reliable and reproducible from readily available starting materials, and the synthetic routes are amenable to large-scale manufacturing and do not require unusual equipment in the manufacturing process. We expect to continue to identify and develop drug candidates that are amenable to cost-effective manufacturing at contract manufacturing facilities.

Sales and Marketing

Our product ZURZUVAE became commercially available in the U.S. in December 2023 as the first and only oral product approved by the FDA specifically for the treatment of adults with PPD. We and Biogen are jointly commercializing ZURZUVAE in the U.S. for the treatment of women with PPD under the Biogen Collaboration Agreement. We and Biogen equally share in all operating profits and losses arising from sales of ZURZUVAE in the U.S., with Biogen recording such sales.

We and Biogen are utilizing a specialty pharmacy distribution model by which ZURZUVAE is shipped directly to women with PPD who are prescribed the treatment. We and Biogen have active field sales forces supported by experienced sales leadership teams and professionals in marketing, access and reimbursement, managed markets, market research, commercial operations, and sales force planning and management. We and Biogen are continuing to engage in discussions with national, regional and government payors to advocate for broad and equitable access to ZURZUVAE for women with PPD with minimal restrictions. Payor coverage for ZURZUVAE for the treatment of women with PPD is currently in place for a majority of commercial and Medicaid covered lives without step therapy or complex prior authorizations, including coverage from all three national Pharmacy Benefit Managers. We expect formulary discussions to continue over the course of 2025.

We and Biogen are focused on helping women with PPD by optimizing access to ZURZUVAE, increasing education and awareness, driving urgency to treat women with PPD, and breaking the stigma associated with PPD. To accomplish these objectives, we are utilizing a broad omnichannel approach that includes both personal and non-personal promotion. Through Sage and Biogen's sales forces, we are engaging in promotional dialogues with healthcare professionals who diagnose and treat women with PPD. These efforts are supplemented by dynamic digital tools that

provide education about PPD to a broader range of healthcare professionals, patients, and patient advocates. Over the course of 2024, we saw prescribing across healthcare professional specialties, with OBGYNs comprising the primary prescriber group. This is notable, as we believe OBGYNs are at the forefront of postpartum care for so many women with PPD given the role they play in a woman's peripartum journey.

To help enable broad and equitable access, we also maintain a patient support program, ZURZUVAE For You, which provides educational resources, help with understanding insurance coverage, and assistance navigating the prescription fulfillment process for women with PPD who are prescribed treatment. This program also includes financial assistance for women with PPD, such as the potential for copay assistance for those with commercial insurance and the potential to be provided product at no cost for other eligible patients.

We and Biogen are also working to help raise awareness of the importance of treating PPD rapidly and removing barriers to treatment. Our commercialization infrastructure also includes capabilities in medical affairs, manufacturing, quality control, drug safety and pharmacovigilance, health economics and outcomes research (HEOR), and compliance.

In addition to our joint commercialization of ZURZUVAE for the treatment of women with PPD in the U.S., the Biogen Collaboration Agreement provides that we will jointly commercialize in the U.S. other Licensed 217 Products if pursued and successfully developed and approved, including sharing equally in sales and marketing activities and profits and losses in the U.S. We have granted Biogen sole rights to commercialize the Licensed 217 Products in the Biogen Territory.

Licenses

We have entered into license agreements with respect to our product and clinical-stage product candidates, which are described below.

Collaboration and License Agreement with Biogen

In November 2020, we entered into the Biogen Collaboration Agreement with Biogen for the development, manufacture and commercialization of Licensed 217 Products and Licensed 324 Products (each, a "Product Class"), which became effective in December 2020. As a result of the SAGE-324 Termination, as of February 17, 2025, all licenses granted by us to Biogen or by Biogen to us regarding the Licensed 324 Products shall expire with respect to the Licensed 324 Products on a worldwide basis. Biogen shall grant to us an irrevocable, perpetual license for any Biogen background technology, Biogen collaboration technology or joint collaboration technology that exists as of February 17, 2025 with respect to the Licensed 324 Products on a worldwide basis, in each case in accordance with the terms of the Biogen Collaboration Agreement. We and Biogen continue to be responsible for our respective share of costs for ongoing activities related to the Licensed 324 Products in accordance with the terms of the Biogen Collaboration Agreement until February 17, 2025.

Under the Biogen Collaboration Agreement, after the effectiveness of the SAGE-324 termination, we and Biogen agreed that we will jointly develop and commercialize the Licensed 217 Products in the U.S., and that Biogen solely will develop and commercialize the Licensed 217 Products in the Biogen Territory. We and Biogen have agreed to share jointly in the performance of the activities under the Biogen Collaboration Agreement in the U.S. and to share all operating profits and losses for activities under the Biogen Collaboration Agreement solely for the U.S. equally. The Biogen Collaboration Agreement provides that Biogen has sole responsibility and decision-making authority with respect to such activities in the Biogen Territory. Biogen is solely responsible for all costs for activities under the Biogen Collaboration Agreement in the Biogen Territory. We have an Opt-Out Right (as defined below) in the U.S. with respect to the Licensed 217 Products.

We have granted to Biogen a non-transferable, sublicensable, except for certain specified exceptions, license to certain of our intellectual property as needed to perform the activities under the Biogen Collaboration Agreement. Such license is co-exclusive with us in the U.S. and exclusive, even as to us, in the Biogen Territory, subject to certain retained rights to allow us to exercise our rights and perform our obligations under the Agreement and with respect to the Shionogi Territory.

Our activities for the Licensed 217 Products in the U.S. are conducted pursuant to joint plans agreed to by us and Biogen, and overseen by a joint steering committee, or the JSC. The JSC is composed of an equal number of representatives from each of us and Biogen.

Under the terms of the Biogen Collaboration Agreement, Biogen paid us an upfront payment of $875.0 million on December 31, 2020. For so long as a Licensed 217 Product is being sold in the U.S., we and Biogen will share equally in all operating profits and losses arising from such Licensed 217 Product in the U.S. The Biogen Collaboration Agreement provides that Biogen will record sales of Licensed 217 Products globally. Consistent with this provision, Biogen records sales of ZURZUVAE in the U.S. We have the right to opt out of such profit- and loss-sharing with respect to the Licensed 217 Products in the U.S., or an Opt-Out Right. If we elect to exercise our Opt-Out Right with respect to the Licensed 217 Products, we have agreed to transition to Biogen applicable development and commercialization activities for such Licensed 217 Products for the U.S., and Biogen has agreed to assume sole operational and financial responsibility for such activities.

The Biogen Collaboration Agreement provides for aggregate regulatory/commercial milestone payments from Biogen to us for Licensed 217 Products of up to $475.0 million, including milestones totaling $75.0 million for the first commercial sale of ZURZUVAE for the treatment of women with PPD in the U.S. and $150.0 million for the first commercial sale of zuranolone in MDD in the U.S., if approved. It also provides for aggregate one-time sales milestone payments from Biogen to us of (i) up to $300.0 million for Licensed 217 Products if we have not exercised our Opt-Out Right with respect to such Licensed 217 Products and (ii) up to $525.0 million for Licensed 217 Products if we have exercised our Opt-Out Right with respect to such Licensed 217 Products. We achieved the milestone totaling $75.0 million for the first commercial sale of ZURZUVAE for the treatment of women with PPD in the U.S. in the fourth quarter of 2023, as a result of the first sale of ZURZUVAE to a distributor, and received the milestone payment in January 2024. Because we and Biogen have agreed not to pursue further development for zuranolone for the treatment of MDD in the U.S., we will not receive the $150.0 million milestone payment for the first commercial sale of ZURZUVAE for the treatment of MDD in the U.S.

Biogen has also agreed to pay us tiered royalties based on net sales of the Licensed 217 Products in the Biogen Territory of high-teens to low-twenties percentages. If we have exercised our Opt-Out Right in the U.S. with respect to Licensed 217 Products, Biogen has agreed to pay us specified royalties based on net sales of Licensed 217 Products. Royalty payments may be reduced in certain specified customary circumstances. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may never receive additional milestone payments or any royalty payments from Biogen.

During the term of the Biogen Collaboration Agreement, neither us nor Biogen nor any of our respective affiliates is permitted outside of the Biogen Collaboration Agreement to directly or indirectly develop, manufacture, conduct medical affairs activities or commercialize certain products in specified indications, or enter into agreements or arrangements with third parties to perform any of the above activities.

Unless earlier terminated, the Biogen Collaboration Agreement expires on a Licensed Product-by-Licensed Product and country-by-country basis on the later of (i) in the Biogen Territory, the expiration of the royalty term for such Licensed Product in such country or (ii) in the U.S., until the parties agree to permanently stop commercializing such Licensed Product. Biogen may terminate the Biogen Collaboration Agreement for convenience in its entirety or on a Product Class-by-Product Class basis, as it did with the SAGE-324 Termination, or as to a region by providing advance written notice. Either us or Biogen may terminate the Biogen Collaboration Agreement (i) in the event of a material breach in whole or in part, by the other party subject to a cure period and (ii) in the event of the insolvency of the other party, in each case subject to specified conditions.

In connection with the execution of the Biogen Collaboration Agreement, we and BIMA also entered into a stock purchase agreement, or the Biogen Stock Purchase Agreement, for the sale and issuance of 6,241,473 shares of our common stock, or the Biogen Shares, to BIMA at a price of approximately $104.14 per share, a premium of 40% over the volume-weighted average share price for the 30 days ending on the day prior to entry into the Biogen Stock Purchase Agreement, for an aggregate purchase price of $650.0 million. The sale of the Biogen Shares was consummated on December 31, 2020.

We have granted BIMA specified demand and piggyback registration rights with respect to the Biogen Shares. The Biogen Stock Purchase Agreement also includes standstill provisions and a voting agreement with respect to the Biogen Shares. Pursuant to the terms of the Biogen Stock Purchase Agreement, BIMA has agreed not to, and to cause its affiliates not to, directly or indirectly acquire our securities, seek or propose a tender or exchange offer or merger between us and BIMA, solicit proxies or consents with respect to any matter, or undertake other specified actions, in each case subject to specified conditions. The standstill restrictions terminate on the earliest of (i) a specified period of time after a regulatory milestone under the Biogen Collaboration Agreement, (ii) the date one year following the termination of the Biogen Collaboration Agreement and (iii) December 28, 2027.

For additional information related to the Biogen Collaboration Agreement, see the Risk Factor captioned "*Our plans to explore strategic alternatives and our rejection of an unsolicited, non-binding acquisition proposal from Biogen to acquire all of our outstanding shares not owned by Biogen may have a material adverse effect on our business*" under Part I, Item 1A, "Risk Factors" of this Annual Report.

Collaboration Agreement with Shionogi & Co., Ltd.

In June 2018, we entered into a collaboration agreement with Shionogi. Pursuant to this agreement, Shionogi is responsible for all clinical development, regulatory filings and commercialization of products containing zuranolone for the treatment of MDD and potentially other indications in the Shionogi Territory. Shionogi made an upfront payment of $90.0 million in 2018, and we will be eligible to receive additional payments of up to $485.0 million if certain regulatory and commercial milestones are achieved by Shionogi.

Under the terms of the agreement, the potential future milestone payments include up to $70.0 million for the achievement of specified regulatory milestones, up to $30.0 million for the achievement of specified commercialization milestones, and up to $385.0 million for the achievement of specified net sales milestones. The potential future milestone payments for achievement of specified regulatory milestones was reduced to $55.0 million upon failure to received FDA approval of zuranolone for the treatment of MDD in the U.S. prior to December 31, 2023. We will receive tiered royalties on sales of zuranolone in the Shionogi Territory, if development efforts are successful, with tiers averaging in the low to mid-twenty percent range, subject to other terms of the agreement. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any additional milestone payments or any royalty payments from Shionogi.

As between us and Shionogi, we maintain exclusive rights to develop and commercialize zuranolone outside of the Shionogi Territory. The upfront cash payment and any payments for milestones and royalties are non-refundable and non-creditable.

The agreement with Shionogi will terminate on a licensed product-by-licensed product basis on the date on which the royalty term has expired in each country in the Shionogi Territory for such licensed product and will ultimately expire upon the expiration of the last-to-expire royalty term. Shionogi may remove South Korea or Taiwan from the covered territories, for any reason or no reason upon 180 days' prior written notice. Shionogi may terminate the agreement in its entirety for any reason or no reason upon 180 days' prior written notice. Shionogi may also terminate the agreement in the event of a serious adverse event or a clinical failure upon 60 days' written notice to us. Either party may terminate this agreement early in the event of an uncured material breach within 180 days' after notice is delivered to the other party.

Intellectual Property

We strive to protect the proprietary know-how and technology that we believe is important to our business, including seeking and maintaining patents intended to cover our product candidates and compositions, their methods of use and processes for their manufacture, and any other aspects of inventions that are commercially important to the development of our business. We may also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. To protect our rights to our proprietary know-how and technology, we require all employees, as well as our consultants and contract research organizations, or CROs, when feasible, to enter into agreements that generally require disclosure and assignment to us of ideas, developments, discoveries and inventions made by these employees, consultants, and CROs in the course of their service to us.

We plan to continue to expand our intellectual property estate by filing patent applications directed to compositions, methods of use, treatment and patient selection, formulations and manufacturing processes created or identified from our ongoing development of our product candidates. Our success will depend on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; preserve the confidentiality of our trade secrets; and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how and continuing technological innovation and may pursue in-licensing opportunities to develop and maintain our proprietary position. We seek to obtain domestic and international patent protection, and endeavor to promptly file patent applications for new commercially valuable inventions.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and patent scope can be reinterpreted by the courts after issuance. Moreover, many jurisdictions, including the U.S., permit third parties to challenge issued patents in administrative proceedings, which may result in further narrowing or even cancellation of patent claims. We cannot predict whether the patent applications we are currently pursuing, or may in the future pursue, will issue as patents in any particular jurisdiction or whether the claims of any issued patents will be enforceable or provide sufficient protection from competitors.

Because patent applications in the U.S. and certain other jurisdictions are maintained in secrecy for 18 months or potentially even longer, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by our issued patents, our pending patent applications or of patent applications we may file in the future. Moreover, we may have to participate in interference proceedings or derivation proceedings declared by the U.S. Patent and Trademark Office, or U.S. PTO, or similar proceedings outside the U.S., to determine priority of invention.

Patents

We hold issued patents and pending patent applications in the U.S., and in certain foreign countries. Our intellectual property holdings include, but are not limited to:

- One issued U.S. patent, exclusively licensed to us, covering a method of using our proprietary brexanolone formulation to treat PPD, which will expire in 2033; one U.S. issued patent and one granted patent in Europe covering our proprietary formulation of brexanolone, which will expire in 2033; and one U.S. issued patent covering the dosage regimen of brexanolone to treat PPD, which will expire in 2037;
- Pending U.S. and foreign patent applications covering certain aspects of brexanolone, including courses of treatment, dosage regimens, methods for manufacturing, and additional uses of the formulation of brexanolone to treat various brain health diseases and disorders, including PPD;
- One issued U.S. patent covering the composition of matter of zuranolone, three issued U.S. patents covering methods of using zuranolone, one granted European patent covering the composition of matter of zuranolone, and one granted European patent covering methods of using zuranolone, each of which expires in April 2034, subject to any potential extensions; one issued U.S. patent covering certain solid forms of zuranolone, and one issued U.S. patent covering methods of using certain solid forms of zuranolone, each of which expires in August 2037, subject to any potential extensions; and pending U.S. and foreign patent applications covering zuranolone, uses of zuranolone to treat various brain health diseases and disorders, and solid forms of zuranolone;
- Issued patents covering the composition of matter for SAGE-324 in Europe and Japan, expiring in May 2035, subject to any potential extensions, and U.S. and foreign patent applications covering SAGE-324, SAGE-319, and many other modulators of the $GABA_A$ receptor and uses of these compounds to treat various brain health diseases and disorders;
- Two issued U.S. patents covering composition of matter and method of use of SAGE-689 which expire in December 2033, subject to any potential extensions, and U.S. and foreign patent applications covering SAGE-689 and uses of SAGE-689 to treat various brain health diseases and disorders. These patents and patent applications are co-owned with Washington University, and Sage has an exclusive license to Washington University's rights in these patents and patent applications; and

- U.S. and foreign patents and patent applications covering modulators of the NMDA receptor, and uses of these compounds to treat various brain health diseases and disorders.

Patent Term

The base term of a U.S. patent is 20 years from the filing date of the earliest-filed non-provisional patent application from which the patent claims priority. The term of a U.S. patent can be lengthened by patent term adjustment, which compensates the owner of the patent for administrative delays at the U.S. PTO. In some cases, the term of a U.S. patent, including any accrued patent term adjustment, is shortened by terminal disclaimer that reduces its term to that of an earlier-expiring patent.

The term of a U.S. patent may also be eligible for patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act, to account for at least some of the time the drug is under development and regulatory review after the patent is granted. With regard to a drug for which FDA approval is the first permitted marketing of the active ingredient, the Hatch-Waxman Act allows for extension of the term of one U.S. patent that includes at least one claim covering the composition of matter of an FDA-approved drug, an FDA-approved method of treatment using the drug, and/or a method of manufacturing the FDA-approved drug. The extended patent term cannot exceed the shorter of five years beyond the non-extended expiration of the patent or 14 years from the date of the FDA approval of the drug. Some foreign jurisdictions, including Europe and Japan, also have patent term extension provisions, which allow for extension of the term of a patent that covers a drug approved by the applicable foreign regulatory agency. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extension on patents covering those products, their methods of use, and/or methods of manufacture.

Trade Secrets

In addition to patents, we may rely on trade secrets and know-how to develop and maintain our competitive position. Companies typically rely on trade secrets to protect aspects of their business that are not amenable to, or that they do not consider appropriate for, patent protection. We protect trade secrets, if any, and know-how by establishing confidentiality agreements and invention assignment agreements with our employees, and, where feasible, with consultants, scientific advisors, contractors and certain other entities with whom we do business. These agreements generally provide that all confidential information developed or made known during the course of an individual or entity's relationship with us must be kept confidential during and after the relationship. These agreements also generally provide that all relevant inventions resulting from work performed for us or relating to our business and conceived or completed during the period of employment or assignment, as applicable, shall be our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, designed to guard against misappropriation of our proprietary information by third parties.

Competition

The biopharmaceuticals industry is highly competitive. There are many public and private companies, universities, governmental agencies and other research organizations actively engaged in the research and development of products that may be similar to our product or product candidates or address similar markets. It is probable that the number of companies seeking to develop products and therapies similar to our products or targeting similar indications will increase.

Currently, the only pharmacological therapies specifically approved for the treatment of PPD are ZURZUVAE and ZULRESSO. We discontinued commercial availability of ZULRESSO in the U.S. as of December 31, 2024. ZURZUVAE currently competes with the current standard of care for PPD, which commonly consists of psychotherapy; however, patients with moderate or severe PPD are often prescribed antidepressant medications such as SSRIs and SNRIs. ZURZUVAE may also face competition from drugs currently in development, if successfully developed and approved in the future for the treatment of PPD, including potentially LPCN 1154, an oral formulation of the neuroactive steroid brexanolone under development by Lipocine, Inc. under the streamlined 505(b)(2) regulatory pathway, which allows for approval of an abbreviated NDA by the FDA, and BRII-296, an intramuscular formulation of brexanolone being developed by Brii Biosciences.

In the field of neuroactive steroids focused specifically on modulation of $GABA_A$ receptors, we also face competition from a number of companies, including Marinus Pharmaceuticals, Inc. (acquired by Immedica Pharma AB),

which received FDA approval of ganaxolone, a known $GABA_A$ positive allosteric modulator neuroactive steroid, to treat seizures associated with CDKL5 deficiency disorder, a rare, genetic epilepsy. Other $GABA_A$ competitors include darigabat, which is being developed by Cerevel Therapeutics, Inc. (acquired by AbbVie Inc.) for the treatment of epilepsy and panic disorder.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and human resources than we do, and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and the commercialization of those treatments. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. We expect competition in the indications we are pursuing will focus on efficacy, safety, convenience, availability, and price. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are perceived to be safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may 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.

Government Regulation

Government authorities in the U.S. at the federal, state and local level and in other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring/pharmacovigilance, safety and periodic reporting, marketing and export and import of drug products. Generally, before a new drug can be marketed in a given jurisdiction, considerable data demonstrating its quality, safety and efficacy must be obtained and/or generated, organized into a format specific to each regulatory authority, submitted for review and the drug must be approved by the relevant regulatory authority or authorities.

U.S. Drug Development

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

Our product candidates must be approved by the FDA through the NDA process before they may be legally marketed in the U.S. The process required by the FDA before a drug may be marketed in the U.S. requires substantial time, effort and financial resources and generally involves the following:

- Completion of extensive non-clinical studies and testing, including non-clinical laboratory tests, animal studies and formulation studies, in accordance with applicable regulations, including the FDA's current Good Laboratory Practice, or GLP, regulations;
- Submission to the FDA of an Investigational New Drug, or IND, application, which must become effective before human clinical trials may begin;
- Approval by an independent institutional review board, or IRB, or ethics committee representing each clinical trial site before each trial may be initiated;

- Performance of adequate and well-controlled human clinical trials in accordance with applicable IND and other clinical trial-related regulations, sometimes collectively referred to as good clinical practice, or GCP, to establish the safety and efficacy of the proposed drug for each proposed indication;
- Submission to the FDA of an NDA for marketing approval of the new drug;
- Determination by the FDA within 60 days of its receipt of an NDA to accept and file the NDA for review;
- Satisfactory completion of a potential FDA pre-approval inspection of the manufacturing facility or facilities where the drug is 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 non-clinical and/or clinical trial sites that generated the data in support of the NDA; and
- Payment of applicable user fees and FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee and scheduling by the DEA, if applicable, prior to any commercial marketing or sale of the drug in the U.S.

The data required to support an NDA are generated in two distinct development stages: non-clinical and clinical. For new chemical entities, the non-clinical development stage generally involves synthesizing the active component, developing the formulation and determining the manufacturing process, as well as carrying out non-human toxicology, pharmacology and drug metabolism studies in the laboratory, which are typically intended to support subsequent clinical testing. Non-clinical tests include laboratory evaluations of product chemistry, formulation, stability and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product. The conduct of the non-clinical tests must comply with federal laws and regulations, including, for animal studies, the Animal Welfare Act and GLPs. The sponsor must submit the results of the non-clinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. These studies are typically referred to as IND-enabling studies.

An IND is a request for authorization from the FDA to administer an investigational drug product to humans in the context of a clinical study. An IND must become effective before human clinical trials may begin. The central focus of an IND submission is on the general investigational plan and the protocols for human trials. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials, including whether subjects will be exposed to unreasonable health risks, and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that could cause the trial to be suspended or terminated.

The clinical stage of development generally involves the administration of the drug candidate to healthy volunteers and then to patients with the disease or condition being studied under the supervision of qualified investigators, which generally are physicians not employed by or under the trial sponsor's control. Clinical trials must be conducted in accordance with GCPs, which establish standards for conducting, recording data from, and reporting the results of, clinical trials, and are intended to assure that the data and reported results are credible and accurate, and that the rights, safety, and well-being of study participants are protected. GCPs include the requirement that all research subjects provide their informed consent for their participation in any given clinical trial. Clinical trials are conducted under protocols describing, among other details, 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 the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an IRB at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants, and considers such items as whether the risks to individuals participating in the clinical trials 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 trial subject or his or her legal representative and monitors the clinical trial until completed. Companies sponsoring the clinical trials, investigators, and

IRBs also must comply with, as applicable, regulations and guidelines for obtaining informed consent from the study patients, following the protocol and investigational plan, adequately monitoring the clinical trial, and timely reporting of adverse events. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

A sponsor who wishes to conduct a clinical trial outside the U.S. may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. Foreign studies conducted under an IND must meet the same requirements that apply to studies being conducted in the U.S. If a foreign clinical trial is not conducted under an IND, the FDA will accept the study as support for an NDA so long as the clinical trial is well-designed and well-conducted, conducted in compliance with GCPs, including review and approval by an independent ethics committee and compliance with informed consent principles, and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary.

Clinical Trials

Clinical trials are generally conducted in three phases that may overlap, known as Phase 1, Phase 2 and Phase 3 clinical trials.

- Phase 1 clinical trials generally involve a small number of healthy volunteers who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and the early safety profile of the drug.
- Phase 2 clinical trials typically involve studies in patients afflicted with the target disease to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, as well as identification of possible adverse effects and safety risks and preliminary evaluation of efficacy.
- Phase 3 clinical trials generally involve large numbers of patients afflicted with the target disease at multiple sites (typically from several hundred to several thousand subjects), 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 and labeling. Phase 3 clinical trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended for drugs intended for chronic dosing to mimic the actual use of a product during marketing.

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

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, any clinically important increased rates of serious suspected adverse events compared to those listed in the protocol or investigator brochure, or findings from other studies or from animal or in vitro testing that suggests a significant risk for human subjects. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. Success in one phase does not mean that the results will be observed in subsequent phases. Each phase may involve multiple studies. If concerns arise about the safety of the product candidate, the FDA or other regulatory authorities can stop clinical trials by placing them on a "clinical hold" pending receipt of additional data, which can result in a delay or termination of a clinical development program. The sponsoring company, the FDA, or the IRB may suspend or terminate a clinical trial at any time on various grounds, including a finding that the patients are being exposed to an unacceptable health risk.

Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for

whether or not a trial may move forward at designated check points based on access to certain data from the trial, and may suspend a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk.

In December 2022, with the passage of Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, actions plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans.

Sponsors of certain clinical trials are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health, or NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. The failure to submit clinical trial information to clinicaltrials.gov, as required, is a prohibited act under the FDCA with violations subject to potential enforcement, including warnings and civil monetary penalties of up to $10,000 for each day the violation continues.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug 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 drug candidate and, among other things, we must develop methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

NDA and FDA Review Process

The results of non-clinical studies and of the clinical trials, together with other detailed information, including extensive manufacturing information and information on the composition of the drug and proposed labeling, are submitted to the FDA as part of an NDA requesting approval to market the drug for one or more specified indications. The FDA reviews an NDA to determine, among other things, whether a drug is safe and effective for its intended use and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. FDA approval of an NDA must be obtained before a drug may be marketed in the U.S.

In addition, under the Pediatric Research Equity Act certain NDAs or supplements to an NDA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. Under the Best Pharmaceuticals for Children Act, the FDA may also issue a written request asking a sponsor to conduct pediatric studies related to a particular active moiety; if the sponsor agrees and meets certain requirements, the sponsor may be eligible to receive additional marketing exclusivity for its drug product containing such active moiety.

Under The Prescription Drug Fee User Act, or PDUFA, each NDA must be accompanied by a user fee, unless subject to a waiver. The FDA adjusts the PDUFA user fees on an annual basis. According to the FDA's fee schedule, effective through September 30, 2025, the user fee for an application requiring clinical data, such as an NDA, is approximately $4.3 million. PDUFA also imposes an annual prescription drug program fee for human drugs of approximately $0.4 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-designated indication.

The FDA reviews all NDAs submitted before it accepts them for filing, and may request additional information rather than accepting an NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA aims to complete its initial review of an NDA and respond to the

applicant within 10 months from the filing date for a standard NDA and within six months from the filing date for a priority NDA. The FDA does not always meet its PDUFA target action dates for standard and priority NDAs, and the review process is often significantly extended by FDA requests for additional information or clarification.

After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. Before approving an NDA, the FDA will generally conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether the facilities comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications.

Before approving an NDA, the FDA may also audit data from clinical trials to ensure compliance with GCP requirements and integrity of the data submitted in the NDA. With the passage of FDORA, Congress clarified the FDA's authority to conduct inspections by expressly permitting inspection of facilities involved in the preparation, conduct, or analysis of clinical and non-clinical studies submitted to the FDA as well as other persons holding study records or involved in the study process.

The FDA may also re-analyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. The review and evaluation process for an NDA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all. Additionally, the FDA may refer applications for novel drug products or drug products that 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. For example, the advisory committee may recommend or the FDA may determine that a Risk Evaluation and Mitigation Strategy, or REMS, program is necessary to ensure safe use of the product. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

After the FDA evaluates an NDA, it may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A complete response letter indicates that the review cycle of the application is complete and the application is not ready for approval. A complete response letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The complete response letter may require additional clinical data and/or one or more additional pivotal Phase 3 clinical trials, and/or other significant and time-consuming requirements related to clinical trials, non-clinical studies or manufacturing. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such additional data and information are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive, and the FDA may interpret data differently than we interpret the same data.

There is no assurance that the FDA will ultimately approve a drug product for marketing in the U.S., and we may encounter significant difficulties or costs during the review process. If a product receives marketing approval, the approval may be significantly limited to specific patient populations and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA typically requires that certain contraindications, warnings or precautions be included in the product labeling, and may condition the approval of the NDA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-marketing testing or clinical trials and surveillance to monitor the effects of approved products. For example, the FDA may require Phase 4 testing which may involve clinical trials designed to further assess a drug's safety and/or efficacy and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also place other conditions on approvals including the requirement for a REMS to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS if the FDA determines that a REMS is required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any limitations on approval, marketing or use for any of our products could restrict the commercial promotion, distribution, prescription or dispensing

of those products. Product approvals may be withdrawn for non-compliance with regulatory requirements if problems occur following launch, or if the FDA determines that the product is no longer safe or effective.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug product intended to treat a "rare disease or condition," which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S., or more than 200,000 individuals in the U.S., if there is no reasonable expectation that the cost of developing and making a drug product available in the U.S. for that disease or condition will be recovered from sales of the product. If orphan product designation is sought, it must be requested before submitting an NDA for the drug for the proposed rare disease or condition. If the FDA grants orphan drug designation, the common name of the therapeutic agent and its designated orphan use are disclosed publicly by the FDA. Orphan product designation does not, by itself, convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other sponsors' applications to market the same drug for the indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Orphan exclusivity operates independently from other regulatory exclusivities and other protection against generic competition, including patents that we hold for our products. A sponsor of a product application that has received an orphan drug designation may also be granted tax incentives for clinical research undertaken to support the application. In addition, the FDA may coordinate with the sponsor on research study design for an orphan drug and may exercise its discretion to grant marketing approval on the basis of more limited product safety and efficacy data than would ordinarily be required, based on the limited size of the applicable patient population.

Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity, or obtain approval for the same product but for a different indication than that for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same product as defined by the FDA, or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. The FDA can revoke a product's orphan drug exclusivity under certain circumstances, including when the holder of the approved orphan drug application is unable to assure the availability of sufficient quantities of the drug to meet patient needs. Orphan drug status in the EU has similar, but not identical, benefits. In the EU, orphan medicinal products enjoy ten years of orphan market exclusivity. In April 2023, the European Commission published a proposal to reform EU pharmaceutical law. This proposal intends to change the legislation regarding orphan medicinal products. In April 2024, the European Parliament adopted its position on the legislation, in which they set the baseline period for orphan market exclusivity at nine years (instead of the current ten years), which could be extended up to eleven years when the product meets specific requirements. The legislative process for this reform is expected to take several years, and adoption of the new legislation is not expected to take place before 2026. It is therefore currently uncertain if the proposal will be adopted in its current form, with the proposed modification of orphan market exclusivity, and it is uncertain if and when the revised legislation would enter into force.

In September 2021, the Court of Appeals for the 11th Circuit held that, for the purpose of determining the scope of market exclusivity, the term "same disease or condition" in the statute means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the specifically designated "indication or use." Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, the FDA announced that, in matters beyond the scope of that court order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved.

Expedited Development and Review Programs

The FDA has several programs that are intended to expedite or facilitate the process for reviewing new drugs that are intended to treat serious or life-threatening conditions and/or demonstrate the potential to address unmet medical needs for the condition and/or, if approved, would provide meaningful therapeutic benefit over existing treatments. Fast Track designation and Breakthrough Therapy designation are two of these programs and apply to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug or biologic may request the FDA to designate the drug as a Fast Track product at any time during the development of the product and may request the FDA to designate the drug as a Breakthrough Therapy based on preliminary clinical evidence that meets the criteria outlined in the FDA's programs. Under the Fast Track or Breakthrough Therapy expedited programs, the FDA may review sections of the marketing application on a rolling basis before the complete NDA is submitted if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

Any product submitted to the FDA for marketing, including under a Fast Track or Breakthrough Therapy program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval.

Any product is eligible for priority review if it treats a serious condition and, if approved, would offer a significant improvement in the safety and effectiveness of treatment, diagnosis or prevention compared to marketed products. Significant improvement may be shown by evidence of increased effectiveness for the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months from the date of the NDA filing.

A product may also be eligible for accelerated approval if the product is intended to treat a serious or life-threatening illness and, if approved, would provide meaningful therapeutic benefit over existing treatments. Accelerated approval for a product means that it may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. If the FDA concludes that a drug shown to be effective can be safely used only if distribution or use is restricted, it will require such post-marketing restrictions, as it deems necessary to assure safe use of the drug, such as:

- distribution restricted to certain facilities or physicians with special training or experience; or
- distribution conditioned on the performance of specified medical procedures.

The limitations imposed would be commensurate with the specific safety concerns presented by the drug. In addition, the FDA currently requires pre-approval of promotional materials as a condition for accelerated approval, which could adversely impact the timing of the commercial launch of the product.

With the passage of FDORA, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized the FDA to require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded, require the sponsor to submit progress reports on its post-approval studies to the FDA every six months (until the study is completed) and use expedited procedures to withdraw accelerated approval of an NDA, if the confirmatory trial fails to verify the product's clinical benefit. Further, FDORA requires the agency to publish on its website "the rationale for why a post-approval study is not appropriate or necessary" whenever it decides not to require such a study upon granting accelerated approval.

Fast Track designation, priority review, accelerated approval and Breakthrough Therapy designation do not change the standards for approval, but may expedite the development or approval process.

Pediatric Trials

The Food and Drug Administration Safety and Innovation Act, which was signed into law on July 9, 2012, amended the FDCA to require that a sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-Phase 2 meeting or as may be agreed between the sponsor and the FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies, along with supporting information. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from non-clinical studies, early phase clinical trials, and/or other clinical development programs. The FDA, if it learns of new information, may also request that the sponsor amend the initial PSP. The FDA may send a non-compliance letter to sponsors who have failed to submit their required pediatric assessments and have failed to seek or obtain a deferral, deferral extension or waiver, or have failed to request approval for a required pediatric formulation.

Post-Marketing Requirements

Following approval of a new product, a pharmaceutical company and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting to the applicable regulatory authorities of adverse experiences with the product, providing the regulatory authorities with updated safety and efficacy information, product sampling and distribution requirements, and complying with promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the Internet.

Although physicians may legally prescribe available drugs for off-label uses, manufacturers may not market or promote such off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in non-promotional, non-misleading communication regarding off-label information, such as distributing or discussing certain scientific or medical journal information. For example, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval.

Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require the applicant to develop additional data or conduct additional non-clinical studies and clinical trials. As with new NDAs, the review process is often significantly extended by FDA requests for additional information or clarification. Any distribution of prescription drug products and pharmaceutical samples must comply with the U.S. Prescription Drug Marketing Act, if applicable, and the Drug Supply Chain Security Act.

FDA regulations also require that approved products be manufactured in specific approved facilities and in accordance with cGMP. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. NDA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These manufacturers must comply with cGMP regulations that require, among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP.

Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. The PREVENT Pandemics Act, which

was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug or biologic undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside the United States prior to being imported or offered for import into the United States.

Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. The discovery of violative conditions, including failure to conform to cGMPs, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute products manufactured, processed or tested by them. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA, including, among other things, recall or withdrawal of the product from the market.

Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, administrative enforcement, warning or untitled letters from the FDA, mandated corrective advertising or communications with doctors, and civil penalties or criminal prosecution, among others. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

Other Regulatory Matters

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the U.S., the other divisions of the Department of Health and Human Services, or HHS; the U.S. Department of Justice; the DEA; the Consumer Product Safety Commission; the Federal Trade Commission; the Occupational Safety and Health Administration; the Environmental Protection Agency; and state and local governments.

In the U.S., a drug product approved by the FDA may also be subject to regulation under the Controlled Substances Act, or CSA, as a controlled substance. The CSA is administered by the DEA and establishes, among other things, certain registration, security, recordkeeping, reporting, import, export and other requirements for controlled substances. The CSA classifies controlled substances into five schedules: Schedule I, II, III, IV or V. FDA approved pharmaceutical products may be listed in Schedule II, III, IV or V, with Schedule II substances considered to present the highest potential for abuse or dependence and Schedule V substances the lowest relative risk of abuse among such substances. An approved drug product or drug candidate that has not yet been approved by the FDA may be subject to scheduling as a controlled substance under the CSA, depending on the drug's potential for abuse. For a drug approved by the FDA and determined to require control under the CSA, the CSA requires the DEA to issue an interim final order scheduling the drug within 90 days after the DEA receives notice from HHS that the FDA has approved the drug and the DEA receives from HHS the scientific and medical evaluation completed by the FDA. Following recommendation by the FDA, zuranolone and brexanolone each received a Schedule IV classification from the DEA.

In the U.S., arrangements and interactions with healthcare providers, third-party payors, patients and others expose us to broadly applicable anti-fraud and abuse, anti-kickback, false claims and other healthcare laws and regulations. These broadly applicable laws and regulations may constrain the business or financial arrangements or relationships through which we sell, market and distribute our approved products and any future products that may obtain marketing approval. In the U.S., federal and state healthcare laws and regulations that may affect our operations include:

- The federal Anti-Kickback Statute, which makes it illegal for any person, including a company marketing a prescription drug (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer, or pay any remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, that is intended to induce or reward the referral of an individual or purchase, lease or order, or the arranging for or recommending the purchase or order, of a particular item or service, for which payment may be made in whole or in part under a federal healthcare program, such as Medicare or Medicaid. This statute has been interpreted to apply to arrangements between pharmaceutical companies on one hand and prescribers, patients, purchasers

and formulary managers on the other. Liability under the Anti-Kickback Statute may be established without proving actual knowledge of the statute or specific intent to violate it. In addition, the government may assert that a claim, including items or services resulting from a violation of the federal Anti-Kickback Statute, constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Although there are a number of statutory exemptions and regulatory safe harbors to the federal Anti-Kickback Statute protecting certain common business arrangements and activities from prosecution or regulatory sanctions, the exemptions and safe harbors are drawn narrowly. Practices that involve remuneration to those who prescribe, purchase, or recommend pharmaceutical and biological products, including certain discounts, or engaging such individuals as consultants, advisors, or speakers, may be subject to scrutiny if they do not fit squarely within an exemption or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. Moreover, there are no safe harbors for many common practices, such as educational and research grants, charitable donations, product support and patient assistance. Violations of this law may be punishable by up to ten years in prison, criminal fines, damages, administrative civil money penalties, and the potential for exclusion from participation in federal healthcare programs.

- The federal civil False Claims Act, which prohibits anyone from, among other things, knowingly presenting, or causing to be presented claims for payment of government funds that are false or fraudulent, or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim or knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government. Actions under the False Claims Act may be brought by the federal government or as a qui tam action by a private individual in the name of the government. Many pharmaceutical manufacturers have been investigated and have reached substantial financial settlements with the federal government under the False Claims Act for a variety of alleged improper activities. The government may deem companies to have "caused" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, our activities relating to the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state, and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. Penalties for a False Claims Act violation may include three times the actual damages sustained by the government, plus significant civil penalties for each separate false or fraudulent claim, and the potential for exclusion from participation in federal healthcare programs.
- Numerous federal and state laws, including state data breach notification laws, state health information and/or genetic privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act and the California Consumer Privacy Act), govern the collection, use, and disclosure and protection of health-related and other personal information. Failure to comply with these laws and regulations could result in government enforcement actions and create liability, private litigation, or adverse publicity. In addition, we or our collaborators may obtain health information from third parties, such as hospitals, healthcare professionals, and research institutions, that are subject to privacy and security requirements under the federal Health Insurance Portability and Accountability Act of 1996, and its implementing regulations, or collectively, HIPAA. HIPAA imposes privacy and security obligations on covered entity healthcare professionals, health plans, and healthcare clearinghouses, as well as their "business associates" – independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service for or on behalf of a covered entity. Although we are not directly subject to the HIPAA information privacy and security provisions – other than with respect to providing certain employee benefits – we could potentially be subject to criminal penalties if we or our agents knowingly receive individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. In addition, HIPAA does not replace federal, state, or other laws that may grant individuals even greater privacy protections.
- The HIPAA fraud provisions, which impose criminal and civil liability for knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors, and prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false fictitious or fraudulent statement or entry, in connection with the delivery of or payment for healthcare benefits, items or services.
- The federal Physician Payment Sunshine Act, implemented as the Open Payments Program, which requires manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under

Medicare, Medicaid or the Children's Health Insurance Program, or CHIP, (with certain exceptions) to report annually to the Centers for Medicare & Medicaid Services, or CMS, the agency that administers the Medicare and Medicaid programs, information related to direct or indirect payments and other transfers of value to physicians, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives, and teaching hospitals, as well as ownership and investment interests held in the company by physicians and their immediate family members. The reportable information is publicly available on a searchable website.

- Analogous state and local laws and regulations, such as state anti-kickback and false claims laws, which may apply to items or services reimbursed under Medicaid and other state programs or, in several states, regardless of the payor. We are also subject to other state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare professionals; state laws that restrict the ability of manufacturers to offer co-pay support to patients for certain prescription drugs; state laws that require drug manufacturers to report information related to clinical trials, or information related to payments and other transfers of value to physicians and other healthcare professionals or marketing expenditures; state laws and local ordinances that require identification or licensing of sales representatives; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Substantial resources are necessary to ensure that our business arrangements and interactions with healthcare professionals, third-party payors, patients and others comply with applicable healthcare laws and regulations. Although compliance programs can mitigate the risk of investigation, prosecution, and/or liability for violations of these laws, the risks cannot be entirely eliminated. It is possible that federal or state governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law, and if we are found to be in violation of any of these laws or any other federal or state governmental regulations, we may be subject to significant civil, criminal and administrative penalties, imprisonment, damages, fines, exclusion from government-funded healthcare programs such as Medicare and Medicaid, or the curtailment or restructuring of our operations. Any action against us for violation of these laws or regulations, 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.

Numerous other laws may apply to our products. 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 Patient Protection and Affordable Care Act, as amended, and its implementing regulations (collectively referred to herein as the ACA (addressed further below in the section on "U.S. Healthcare Reform")). If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Many states impose various requirements on pharmaceutical manufacturers to report development costs and pricing information when prices are increased. Penalties for late or faulty reporting can be significant. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities are also potentially subject to federal and state consumer protection and unfair competition laws.

The handling of any controlled substances must comply with the CSA and Controlled Substances Import and Export Act.

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, issuance of warning or untitled letters, recall or 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. Federal regulators, state attorneys general, and plaintiffs' attorneys have been and will likely continue to be active in this space. 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.

Many of these laws differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Many of the state laws enable a state attorney general to bring actions and provide private rights of action to consumers as enforcement mechanisms. There is also heightened sensitivity around certain types of health information, such as sensitive condition information or the health information of minors, which may be subject to additional protections. Compliance with these laws is difficult, constantly evolving, and time consuming. Changes in statutes, regulations or the interpretation of existing laws or regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of our drug candidates, if any, some of our U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA, or the testing phase, plus the time between the submission date of an NDA and the approval of that application, or the approval phase. This patent term restoration period may be reduced by the FDA if it finds that applicant did not act with due diligence during the testing phase or the approval phase. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. PTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, if circumstances permit, we intend to apply for restoration of patent term for one of our then owned or licensed patents, if any, to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA. Even if, at the relevant time, we have a valid issued patent covering our product, we may not be granted an extension if we were, for example, to fail to apply within applicable deadlines, to fail to apply prior to expiration of relevant patents or otherwise to fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, and we do not have any other exclusivity, our competitors may obtain approval of competing products following our patent expiration and our ability to generate revenues could be materially adversely affected.

Some of our products may also be entitled to certain non-patent-related data exclusivity under the FDCA. The FDCA provides a five-year period of non-patent data exclusivity within the U.S. to the first applicant to obtain approval of an NDA for a new chemical entity, or NCE. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA may not be submitted by another company for another drug containing the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA Orange Book by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for a drug product that contains an active moiety that has been previously approved, if the application contains reports of new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant and that are deemed by the FDA to be essential to the approval of the application (for example, for new indications, dosages or strengths of an existing drug). Three-year exclusivity prevents the FDA from approving ANDAs and 505(b)(2) applications that rely on the information that served as the basis of granting three-year exclusivity. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations, and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a

full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the non-clinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and efficacy. We have obtained five-year NCE exclusivity for brexanolone and zuranolone and plan to seek NCE exclusivity for our current and future product candidates, if eligible. The NCE exclusivity for brexanolone expired in June 2024, five years following approval of ZULRESSO.

European Union Drug Development

In the European Economic Area, or EEA, our future products may also be subject to extensive regulatory requirements. As in the U.S., medicinal products can only be marketed if a marketing authorization from the competent regulatory authorities in the EU has been obtained.

Similar to the U.S., the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC, or the Clinical Trials Directive, has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Clinical Trials Directive in a manner that is often not uniform. This has led to variations in the rules governing the conduct of clinical trials in the individual EU Member States. Under the regime of the Clinical Trials Directive, before a clinical trial can be initiated, it must be approved in each EU Member State where there is a site at which the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more ethics committees. Under the regime of the Clinical Trials Directive, all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ethics committees of the Member State where they occurred.

In order to streamline the regulation of clinical trials across the EU, the EU Parliament has adopted Regulation (EU) No 536/2014, or the EU Clinical Trials Regulation. The EU Clinical Trials Regulation, which repeals and replaces the Clinical Trials Directive, introduces a complete overhaul of the existing regulation of clinical trials for medicinal products in the EU, including a new coordinated procedure for authorization of clinical trials that is reminiscent of the mutual recognition procedure for marketing authorization of medicinal products, and increased obligations on sponsors to publish clinical trial results. The main characteristics of the regulation include: a streamlined application procedure through a single entry point, referred to as the "EU portal"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts.

The EU Clinical Trials Regulation became effective on January 31, 2022, and is applicable directly in all countries of the EEA (which is comprised of 27 Member States of the EU plus Norway, Iceland and Liechtenstein). The EU Clinical Trials Regulation allows for starting and conducting a clinical trial in accordance with the Clinical Trials Directive during a transitional period which ended on January 31, 2023. Clinical trials authorized under the Clinical Trials Directive before January 31, 2023 can continue to be conducted under the Clinical Trials Directive until January 31, 2025. Any application to transition ongoing trials from the Clinical Trials Directive to the new EU Clinical Trials Regulation will need to be submitted and authorized before the end of the transitional period. The EU Clinical Trials Regulation is intended to simplify and streamline the approval of clinical trials in the EEA.

In the EU, pediatric data or an approved Pediatric Investigation Plan, or PIP, or waiver, is required to have been approved by the European Medicines Agency, or EMA, prior to submission of a marketing authorization application to the EMA or the competent authorities of the EU Member States. In some EU countries, we may also be required to have an approved PIP before we can begin enrolling pediatric patients in a clinical trial.

European Union Drug Review and Approval and Post-marketing Requirements

In the EEA, medicinal products can only be commercialized after a related marketing authorization has been granted. Marketing authorization for medicinal products can be obtained through several different procedures. These are through a centralized, mutual recognition procedure, decentralized procedure, or national procedure (if marketing authorization is sought for a single EU Member State). The centralized procedure allows a company to submit a single application to the EMA. If a related positive opinion is provided by the EMA, the European Commission will grant a centralized marketing authorization that is valid in all EEA countries.

The United Kingdom, or UK, withdrew from the EU on January 31, 2020, commonly referred to as Brexit. Marketing authorizations granted through the EU centralized procedure continue to be valid in Northern Ireland by virtue of the Northern Ireland Protocol, but such EU marketing authorizations are not valid in the rest of the UK (England, Wales and Scotland, or collectively Great Britain). EU marketing authorizations existing as at the end of the Brexit transition period on December 31, 2020, were automatically converted into Great Britain marketing authorizations as of January 1, 2021. Until the end of 2023, a marketing authorization for Great Britain can be applied for on an expedited timetable through the UK European Commission Decision Reliance Procedure, after having received a positive opinion from the EMA's Committee for Medicinal Products for Human Use. Beginning on January 1, 2024, the new International Recognition Procedure, or IRP, has replaced the UK European Commission Decision Reliance Procedure. The decentralised reliance procedure has been incorporated under the umbrella of the IRP. Under the IRP, a marketing authorization for Great Britain can be obtained on the basis of a marketing authorization granted in the U.S. or the EU.

The EU centralized procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for products containing a new active substance that is not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or for which grant of centralized marketing authorization is in the interest of patients in the EU.

The decentralized authorization procedure permits companies to file identical applications for authorization to several EU Member States simultaneously for a medicinal product that has not yet been authorized in any EU Member State. The competent authorities of a single EU Member State, the reference member state, is appointed to review the application and provide an assessment report. The competent authorities of the other EU Member States, the concerned member states, are subsequently required to grant marketing authorization for their territories on the basis of this assessment. The only exception to this is where an EU Member State considers that there are concerns of potential serious risk to public health related to authorization of the product. In these circumstances, the matter is submitted to the Heads of Medicines Agencies for review. The mutual recognition procedure allows companies that have a medicinal product already authorized in one EU Member State to apply for this authorization to be recognized by the competent authorities in other EU Member States.

The maximum timeframe for the evaluation of a marketing authorization application in the EU is 210 days, not including clock stops during which applicants respond to questions from the competent authority. The initial marketing authorization granted in the EU is valid for five years. The authorization may be renewed and valid for an unlimited period unless the national competent authority or the European Commission decides on justified grounds to proceed with one additional five-year renewal period. The renewal of a marketing authorization is subject to a re-evaluation of the risk-benefit balance of the product by the national competent authorities or the EMA.

The holder of an EU marketing authorization for a medicinal product must also comply with the EU's pharmacovigilance legislation. This includes requirements to conduct pharmacovigilance, or the assessment and monitoring of the safety of medicinal products.

Various requirements apply to the manufacture and distribution of medicinal products in the EU market. Manufacture of medicinal products in the EU requires a manufacturing authorization, and import of medicinal products into the EU requires a manufacturing authorization allowing for import. The manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, or APIs, including the manufacture of APIs outside of the EU with the intention to import the APIs into the EU. Similarly, the distribution of medicinal products within the EU is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of the EU Member States. Marketing authorization holders and/or manufacturing authorization holders and/or distribution authorization holders may be subject to civil, criminal or administrative sanctions, including suspension of manufacturing authorization, in case of non-compliance with the EU or EU Member States' requirements applicable to the manufacturing of medicinal products.

In the EU, the advertising and promotion of medicinal products are subject to EU Member States' laws governing promotion of medicinal products, interactions with physicians and other healthcare professionals, misleading and comparative advertising and unfair commercial practices. For example, applicable laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities in connection with a marketing authorization approval. The SmPC is the document that provides information to physicians concerning the safe and effective use of the product. Promotional activity that does not comply with the SmPC is considered off-label and is prohibited in the EU. Breaches of the rules governing the promotion of medicinal products in the EU could be penalized by civil, criminal or administrative sanctions, which may include fines and imprisonment. These laws may further limit or restrict the advertising and promotion of medicinal products to the general public and may also impose limitations on promotional activities with healthcare professionals.

European Union Regulatory Data Exclusivity

In the EU, innovative medicinal products that are subject to marketing authorization on the basis of a full dossier, and do not fall within the scope of the concept of global marketing authorization, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. The concept of global marketing authorization prevents the same marketing authorization holder or members of the same group, or companies that have concluded tacit or explicit agreements concerning the marketing of the same medicinal product, from obtaining separate data and market exclusivity periods for medicinal products that contain the same active substance. This data exclusivity, if granted, prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic application or biosimilar application for eight years from the date of authorization of the innovative product, after which a generic or biosimilar marketing authorization application can be submitted, and the innovator's data may be referenced. However, the generic product or biosimilar products cannot be marketed in the EU for a further two years thereafter. The overall ten-year period may be extended for a further year to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. In April 2023, the European Commission published a proposal to reform the current European pharmaceutical legislative framework with a new Directive and Regulation to reduce the regulatory data protection period. The European Commission proposed to reduce the baseline regulatory data protection from eight years to six years. In the adopted position of the European Parliament, the baseline of eight years of data protection will be reduced to seven and a half years. The legislative process for this reform is expected to take several years, and adoption of the new legislation is not expected to take place before 2026. It is currently uncertain if the proposal will be adopted in its current form, with the modification of regulatory data protection, and it is uncertain if and when the revised legislation would enter into force.

European Union Orphan Designation and Exclusivity

In the EU, orphan drug designations are granted by the European Commission based on a scientific opinion by the EMA's Committee for Orphan Medicinal Products in relation to medicinal products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the EU and in relation to which there exists no satisfactory method of diagnosis, prevention, or treatment (or the product would be a significant benefit to those affected). Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the medicinal product.

Orphan medicinal products are entitled to ten years of exclusivity in all EU Member States. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities of the product. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if the similar product is deemed safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if it is established that the criteria for orphan designation are no longer met, such as if

it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

In addition, grant of orphan designation by the European Commission also entitles the holder of this designation to financial incentives such as reduction of fees or fee waivers. Orphan drug designation must be requested before submitting an application for marketing authorization. Orphan drug designation does not, in itself, convey any advantage in, or shorten the duration of, the regulatory review and authorization process. In April 2023, the European Commission published a proposal to reform EU pharmaceutical law regarding orphan medicinal products that, if adopted in its current form, would shorten the baseline for the orphan market exclusivity from ten years to nine years. The orphan market exclusivity period could, however, be extended up to eleven years if specific requirements are met.

European Union Data Protection

EU Member States and other jurisdictions where we may in the future operate, including the UK, have adopted data protection laws and regulations, which impose significant compliance obligations. For example, the General Data Protection Regulation, or GDPR, imposes strict obligations and restrictions on the processing of personal data, including ensuring the lawfulness of processing personal data (including having a lawful basis for processing personal data, which may require in certain instances obtaining valid consent of the individuals to whom the personal data relates , providing detailed information about the processing activities to the individuals, having appropriate contractual arrangements for sharing personal data with third parties where required (such as with vendors or clinical trial sites), ensuring that appropriate transfer mechanisms are used for transferring personal data out of the European Economic Area and/or the UK to other countries, including the U.S., having appropriate technical and organizational security and confidentiality measures in place to protect personal data, reporting in certain instances personal data breaches to data protection authorities and/or affected individuals, appointing data protection officers, conducting data protection impact assessments, responding to and handling of privacy rights requests, and having appropriate policies and procedures in place to be able to demonstrate compliance with the GDPR. Violation of these data protection obligations may result in the imposition of substantial potential fines.

With regard to transfer of personal data, the GDPR restricts the ability of companies to transfer personal data from the EEA, including the EU, UK, and Switzerland, to the U.S. and other countries, which may adversely affect our ability to transfer personal data or otherwise may cause us to incur significant costs for implementing lawful transfer mechanisms, conducting data transfer impact assessments, and implementing additional measures where necessary to ensure that any personal data transferred are adequately protected in a manner essentially equivalent to the EEA. The GDPR provides different transfer mechanisms we can use to lawfully transfer personal data from the EU to countries outside the EU. An example is relying on adequacy decisions of the European Commission, such as the EU-U.S. Data Privacy Framework. In October 2022, President Biden issued an executive order to implement EU-U.S. data privacy safeguards. In July 2023, the European Commission adopted its adequacy decision for the EU-U.S. Data Privacy Framework. The adequacy decision concludes that the U.S. ensures an adequate level of protection, compared to that of the EU for personal data transferred from the EU to U.S. companies participating in the EU-U.S. Data Privacy Framework. The adequacy decision on the EU-U.S. Data Privacy Framework covers data transfers from any public or private entity in the EEA to U.S. companies participating in the EU-U.S. Data Privacy Framework. With the adoption of the adequacy decision, EU entities are able to transfer personal data to U.S. companies participating in the EU-U.S. Data Privacy Framework without having to put in place additional data protection safeguards. Another example of a lawful transfer mechanism is using the EU Standard Contractual Clauses as approved by the European Commission in June 2021, which are the most common transfer mechanism used to transfer personal data out of the EU to controllers or processors outside the EEA that are not directly subject to the GDPR. In order to use the EU Standard Contractual Clauses mechanism, the exporter and the importer must ensure that the importer can guarantee an adequate level of personal data protection in the importing country that is essentially equivalent to that of the EEA. Compliance with EU data transfer obligations involves conducting transfer impact assessments, which includes documenting detailed analyses of data access and protection laws in the countries in which data importers are located, which can be costly and time-consuming. Data importers must also expend resources in analyzing their ability to comply with transfer obligations, including implementing new safeguards and controls to further protect personal data.

In addition, the privacy and data security landscape in the EU continues to remain in flux. Brexit has created uncertainty with regard to future data protection regulation in the UK. The European Commission has adopted an

adequacy decision concerning the level of data protection in the UK. Personal data may now flow freely from the EEA to the UK; however, the European Commission may suspend the adequacy decision if it decides that the UK no longer provides for an adequate level of data protection.

Data protection authorities from the different EU Member States and the UK may interpret the GDPR and applicable related national laws differently, may impose additional requirements under local data protection laws, and amend or update local data protection laws. In addition, regulatory guidance on implementation and compliance practices may be updated or otherwise revised, which adds to the complexity of processing personal data in the EEA. Enforcement by European and UK regulators is generally active, and failure to comply with the GDPR or applicable Member State and/or UK local law may result in warnings, compliance orders and fines (including possible fines of up to 4% of global annual turnover for the preceding financial year or €20 million (whichever is higher) for the most serious infringements). The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with data protection authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR.

Compliance with these privacy data protection laws and regulations is onerous, constantly evolving, time consuming, and requires a flexible privacy framework and substantial resources. Compliance efforts will likely be an increasing and substantial cost in the future. We may be required to expend significant capital and other resources to ensure ongoing compliance with applicable privacy and data protection laws, to protect against security incidents, or to alleviate issues caused by such incidents. In addition, if our efforts to comply with applicable privacy and data protection laws and regulations are not successful, it could adversely affect our business. Failure to comply with such laws and regulations could result in government enforcement actions and create liabilities, including but not limited to imposition of significant penalties, private litigation (including class actions) and/or adverse publicity that could negatively affect our business.

Regulation in the Rest of the World

For other countries outside of the U.S., UK and EU, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

Approval by a regulatory authority in one jurisdiction does not guarantee approval by comparable regulatory authorities in other jurisdictions. If we fail to comply with applicable foreign regulatory requirements applicable to a given country, we may not be able to obtain regulatory approval for our product candidates in such country if we choose to seek such approval, or we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Coverage and Reimbursement

U.S. Healthcare Reform

The containment of healthcare costs continues to remain a priority of federal and state governments, and the prices of drugs have been a focus in recent efforts. Changes in government legislation or regulation and changes in governmental health benefit programs' or commercial payors' policies governing reimbursement for our products, if successfully developed and approved, may reduce reimbursement of our products' costs to physicians, pharmacies, patients, and distributors. The U.S. federal government and state legislatures, as well as foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and utilization management requirements, such as requirements for substitution of generic products or therapeutic equivalents. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with

existing controls and measures, could limit our net revenue and results for products, if any, we commercialize in the future.

The pricing and reimbursement environment for our products may change in the future and become more challenging due to state and federal healthcare reform measures. The American Recovery and Reinvestment Act of 2009, or ARRA, for example, allocated new federal funding to compare the effectiveness of different treatments for the same condition. The plan for the research was published in 2012 by HHS, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures are made to Congress. Although ARRA does not mandate the use of the results of comparative effectiveness studies for reimbursement purposes, it is not clear what effect, if any, the research will have on the sales of any products for which we receive marketing approval or on the reimbursement policies of public and private payors. It is possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of any product for which we receive marketing approval. For example, if third-party payors find our products not to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The ACA was a sweeping measure intended to expand healthcare coverage within the U.S., primarily through the imposition of health insurance mandates on employers and individuals, the provision of subsidies to eligible individuals enrolled in plans offered on the health insurance exchanges, and the expansion of the Medicaid program. This law has substantially changed the way healthcare is financed by both governmental and private insurers and has significantly impacted the pharmaceutical industry. Changes that may affect our business include those governing enrollment in federal healthcare programs, reimbursement changes, rules regarding prescription drug benefits under the health insurance exchanges, changes to the Medicaid Drug Rebate Program, expansion of the Public Health Service Act's 340B drug pricing program, or 340B program, and fraud and abuse enforcement. Further changes made by the ACA include those to the Medicare Part D program establishing benefits for patients within a coverage gap in the Medicare Part D prescription drug program (commonly known as the "donut hole"), which was subsequently modified by the Inflation Reduction Act (as outlined below).These changes have impacted previously existing government healthcare programs and have resulted in the development of new programs, including Medicare payment for performance initiatives and improvements to the Medicare physician quality reporting system and feedback program.

One of the goals of ACA was to expand coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, among other things, the ACA increased minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program and extended manufacturers' Medicaid rebate liability to drugs dispensed to individuals who are enrolled in Medicaid managed care organizations. The ACA also requires manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid or CHIP (with certain exceptions) to report annually to CMS information related to direct or indirect payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investment interests held in the company by physicians and their immediate family members. Since 2022, applicable manufacturers also are required to report information regarding payments and transfers of value provided to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives. Failure to submit required information may result in civil monetary penalties of $1,000 to $10,000 for each payment or ownership interest that is not timely, accurately, or completely reported (annual maximum of $150,000), and $10,000 to $100,000 for each knowing failure to report (annual maximum of $1 million).

Some states have elected not to expand their Medicaid programs by raising the income limit to 133% of the federal poverty level for the ACA expansion population, as is permitted under the ACA. For each state that does not choose to expand its Medicaid program, there may be fewer insured patients overall, which could impact sales of our products that are approved and that we successfully commercialize, and our business and financial condition. Where Medicaid patients receive insurance coverage under any of the new options made available through the ACA, the possibility exists that manufacturers may be required to pay Medicaid rebates on drugs used under these circumstances, a decision that could impact manufacturer revenues.

Certain provisions of the ACA have been subject to judicial challenges as well as efforts to modify them or to alter their interpretation or implementation. For example, the U.S. Tax Cuts and Jobs Act of 2017 included a provision

repealing the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." We expect that the ACA, its implementation, efforts to challenge or modify the ACA or its implementing regulations, or portions thereof, and other healthcare reform measures that may be adopted in the future, could have a material adverse effect on our industry generally and on our ability to commercialize our product candidates, if approved.

Other legislative changes relating to reimbursement have been adopted in the U.S. since the ACA was enacted. For example, the Budget Control Act of 2011, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals for spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction, which triggered the legislation's automatic reductions. In concert with subsequent legislation, this has resulted in aggregate reductions to Medicare payments to providers of, on average, 2% per fiscal year through 2030 (with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, due to the COVID-19 pandemic). In December 2021, President Biden signed a law that provided for 1% Medicare sequestration in the second quarter of 2022 and the full 2% sequestration thereafter until 2030.This sequestration is currently set at 2% and will increase to 2.25% for the first half of fiscal year 2030, to 3% for the second half of fiscal year 2030, and to 4% for the remainder of the sequestration period that lasts through the first six months of fiscal year 2031. As long as these cuts remain in effect, they could adversely impact payment for any products we may commercialize in the future. We expect that additional federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, and in turn could significantly reduce the projected value of certain development projects and reduce our profitability.

Further, the Inflation Reduction Act of 2022, or IRA, among other things, established a Medicare Part B inflation rebate scheme, under which, generally manufacturers will owe rebates if the average sales price of a Part B drug increases faster than the pace of inflation. Failure to timely pay a Part B inflation rebate is subject to a civil monetary penalty. The IRA also establishes a Medicare Part D inflation rebate scheme, under which generally manufacturers will owe rebates if the average manufacturer price of a Part D drug increases faster than the pace of inflation. The IRA also creates a drug price negotiation program under which the prices for Medicare units of certain high Medicare spend drugs and biologics without generic or biosimilar competition will be capped by reference to, among other things, a specified non-federal average manufacturer price, starting in 2026. Failure to comply with requirements under the drug price negotiation program is subject to an excise tax and/or a civil monetary penalty. The IRA further makes several changes to the Medicare Part D benefit, including a limit on annual out-of-pocket costs, and replacement of the coverage gap discount program with a new manufacturer discount program beginning in 2025, under which manufacturers are, in general, to provide a 10% discount on a covered Part D drug where a beneficiary is in the initial phase of Part D coverage and a 20% discount where a beneficiary is in the catastrophic phase of Part D coverage. Congress continues to examine various policy proposals that may result in pressure on the prices of prescription drugs in the government health benefit programs. The IRA or other legislative change could impact the market conditions for our product candidates.

Additional legislative changes, regulatory changes, or guidance could be adopted, which may impact potential marketing approvals and reimbursement for our product candidates, if approved. For example, there has been increasing legislative, regulatory, and enforcement interest in the U.S. with respect to drug pricing practices. There have been several Congressional inquiries and proposed and enacted federal and state legislation and regulatory initiatives designed to, among other things, bring more transparency to product pricing, evaluate the relationship between pricing and manufacturer patient programs, and reform government healthcare program reimbursement methodologies for drug products. Individual states in the U.S. have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including by requiring pharmaceutical manufacturers to report to state agencies when they introduce new drugs to market with prices over a certain threshold, or when they increase the price of a drug over a certain threshold. Additionally, some individual states have begun establishing Prescription Drug Affordability Boards, or PDABs, to conduct affordability reviews for certain drugs, including high cost drugs and drugs with qualifying price increases. In some of these states, the PDAB has authority to set upper payment limits on what certain purchasers and payers may pay or reimburse for drugs that are found to pose an affordability challenge in the state. If healthcare policies or reforms intended to curb healthcare costs are adopted, the prices that we charge for any approved products may be limited, our commercial opportunity may be limited and/or our revenues from sales of our product and any future products, if approved, may be negatively impacted.

It is possible that the above-mentioned measures, as currently enacted or may be amended in the future, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and

other healthcare funding, more rigorous coverage criteria, and new payment methodologies and additional downward pressure on coverage and payment and the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of additional cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products. We cannot be sure whether additional legislative changes will be enacted in the U.S. or outside of the U.S., or whether regulatory changes, guidance or interpretations will be changed, or what the impact of such changes on our product candidates, if any, may be.

Pharmaceutical Pricing and Reimbursement

Sales of ZURZUVAE and any product candidates we successfully develop in the future depend on the availability and extent of coverage and reimbursement from third-party payors, which are increasingly reducing reimbursements for medical products and services. Decreases in third-party reimbursement for our products or a decision by a third-party payor not to cover a product or to manage utilization by, for example, requiring prior authorization or step edits, could reduce physician usage of our products and have a material adverse effect on our sales, results of operations and financial condition. In the U.S., healthcare professionals are reimbursed for covered services and products through Medicare, Medicaid, and other government healthcare programs, as well as through commercial insurance and managed healthcare organizations. Additional legislative changes, regulatory changes, or guidance could be adopted that may impact coverage and reimbursement for our products. For example, effective in April 2022, Congress expanded the availability of postpartum coverage under Medicaid and CHIP.

No uniform policy of coverage and reimbursement for drug products exists. Further, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be set because the process for determining whether a third-party payor will provide coverage for a drug product may be separate from the process for determining the reimbursement amount for the drug product. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will each be made on a payor-by-payor basis. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

We participate in the Medicaid Drug Rebate Program and other governmental programs. The Medicaid Drug Rebate Program and other governmental programs impose obligations to report certain pricing data to the federal government as well as other compliance obligations. Other programs impose limits on the price we are permitted to charge certain entities for our products. Statutory and regulatory changes or other agency action regarding these programs and their requirements could negatively affect the coverage and reimbursement by these programs of our products for which we receive regulatory approval and could negatively impact our results of operations or expand our rebate liability.

Under the Medicaid Drug Rebate Program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being available for our drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data we report on a monthly and quarterly basis to CMS, the federal agency that administers the Medicare and Medicaid programs. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug, which, in general, represents the lowest price available from the manufacturer to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity, or governmental entity in the U.S. in any pricing structure, calculated to include all sales and associated rebates, discounts, and other price concessions. Where our average manufacturer price increases faster than the pace of inflation, we may be subject to an additional rebate in the amount that our average manufacturer price has exceeded the pace of inflation. As of January 1, 2024, there is no longer a cap on the rebate amount, and our rebate liability could increase accordingly.

The ACA made significant changes to the Medicaid Drug Rebate Program, and CMS issued a final regulation to implement the changes to the Medicaid Drug Rebate Program under the ACA. CMS also issued a final regulation that modified prior Medicaid Drug Rebate Program regulations to permit reporting multiple best price figures with regard to value-based purchasing arrangements; and provide definitions for "line extension," "new formulation," and related terms, with the practical effect of expanding the scope of drugs considered to be line extensions that are subject to an alternative rebate formula. Our failure to comply with these price reporting and rebate payment options could negatively impact our financial results. In September 2024, CMS further modified the regulations governing the Medicaid Drug Rebate Program, which could increase our costs and the complexity of compliance, impact rebate liabilities, and be time-consuming to implement.

Federal law requires that any company that participates in the Medicaid Drug Rebate Program also participate in the 340B drug pricing program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B program, which is administered by the Health Resources and Services Administration, or HRSA, requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The ACA expanded the list of covered entities to include certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, but exempts "orphan drugs" from the ceiling price requirements for these covered entities. The 340B ceiling price is calculated using a statutory formula, which is based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate Program, and, in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. Changes to the definition of average manufacturer price and the Medicaid Drug Rebate amount also could affect our 340B ceiling price calculations and negatively impact our results of operations.

HRSA issued a final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that are found to have knowingly and intentionally overcharged covered entities. It is unclear how HRSA will apply its enforcement authority under the regulation. We also are required to report our 340B ceiling prices to HRSA on a quarterly basis, and HRSA then publishes them to covered entities. Moreover, via final regulation, HRSA established an administrative dispute resolution, or ADR, process for claims by covered entities that a manufacturer has engaged in overcharging, and by manufacturers that a covered entity violated the prohibitions against diversion or duplicate discounts. Such claims are to be resolved through an ADR panel of government officials rendering a decision that could be appealed in federal court. HRSA issued a final rule that, effective June 2024, modified aspects of the ADR process, which could impact the procedures that are used to determine whether we owe additional 340B discounts. An ADR proceeding could subject a manufacturer to onerous procedural requirements and result in additional liability.

Federal law also requires all manufacturers to report the average sales price for drugs payable under the Medicare Part B program regardless of whether they are enrolled in the Medicaid Drug Rebate Program. Manufacturers calculate the average sales price based on a statutorily defined formula as well as regulations and interpretations of the statute by CMS. CMS uses these submissions to determine payment rates for drugs under Medicare Part B. Starting in 2023, manufacturers must pay refunds to Medicare for single source drugs or biologics, or biosimilar biological products, reimbursed under Medicare Part B and packaged in single-dose containers or single-use packages, for units of discarded drug reimbursed by Medicare Part B in excess of 10 percent of total allowed charges under Medicare Part B for that drug. Manufacturers that fail to pay refunds could be subject to civil monetary penalties of 125% of the refund amount.

Statutory or regulatory changes or CMS guidance could affect the average sales price calculations for our approved products and the resulting Medicare payment rate, and could negatively impact our results of operations. Also, the Medicare Part B drug payment methodology is subject to change based on legislation enacted by Congress.

Congress also could enact additional changes that affect our overall rebate liability and the information we report to the government as part of price reporting calculations, which could impact the market conditions for our products. We further expect continued scrutiny on government price reporting and pricing more generally from Congress, agencies, and

other bodies, and are seeing an increase in state interest in price reporting, transparency, and other policies to address drug pricing concerns.

Pricing and rebate calculations vary among products and programs. The calculations are complex and are often subject to interpretation by us, governmental or regulatory agencies and the courts. The Medicaid rebate amount will be computed each quarter based on our submission to CMS of our current average manufacturer prices and best prices for the quarter. If we become aware that our Medicaid reporting for a prior period was incorrect, or has changed as a result of recalculation of the pricing data, we are obligated to resubmit the corrected data for a period not to exceed three years from the period in which the data originally were due. Such restatements and recalculations would increase our costs for complying with the laws and regulations governing the Medicaid Drug Rebate Program. Any corrections to our rebate calculations could result in an overage or underage in our rebate liability for past quarters, depending on the nature of the correction. Price recalculations also may affect the ceiling price at which we are required to offer our products to covered entities under the 340B program, and may require us to issue refunds to 340B covered entities, which can be costly and burdensome.

Further, the IRA establishes Medicare Part B and Part D inflation rebate schemes (the first Part B inflation rebate period was in the first quarter of 2023; the first Part D inflation rebate period was in the fourth quarter of 2022 through the third quarter of 2023) and a drug price negotiation program, with the first negotiated prices to take effect in 2026. It also makes several changes to the Medicare Part D benefit, including the creation of a new manufacturer discount program in place of the current coverage gap discount program (beginning in 2025). Manufacturers may be subject to civil monetary penalties for certain violations of the negotiation and inflation rebate provisions and an excise tax during a noncompliance period under the negotiation program. Drug manufacturers may also be subject to civil monetary penalties with respect to their compliance with the new Part D manufacturer drug discount program.

We could be held liable for errors associated with our submission of pricing data. Civil monetary penalties can be applied if we are found to have made a misrepresentation in the reporting of our average sales price for each misrepresentation and for each day in which the misrepresentation was applied, or if we are found to have charged 340B covered entities more than the statutorily mandated ceiling price. In addition to retroactive rebates and the potential for 340B program refunds, if we are found to have knowingly submitted false average manufacturer price or best price information to the government, or to have misrepresented that information, we may be liable for significant civil monetary penalties per item of false information. Our failure to submit monthly/quarterly average manufacturer price and best price data on a timely basis could result in a significant civil monetary penalty per day for each day the information is late beyond the due date. Such failures also could be grounds for CMS to terminate our Medicaid drug rebate agreement, pursuant to which we participate in the Medicaid program, or, if we fail to comply with 340B program requirements, HRSA could decide to terminate our 340B program participation agreement. In the event that CMS terminates our rebate agreement or HRSA terminates our 340B program participation agreement, no federal payments would be available under Medicaid or Medicare Part B for our covered outpatient drugs.

CMS and the Office of Inspector General have pursued manufacturers that were alleged to have failed to report these data to the government in a timely manner. Governmental agencies may also make changes in program interpretations, requirements or conditions of participation, some of which may have implications for amounts previously estimated or paid. We cannot guarantee that our submissions will not be found by CMS to be incomplete or incorrect.

In order to be eligible to have our products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by the Department of Veterans Affairs, or VA, Department of Defense, or DoD, Public Health Service, and Coast Guard (collectively, the Big Four agencies) and certain federal grantees, we are required to participate in the VA Federal Supply Schedule, or FSS, pricing program, established under Section 603 of the Veterans Health Care Act of 1992. Under this program, we are obligated to make our "covered" drugs (*i.e.*, innovator drugs and biologics) available for procurement on an FSS contract and charge a price to the Big Four agencies that is no higher than the Federal Ceiling Price, or FCP, which is a price calculated pursuant to a statutory formula. The FCP is derived from a calculated price point called the "non-federal average manufacturer price", or Non-FAMP, which we are required to calculate and report to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to significant civil monetary penalties for each item of false information. The FSS contract also contains extensive disclosure and certification requirements. In

addition, Section 703 of the National Defense Authorization Act for FY 2008, requires us to pay quarterly rebates to DoD on utilization of covered drugs that are dispensed through DoD's Tricare network pharmacies to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP for the calendar year that the product was dispensed. If we overcharge the government in connection with the FSS contract or Tricare Retail Pharmacy Rebate Program, whether due to a misstated FCP or otherwise, we will be required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and any response to government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In addition, in many foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU Member States have the power to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. An EU Member State may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved. Historically, products launched in the EU do not follow price structures of the U.S., and generally prices tend to be significantly lower.

In various EU Member States, we expect to be subject to continuous cost-cutting measures, such as lower maximum prices, lower or lack of reimbursement coverage and incentives to use cheaper, usually generic, products as an alternative. Health Technology Assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including countries representing major markets. The HTA process, which is governed by the national laws of these countries, is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. On January 31, 2018, the European Commission presented a proposal for a regulation on health technologies assessment. The proposal was adopted in December 2021 and will apply as of January 2025. This EU HTA regulation is intended to boost cooperation among EU Member States in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas.

Employees and Human Capital

Our mission to pioneer solutions to deliver life-changing brain health medicines so every person can thrive depends on our ability to attract, develop, engage, and retain the industry's highest quality talent across all dimensions of diversity. This understanding guides our approach to recruiting, managing and supporting our human capital resources. At Sage, we strive for a best-in-class working culture and a spirit of collaboration and inclusivity with a goal of supporting our team members and their families while we work to achieve our mission and evolve our business and culture as we grow. At Sage, we believe every voice matters and every contribution counts.

General Information. As of February 4, 2025, we employed 353 full-time employees, including 122 in research and development and 231 in selling, general and administrative and no part-time employees. Approximately 17 of our employees hold M.D. or Ph.D. degrees. We have never had a work stoppage, and none of our employees are represented by a labor organization or under any collective-bargaining arrangements. We consider our employee relations to be good.

Diversity, equity, and inclusion

We are committed to taking action to integrate diversity, equity, inclusion, and equal opportunity to foster a diverse workforce, sense of belonging and innovative thinking. We have four core areas of focus:

- **Experience:** Foster a diverse and inclusive culture that enables a sense of belonging and innovative thinking.
- **Talent:** Recruit and develop diverse, high-performing individuals and teams.
- **External:** Identify and partner with diverse community organizations and vendors to increase diversity in our ecosystem.
- **Patients:** Continue to grow and nurture long-term and transparent relationships to ensure diverse voices are represented.

Our commitment to diversity, equity, and inclusion is a core focus of our leadership team: three of our seven leadership team members are women and/or from diverse racial and ethnic groups. As of year-end 2024, approximately 62% of our U.S. workforce identified as female and 31% identified as racially or ethnically diverse.

Compensation, Benefits and Ongoing Professional Development

Our vision is to fearlessly lead the way to create a world with better brain health, which requires everyone to consistently give their best. We aim to spur every single employee on to realize their true potential. To do this, we appreciate what it takes to be at one's best, which is why we prioritize the health and well-being of all team members. To promote our employees' continued well-being and development, we offer a variety of inclusive benefits and opportunities. We offer comprehensive work-life and income protection benefits, including health, dental, vision, life insurance, disability and retirement savings programs, paid time off and family leave, family planning, mental health days, caregiving support, a "be well" subsidy, technology benefits, tuition reimbursement, and an employee assistance program. We continue to prioritize the needs of our employees through a robust listening strategy and are focused on assessing and responding to evolving needs.

Our employees are encouraged to take advantage of an array of professional and career development resources delivered through a variety of venues, including continued learning courses, online learning, company-wide coaching, podcasts, and leadership circles. We believe our investment in learning and growth gives us a competitive edge and our strategies are focused on optimal performance, ongoing professional growth, and future of work capabilities, with the following areas of focus:

- **Foster critical leadership capabilities**: Build a culture where leaders drive inclusion, performance, curiosity, and personal and professional growth.
- **Create a change agile and integrated organization**: Maximize our ability to collaborate and forge new pathways in the face of change.

- **Strengthen our commitment to personal and professional growth**: Increase engagement and retention through learning investment in individual employees.

We are committed to fostering an environment in which everyone feels valued, respected, and empowered to contribute and provided access to the resources and opportunities to do their best work, while we strive to make a positive difference for patients and their families.

Corporate Information

We commenced operations on January 19, 2011 as Sterogen Biopharma, Inc. On September 13, 2011, we changed our name to Sage Therapeutics, Inc. under our Second Amended and Restated Certificate of Incorporation. Our mailing address and executive offices are located at 55 Cambridge Parkway, Cambridge, Massachusetts and our telephone number at that address is (617) 299-8380. We maintain an Internet website at the following address: www.sagerx.com. The information on our website is not incorporated by reference in this Annual Report or in any other filings we make with the Securities and Exchange Commission, or SEC.

We make available on or through our website certain reports and amendments to those reports that we file with or furnish to the SEC in accordance with the Securities Exchange Act of 1934, as amended. These include our annual reports on Form 10-K, our quarterly reports on Form 10-Q, and our current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make this information available on or through our website free of charge as soon as reasonably practicable after we electronically file the information with, or furnish it to, the SEC.

The SEC maintains an Internet website that contains reports, proxy and information statements, and other information regarding us and other issuers that file electronically with the SEC. The SEC's Internet website address is http://www.sec.gov.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report on Form 10-K, or Annual Report, and in our other public filings before making an investment decision. Our business, prospects, financial condition, or operating results could be harmed by any of these risks, as well as other risks not currently known to us or that we currently consider immaterial. If any such risks or uncertainties actually occur, our business, financial condition or operating results could differ materially from the plans, projections and other forward-looking statements included in this Annual Report, including in the foregoing Business section and later in the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this report and in our other public filings and public statements. The trading price of our common stock could decline due to any of these risks, and as a result, our stockholders may lose all or part of their investment.

Risks Related to Product Development, Regulatory Approval and Commercialization

Our future business prospects depend heavily on our ability, with our collaboration partner, Biogen MA Inc., and Biogen International GmbH, or together, Biogen, to successfully commercialize ZURZUVAE® (zuranolone) for the treatment of women with postpartum depression, or PPD, in the U.S. There is no assurance that our commercialization efforts in the U.S. with respect to ZURZUVAE for the treatment of women with PPD will be successful or that we will be able to generate revenues at the levels or on the timing we expect or at levels or on the timing necessary to support our goals.

Our business currently depends heavily on our ability, along with our collaboration partner, Biogen, to successfully continue to commercialize ZURZUVAE in the U.S. as a treatment for women with PPD. ZURZUVAE was approved by the United States Food and Drug Administration, or FDA, in August 2023 as a treatment for adults with PPD and became commercially available in the U.S. in December 2023. ZURZUVAE is the first oral treatment specifically indicated for adults with PPD. We may never be able to successfully commercialize ZURZUVAE or meet our expectations with respect to revenues or profits from sales. ZURZUVAE may not achieve, or, even if achieved, maintain, broad market acceptance. Healthcare professionals may decide not to use ZURZUVAE as a treatment option for their patients with PPD or may only consider prescribing ZURZUVAE for a subset of women with PPD in their practice who they consider to have particularly severe symptoms relative to other patients suffering from this disease. ZURZUVAE may not achieve brand awareness and adoption among healthcare professionals, including OBGYNs, and our beliefs about the potential for OBGYNs to utilize ZURZUAVE at the forefront of postpartum care may prove to be incorrect. ZURZUVAE also may not achieve or, even if achieved, maintain broad market acceptance from women with PPD who may decide that they do not want to be treated with ZURZUVAE out of concerns about the safety and tolerability profile of ZURZUVAE or use while breastfeeding. ZURZUVAE includes a boxed warning that instructs healthcare professionals to advise patients that ZURZUVAE causes driving impairment due to central nervous system depressant effects, and that people who take ZURZUVAE should not drive a motor vehicle or engage in other potentially hazardous activities requiring complete mental alertness until at least 12 hours after ZURZUVAE administration for the duration of the once-daily 14-day treatment course, which could decrease willingness to prescribe or use ZURZUVAE. The label also includes information about adverse events and other warnings and precautions that may cause a woman with PPD not to consider ZURZUVAE as a treatment option.

ZURZUVAE also may not achieve or, even if achieved, maintain broad market acceptance for the treatment of women with PPD if payors are not willing to provide reimbursement for the treatment or impose significant restrictions on reimbursement. Payors that currently have favorable coverage for ZURZUVAE in PPD may change their policies and may decide to limit reimbursement for ZURZUVAE, including by requiring women with PPD to try other treatments prior to ZURZUVAE, requiring a specific showing of symptom severity on measurements scales, requiring prior consultation with a psychiatrist or other specialist, or imposing other onerous prior authorization requirements, or may deny reimbursement for other reasons or in all cases. Some payors currently require that healthcare professionals attest that the women with PPD for whom they have prescribed ZURZUVAE have severe symptoms. In addition, even if a healthcare professional writes a prescription for ZURZUVAE for the treatment of a woman with PPD, the prescription may not result in product being shipped to the patient and/or the patient taking ZURZUVAE. The healthcare professional or the patient may, for example, not take the steps necessary to obtain reimbursement or to have the prescription filled at

the specialty pharmacy or may find the process of obtaining a prescription through the specialty pharmacy too slow or complicated. There is no guarantee that the infrastructure, systems, processes, policies, relationships and materials we and Biogen have built for the commercialization of ZURZUVAE for the treatment of women with PPD in the U.S. will be sufficient for us to achieve or, even if achieved, maintain success. ZURZUVAE may also not achieve the clinical benefit we expect in women with PPD. Our commercialization of ZURZUVAE in PPD may be negatively impacted by competition from other drugs currently on the market or that may be approved in the future. The number of women with PPD, the unmet need for additional treatment options for women with PPD, and the potential market for ZURZUVAE may be significantly smaller than we expect, or we may encounter other market-related issues in the commercialization of ZURZUVAE for the treatment of women with PPD, including as a result of the price we charge. We and our collaboration partner, Biogen, may not be applying the optimal resources to the launch of ZURZUVAE or we or Biogen may not be able or willing to scale our resources at the right time or at an effective level. Even if we are successful in commercializing ZURZUVAE for the treatment of women with PPD, we expect the revenues from ZURZUVAE for the treatment of women with PPD will be significantly lower than if we had received regulatory approval in major depressive disorder, or MDD.

Our plans to explore strategic alternatives and our rejection of an unsolicited, non-binding acquisition proposal from Biogen to acquire all of our outstanding shares not owned by Biogen may have a material adverse effect on our business.

On January 10, 2025, we received an unsolicited, non-binding acquisition proposal from Biogen to acquire all of our outstanding shares not owned by Biogen for $7.22 per share, or the Biogen Proposal. On January 27, 2025, we announced that our Board of Directors has initiated a process to explore strategic alternatives, and further announced that our Board of Directors unanimously rejected the Biogen Proposal. On January 16, 2025, we commenced litigation against Biogen Inc. and Biogen MA Inc., or together with Biogen Inc., Biogen, in the Delaware Court of Chancery seeking declaratory, injunctive and other relief. In our complaint, we alleged that Biogen breached the standstill provision in the stock purchase agreement we entered into with Biogen on November 27, 2020, or the Biogen Stock Purchase Agreement, by making an unsolicited acquisition proposal and related public disclosures. On this basis, we also sought a temporary restraining order enjoining Biogen from future breaches of the standstill provision. At a hearing held on January 28, 2025, the Delaware Court of Chancery granted our motion for a temporary restraining order against Biogen MA Inc., and entered an implementing order on January 30, 2025, or the TRO Order. Pursuant to the TRO Order, unless consented to by Sage in writing or otherwise ordered by the court, Biogen MA Inc. and its directors, officers, agents, employees, attorneys, representatives, persons in active concert or participation with it, and anyone acting under its direction or control are enjoined from taking any action inconsistent with the Biogen Stock Purchase Agreement's contractual prohibitions against (i) making a public acquisition proposal, (ii) making a private acquisition proposal that is reasonably expected to require public disclosure, or (iii) publicly encouraging any acquisition proposal. Our rejection of the Biogen Proposal, our efforts to enforce the terms of the Biogen Stock Purchase Agreement and our strategic review process may adversely impact our relationship with Biogen, including our efforts to commercialize ZURZUVAE. We cannot be certain that our efforts to date with Biogen, including regarding sales force coordination, engagement with payors, and education efforts related to PPD will not be adversely impacted or that Biogen will continue to make investments related to ZURZUVAE. Any disruption of our relationship with Biogen under our collaboration agreement with Biogen may have an adverse impact on sales of ZURZUVAE, which may in turn materially adversely affect our business, results of operations, financial condition and prospects. We have not set a timetable for the strategic review process, nor have we made any decisions related to any potential strategic alternatives at this time. There can be no assurance that our strategic review process will result in any transaction or other strategic outcome. We do not intend to disclose further developments on this strategic review process unless and until we determine that such disclosure is appropriate or necessary. If we determine to engage in a transaction as a result of our exploration and evaluation of strategic alternatives, our future business, prospects, financial position and operating results could be significantly different than those in historical periods or projected by our management.

Our future business prospects depend heavily on our ability, alone or through our collaborations, to successfully develop, gain regulatory approval of and commercialize our current and future product candidates. We cannot be certain that we will be able to initiate planned clinical trials, to complete ongoing clinical trials or to announce results of such trials with respect to any of our product candidates, on the timelines we expect or at all, or that the results of our clinical trials or other activities under our development programs will be positive. We cannot be certain that we or

our collaborators will be able to advance such product candidates into additional trials or to successfully develop, obtain regulatory approval for, or successfully commercialize any such product candidates, if approved.

Our future business prospects depend heavily on our ability, alone or through our collaborations, to successfully develop and gain regulatory approval of our current and future product candidates. Drug development and obtaining regulatory approval for a product involve a long, expensive and uncertain process, involving a high degree of risk.

Before obtaining regulatory approvals for the commercial sale of any product candidate, non-clinical studies and clinical trials must demonstrate that the product candidate is safe and effective for use in each target indication. We or our collaborators, as applicable, may not be able to demonstrate the efficacy and safety of any of our current product candidates or any future product candidate at each stage of clinical development or we may encounter other issues with any clinical trials or non-clinical studies required for regulatory submissions. Some or all of our or our collaborators' clinical trials may fail to meet their primary or key secondary endpoints, raise safety issues or generate mixed results.

For example, in July 2024, we announced that the KINETIC 2 Study, a Phase 2b dose-ranging clinical trial evaluating SAGE-324 for the treatment of patients with essential tremor, did not meet its primary or secondary endpoints. As a result, we and Biogen announced plans to close our ongoing open label safety study of SAGE-324 and to cease further clinical development of SAGE-324 in essential tremor. Subsequently, in September 2024, Biogen notified us of its termination of our collaboration agreement solely with respect to SAGE-324 on a worldwide basis, effective February 17, 2025. While we are evaluating next steps, if any, for other potential indications for SAGE-324, including seizures in developmental and epileptic encephalopathies, or DEEs, these efforts may be unsuccessful. We may choose not to further develop SAGE-324, or if we do study SAGE-324 in this or other indications, such efforts may result in significant expenditure of time and expense, and we may never achieve positive results from the SAGE-324 program or obtain approval by a regulatory authority.

In addition, based on the results of the Phase 2 DIMENSION, LIGHTWAVE and PRECEDENT Studies evaluating dalzanemdor for the treatment of patients with cognitive impairment associated with Huntington's disease, mild cognitive impairment and mild dementia due to Alzheimer's disease, and cognitive impairment due to Parkinson's disease, respectively, none of which met its primary endpoint, we do not plan to pursue further development of dalzanemdor.

Studying alternate formulations of our product candidates or doses that achieve higher or lower patient exposure may result in unexpected adverse events or raise other safety issues or may otherwise generate negative results. For example, in the KINETIC 2 Study, we evaluated multiple doses, including the same maximum dose of SAGE-324 that we evaluated in prior studies. SAGE-324 did not demonstrate a statistically significant dose-response relationship on the primary endpoint in participants with essential tremor. A dose-relationship was observed, however, in the incidence of central nervous system, or CNS, depressant treatment emergent adverse events, or TEAEs, and in the frequency of TEAEs, leading to study drug discontinuation. We might decide to evaluate different doses, formulations, and durations of dosing for any of our product candidates with other studies or programs in the future. Changes in formulation or the need to refine or scale-up the manufacturing process could also delay development or require us to conduct additional clinical trials or non-clinical studies or conduct post-approval analyses or could lead to different results.

We or our collaborators may not be able to initiate or complete our clinical trials or announce results from our clinical trials on the timelines we expect. We or our collaborators may experience slower than expected activation of sites or enrollment and randomization of patients in our clinical trials, particularly in clinical trials where an in-patient stay or frequent site visits are required, the patient population is small or otherwise difficult to enroll, enrollment criteria are more selective than historically used, there are existing therapies, where other companies are running large clinical trials, or where relevant clinical sites or our vendors are experiencing healthcare staffing shortages or significant turnover. There is also the potential for slower than expected clinical site initiation, problems with the conduct of a study at one or more sites, delays or problems in analyzing data, the potential need for additional analysis or data or the need to enroll additional patients, the negative impact of feedback from the FDA or other regulatory authorities on trial design or analysis of results, the need to make protocol amendments or other unexpected issues, such as adverse events, in any of our clinical trials. These types of delays or issues could lead to delays in the completion of a trial and announcement of results or impact the results of our trials.

Our ongoing and planned development activities may be negatively impacted by a number of factors. Widespread healthcare and vendor staffing shortages and increased competition for patients and clinical sites may make it difficult to enroll patients in our clinical trials and/or identify and activate participating clinical sites for our trials, may cause other delays at clinical trial sites and/or vendors, and may increase the rates of patients withdrawing from our clinical trials following enrollment. Some clinical sites may decline or delay participation in our trials due to capacity and resource constraints. These factors may substantially slow clinical site identification and activation and enrollment in our clinical trials, or cause us to pause trials, which may, in each case, significantly impact our ability to meet our expected timelines, budgets, or other plans.

We or our clinical sites may in the future implement measures to help minimize the number of visits a clinical trial participant is required to make to a site in response to certain events, including by limiting or modifying clinical trial procedures and visits for data collection, or clinical sites may impose other restrictions or limitations on key clinical trial activities such as restrictions related to monitoring of the sites by clinical research organizations. Limitations or modifications to study procedures, study visits or data collection, restrictions on key clinical trial activities such as monitoring or auditing, or other restrictions that may affect data analysis activities may require additional assessment and evaluation from institutional review boards; negatively impact the integrity or completeness of our trial data, the powering of a trial, the integrity or relevance of clinical study endpoints; or impact the timing of availability of results.

The drug development process can take many years and may include post-marketing studies and surveillance, which will require the expenditure of substantial resources. Of the large number of drugs in development in the U.S., only a small percentage will successfully complete the FDA regulatory approval process and will be commercialized. Accordingly, even if we have the requisite financial resources, when needed, to continue to fund our development efforts, we cannot assure you that any of our current or future product candidates will be successfully developed or commercialized either in the U.S. or in any other country. Even if we or our collaborators conduct the trials required by or discussed with the FDA, the FDA may ultimately decide that the design, number and type of trials, number of patients studied or results, even if positive, are not sufficient to file for or gain regulatory approval of our product candidates in the indications we study, or do not support the safety, efficacy or intended profile for our product candidate, as was the case with the complete response letter, or CRL, that the FDA issued related to the new drug application, or NDA, for zuranolone for the treatment of MDD.

We may never be able to generate meaningful revenues from sales of our current or future products at levels or on timing necessary to support our investment and goals, and we may ultimately decide to discontinue commercial availability of products that we are unable to successfully commercialize or as a result of market changes.

We are a commercial-stage company, selling ZURZUVAE in the U.S. market. Even if we or one of our collaborators gains approval of any of our current or future product candidates, we and our collaborators may never be able to successfully commercialize such new product in the approved indications or meet our expectations with respect to timing and revenues or profits from sales of such product. The lack of commercial success at levels or on timing necessary to support our investment and goals, or overall changes to the market, may lead us to discontinue a product and/or voluntarily request the withdrawal of a product's NDA even if successfully developed and approved.

For example, we discontinued commercial availability of our product ZULRESSO® (brexanolone) CIV injection in the U.S. as of December 31, 2024. ZULRESSO was first made commercially available in the U.S. in June 2019. Since launch, our revenues from sales of ZULRESSO were negatively impacted by significant barriers arising from the complex requirements for treatment and, more recently, by the introduction of ZURZUVAE as a treatment for women with PPD. These requirements created significant barriers to treatment with ZULRESSO for women with PPD.

We also encountered other issues and challenges in commercializing ZULRESSO and generating revenues, including:

- Some women with PPD who needed treatment found it too onerous to undergo an infusion or to be treated at a certified healthcare setting overnight for the length of stay required for treatment, or to be enrolled in the registry that is part of the Risk Evaluation and Mitigation Strategy, or REMS, process or have been concerned about the risk of excessive sedation and sudden loss of consciousness.

- More healthcare professionals than we expected were unwilling to accept ZULRESSO as a treatment for women with PPD.
- ZULRESSO competed with lower cost antidepressants.
- Given the complex requirements for treatment, use of ZULRESSO in the U.S. was focused primarily on women with more severe symptoms of PPD.
- We encountered coverage and reimbursement challenges, including restrictions related to the severity of PPD cases for which ZULRESSO would be reimbursed, requirements that other treatments be used prior to ZULRESSO, or other limitations in the scope, breadth, availability or amount of reimbursement covering ZULRESSO or the infusion.
- A number of healthcare settings that were willing to administer ZULRESSO to women with PPD who had commercial insurance were not willing to treat Medicaid patients, which adversely affected our ability to generate revenue from ZULRESSO.

To the extent we face issues with current or future products that impact market acceptance, convenience, availability, reimbursement or other aspects of commercialization, as applicable, these issues could impair our ability to generate revenues or meet our expectations with respect to the amount or timing of revenues for our products. If we decide to discontinue commercial availability and/or voluntarily request the withdrawal of the NDA for any of our products as a result of such challenges, as we did with ZULRESSO, the withdrawal of the product from the marketplace may raise additional potential risks and uncertainties, including from contract terminations or other actions, including by regulatory authorities, which we may not be able to predict. Any issues or hurdles related to our commercialization efforts may materially adversely affect our business, results of operations, financial condition and prospects and could lead us to make significant further changes to the scope and nature of our efforts.

Any product or product candidate that we develop may cause undesirable side effects that limit their commercial profile; delay or prevent further development or regulatory approval; cause regulatory authorities to require labeling statements, such as a boxed warning or a REMS; or result in other negative consequences.

We may observe undesirable side effects or other potential safety issues in nonclinical studies, in clinical trials at any stage of development, as part of an expanded access program, in commercial use or in post-approval studies. Clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients and limited duration of exposure, certain side effects of ZURZUVAE, ZULRESSO, or any other product or product candidate that we may develop, may only be uncovered, or the frequency or severity identified, with a larger number of patients exposed to the product. Those side effects could be serious or life-threatening. If we or others identify any such undesirable side effects, or the increased severity or frequency of any known side effects:

- regulatory authorities may withdraw, withhold or limit their approval of such products;
- the FDA or regulatory authorities outside the U.S. may impose a clinical hold or partial clinical hold which could cause us or our collaborators to have to stop, delay or restrict further development;
- we or our collaborators may, even without a clinical hold, decide to interrupt, delay or halt existing non-clinical studies and clinical trials or stop development;
- we may have difficulty enrolling patients in our clinical trials and completing such trials on the timelines we expect or at all, or we may have to conduct additional non-clinical studies or clinical trials as part of a development program;
- if an NDA for any of our product candidates is reviewed by an advisory committee of the FDA, the advisory committee may recommend against approval of the application or may recommend that the FDA require, as a condition of approval, additional non-clinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions, and the FDA may ultimately agree with the recommendations of the advisory committee;

- we or our collaborators may not be able ultimately to demonstrate, to the satisfaction of regulatory authorities, that our product candidates are safe and that the benefits outweigh the safety risks, and the applicable regulatory authorities may not approve the product candidate;
- regulatory authorities may require the addition of labeling statements, such as a boxed warning or additions to an existing boxed warning, or a contraindication, including as a result of inclusion in a class of drugs for a particular disease, or may require a REMS, or modifications to an existing REMS;
- we or our collaborators may be required to change the way such products are distributed or administered, conduct post-approval studies or change the labeling of the products;
- we or our collaborators may be subject to regulatory investigations and government enforcement actions;
- we or our collaborators may decide to remove such products from the marketplace;
- we or our collaborators could be held liable for injury caused to individuals exposed to or taking our products or product candidates; and
- our reputation may suffer.

We believe that any of these events could prevent us from achieving or maintaining market acceptance of the affected products, could substantially increase the risks to our business, including the risks and costs of developing our product candidates or commercializing our products, and could significantly adversely impact our ability and that of our collaborators to successfully develop, gain regulatory approval for, and commercialize our current product candidates or future products and generate revenues at the levels we expect, or at all.

Obtaining regulatory approval to market any of our product candidates is a complex, lengthy, expensive and uncertain process, and regulatory authorities may delay, limit or deny approval of any of our product candidates for many reasons. Any setback or delay in obtaining regulatory approval for any of our product candidates or in our, or our collaborators', ability to commence or continue marketing of our products, if approved, may have a material adverse effect on our business and prospects.

We are not permitted to market any of our product candidates in the U.S. until we or our collaborators receive approval of an NDA from the FDA or in any foreign countries until we or our collaborators receive the requisite marketing approval from such countries. Obtaining approval of an NDA in the U.S. or marketing approval in any country outside the U.S. is a complex, lengthy, expensive and uncertain process. For example, on August 4, 2023, the FDA issued a CRL related to the NDA for zuranolone for the treatment of MDD. The CRL stated that the NDA did not provide substantial evidence of effectiveness to support the approval of zuranolone for the treatment of MDD and that one or more additional clinical trials would be needed. Regulatory authorities may delay, limit or deny approval of any of our product candidates for many reasons, including, among others:

- we or our collaborators may not be able to demonstrate, to the satisfaction of regulatory authorities, that our product candidates are safe and effective in any indication, as was the case with respect to the NDA for zuranolone for the treatment of MDD, and that the benefits outweigh the safety risks;
- the results of our non-clinical studies and clinical trials may be negative, or may not meet the level of statistical or clinical significance or other criteria required by regulatory authorities for marketing approval;
- regulatory authorities may impose a clinical hold or partial clinical hold prior to the initiation of development or during development of our product candidates, which could cause us to have to stop, delay or restrict further development;
- regulatory authorities may disagree with our interpretation of data from our non-clinical studies and clinical trials, or may not accept data generated at one or more of our sites conducting non-clinical studies or clinical trials which could cause the study or trial to fail;
- regulatory authorities may determine that the number, design, size, conduct, implementation or results of our non-clinical studies or clinical trials are inadequate for regulatory approval or that changes in dosing or drug formulation used in our non-clinical studies or clinical trials require additional trials or studies, even if the

regulatory authorities have previously reviewed and commented on the design and details of our plans, as was the case with respect to the NDA for zuranolone for the treatment of MDD;

- regulatory or other governmental authorities may require that we or our collaborators conduct additional non-clinical studies and clinical trials prior to approval or post-approval;
- regulatory authorities may not approve the formulation, labeling or specifications of any of our product candidates;
- if an NDA for any of our product candidates is reviewed by an advisory committee of the FDA, the advisory committee may recommend against approval of the application or may recommend that the FDA require, as a condition of approval, additional non-clinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions, and the FDA may ultimately agree with the recommendations of the advisory committee;
- regulatory authorities may approve a product candidate for which we or our collaborators are seeking regulatory approval for a more limited patient population than expected or with substantial use restrictions;
- the FDA may require a REMS as a condition of approval or post-approval for our product candidates, as was the case with ZULRESSO, or may modify an existing REMS or may impose other limitations or restrictions, like a boxed warning, as is the case with ZURZUVAE;
- regulatory authorities may determine that the manufacturing processes or facilities of third-party contract manufacturers with which we contract do not conform to applicable requirements, including cGMPs; or
- regulatory authorities may change their approval policies or adopt new regulations.

Further, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA for certain drugs must contain data to assess the safety and effectiveness of the drug in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the sponsor receives a deferral or waiver from the FDA. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. The law requires the FDA to send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. It further requires the FDA to publicly post the PREA Non-Compliance letter and sponsor's response. The applicable legislation in the European Union, or EU, also requires sponsors to either conduct clinical trials in a pediatric population in accordance with a Pediatric Investigation Plan approved by the Pediatric Committee of the European Medicines Agency, or EMA, or to obtain a waiver or deferral from the conduct of these studies by this Committee. For any of our product candidates for which we or our collaborators are seeking regulatory approval in the U.S. or the EU, we cannot guarantee that we will be able to obtain a waiver or alternatively complete any required studies and other requirements in a timely manner, or at all, which could result in an issuance and publication of a PREA Non-Compliance letter and associated reputational harm, our product candidate being considered misbranded and subject to relevant enforcement action, invalidation of the marketing application, and/or financial penalties. Our collaborators are also subject to similar requirements outside of the U.S. and EU and thus the attendant risks and uncertainties.

Any of these factors, many of which are beyond our control, could jeopardize or delay our or our collaborators' ability to obtain regulatory approval for product candidates and successfully market approved products. Even if we or our collaborators receive marketing approval for any of our product candidates, regulatory or other governmental authorities may still impose significant restrictions, including restrictions on the indicated use or marketing, or may impose ongoing requirements for potentially costly post-approval studies. For example, the FDA imposed post-approval obligations in connection with approval of ZURZUVAE. For ZURZUVAE, the FDA is requiring two post-marketing studies: a pharmacokinetic and safety study in adolescent females who have completed puberty and an embryofetal toxicity study in a second species. Although we expect to complete these studies, we may not be able to fulfill these obligations in accordance with the FDA's requirements, or at all. The FDA recommended controlled substance scheduling with respect to ZURZUVAE under the CSA, which ultimately received a Schedule IV classification from the DEA. The FDA may recommend scheduling with respect to any of our current or future product candidates, if approved. In such event, as was the case with ZURZUVAE and ZULRESSO, prior to a product launch, the DEA will need to determine the controlled

substance schedule of the product, taking into account the recommendation of the FDA. The timing of the scheduling process would delay our ability to market any product candidate that is successfully developed and approved. In addition, the scheduling designation itself could impact the commercialization and market opportunity for any product candidate that is successfully developed and approved.

We may seek priority review of future NDA submissions with the FDA, if our development efforts with respect to any of our product candidates are successful, but the FDA may not grant such priority review. Even if the FDA grants priority review for an NDA, the FDA may not meet the applicable review timelines or may elect to extend the timeframe for their review. Delays, resource constraints, and other disruptions at the FDA and other authorities may slow the time necessary for new drugs to be reviewed and/or approved by necessary government authorities, which would adversely affect our business.

Fast Track and Breakthrough Therapy designations from the FDA, PRIority Medicines, or PRIME, designation from the EMA, Innovative Licensing and Access Pathway designation from the Medicines & Healthcare products Regulatory Agency in the United Kingdom, or similar designations in other countries or regions do not necessarily lead to a faster development pathway or regulatory review process, and do not increase the likelihood of regulatory approval. For example, on August 4, 2023, the FDA issued a CRL related to the NDA for zuranolone for the treatment of MDD after previously granting both Fast Track and Breakthrough Therapy designations to zuranolone for MDD. The FDA may withdraw Fast Track designation or Breakthrough Therapy designation, and the EMA may withdraw PRIME designation, if the relevant agency believes that the designation is no longer supported by data from our clinical development programs. For example, in November 2023, the FDA rescinded Breakthrough Therapy Designation for zuranolone for the treatment of MDD.

We or our collaborators may not be able to obtain orphan drug exclusivity for any product candidates we, or they, may develop. Even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition. A similar regulatory scheme governs approval of orphan products by the EMA in the EU. Generally, if a product candidate with an Orphan Drug Designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA, as applicable, from approving another marketing application for the same product for the same therapeutic indication for that time period. The applicable period is seven years in the U.S. and ten years in the EU. The exclusivity period in the EU can be reduced to six years if a product no longer meets the criteria for Orphan Drug Designation, in particular, if the product is sufficiently profitable so that market exclusivity is no longer justified.

In order for the FDA to grant orphan drug exclusivity to one of our products, the Agency must find that the product is indicated for the treatment of a condition or disease with a patient population of fewer than 200,000 individuals annually in the U.S. The FDA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet this standard. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. In addition, even after an orphan drug is approved, a regulatory authority, such as the FDA and EMA, can subsequently approve the same product for the same condition if such regulatory authority concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may also be lost if such regulatory authority determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

The FDA and Congress may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the U.S. Court of Appeals for the Eleventh Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term “same disease or condition” means the designated “rare disease or condition” and could not be interpreted by the FDA to mean the “indication or use.” Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, the FDA announced that, in matters beyond the scope of that court order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved.

We do not know if, when, or how the FDA or other regulatory agencies may change the orphan drug regulations and policies in the future or whether legislative action will be taken, and it is uncertain how any changes might affect our business. Depending on what changes the regulatory authorities or legislatures may make to orphan drug regulations and policies, our business could be adversely impacted.

The number of people with the diseases and disorders for which our products are indicated and for which our product candidates are targeted may be smaller than we expect or our other assumptions with respect to the potential markets for our products and product candidates may not be correct and the markets may be significantly smaller than we expect.

There is no precise method of establishing in any geography over any period of time the actual number of patients with the diseases and disorders for which our products are indicated and our product candidates are targeted. With respect to any indications for which we have developed, are developing, or plan to develop products and product candidates, we estimate the prevalence of the disease or disorder, and our estimates as to prevalence, including the assumptions we apply in determining our estimate, may not be accurate. In each case, there is a range of estimates in the published literature and in marketing studies, which include estimates within the range that are lower than our estimates. For example, our estimates of the prevalence of PPD are higher than estimates reported in some of the published literature and results obtained from certain studies analyzing claims databases and include women who have symptoms of PPD but have not been formally diagnosed with PPD or may not meet all of the diagnostic criteria. We believe these differences may be the result of variations in analytical methodologies and possibly under-diagnosis of PPD as a result of inadequate screening and under-reporting and some patients being reluctant to seek treatment in clinical practice. The actual number of women with PPD or any other indication for which we are pursuing or may elect to pursue development of our product candidates may, however, be significantly lower than we believe. Even if our prevalence estimates are correct, any approved product that we develop may only be indicated for or prescribed to and used by a subset of patients with the relevant disease or disorder. Our assumptions and estimates about the potential markets for ZURZUVAE for the treatment of women with PPD and for our other current and future product candidates in the indications we are or may pursue may not be accurate. In the event the number of patients with the diseases and disorders we are studying is significantly lower than we expect, we or our collaborators may have difficulties in enrolling patients in our clinical trials which may delay or prevent development of our product candidates. If our prevalence estimates with respect to any indication or our other market assumptions are not accurate, the markets for any approved product for these indications may be smaller than we anticipate, which could limit our revenues and our ability to achieve profitability or to meet our expectations with respect to the level and timing of revenues or profits.

Positive results from non-clinical studies and clinical trials of our product candidates are not necessarily predictive of the results of later non-clinical studies and clinical trials of our product candidates in the same indications or other indications. Interim results from non-clinical studies and clinical trials may not be predictive of results of such non-clinical studies or clinical trials once completed. If we cannot replicate the positive results from our earlier non-clinical studies and clinical trials of our product candidates in our later non-clinical studies and clinical trials in the same indications or other indications, or we cannot replicate our interim results in our completed non-clinical studies and clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.

Positive results from non-clinical studies and clinical trials of our product candidates may not necessarily be predictive of the results we or our collaborators may obtain from subsequent non-clinical studies or clinical trials using the same product candidate or other product candidates. Similarly, interim results from non-clinical studies and clinical trials may not be predictive of results of a non-clinical study or clinical trial once completed. For example, despite the results of prior clinical trials, our KINETIC 2, DIMENSION, LIGHTWAVE, and PRECEDENT Studies failed to meet their primary endpoints, as announced in 2024. As a result, we do not plan on continuing development of dalzanemdor, and Biogen terminated our collaboration agreement solely with respect to SAGE-324 on a worldwide basis, effective February 17, 2025. We are evaluating next steps, if any, for other potential indications of SAGE-324, including seizures in DEEs, and we may choose not to further develop SAGE-324 in any indication.

We or our collaborators may also observe safety issues in clinical trials or non-clinical studies of our product candidates that we or they did not observe or appreciate in earlier stage clinical studies or non-clinical studies, or a different rate or severity of events, including as a result of an increase in dosing or in frequency or duration of dosing, studying a different patient population or different indication than previously studied, or administering a product

candidate with a concomitant medication. For example, in the KINETIC 2 Study, for which we reported negative results in July 2024, we observed a dose-relationship in the incidence of CNS depressant TEAEs and in the frequency of TEAEs leading to study drug discontinuation in the study. Any of our studies may result in unexpected adverse events or raise other safety issues or may otherwise generate negative results.

The results from non-clinical animal models may not be replicated in clinical trials, including, for example, in future clinical trials of SAGE-319 or any of our other product candidates. Many product candidates, including many targeting central nervous system disorders, with promising non-clinical profiles have failed to demonstrate similar safety, non-toxicity and efficacy in humans.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later-stage clinical trials after achieving positive results in earlier-stage development, and we cannot be certain that we will not face similar setbacks. Many drugs have failed to replicate efficacy and safety results in larger, longer or more complex later stage trials. Moreover, non-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in non-clinical studies and clinical trials nonetheless failed to obtain FDA approval. If we or our collaborators fail to produce positive results in our ongoing and planned non-clinical studies or clinical trials of any of our product candidates, the development timeline and regulatory approval and commercialization prospects for our product candidates, and, correspondingly, our business and financial prospects, would be materially adversely affected.

Failures or delays by us or our collaborators in the commencement, enrollment or completion of our ongoing and planned clinical trials of our current and future product candidates could cause us not to meet our expected timelines or result in increased costs to us, and could delay, prevent or limit our ability to gain regulatory approval of any such product candidate and to generate revenue from resulting products, if any.

Successful completion of clinical trials at each applicable stage of development is a prerequisite to submitting an NDA to the FDA or equivalent filings outside the U.S. and, consequently, the ultimate approval and commercial marketing of any of our product candidates for the indications in which we develop them. We do not know whether we, or our collaborators, will complete and announce the results of any of our ongoing clinical trials, or whether future trials will begin, as planned or expected, if at all, as the commencement, enrollment, completion and announcement of results of clinical trials can be delayed or prevented for a number of reasons, including, among others:

- denial by the FDA or other regulatory authority of permission to proceed with our planned clinical trials or any other clinical trials we may initiate, or placement of one or more clinical trials on full or partial clinical hold;
- delay or inability to satisfy the requirements of the FDA to commence clinical trials, including chemistry, manufacturing and control, or CMC, requirements, or to file or receive approvals of additional investigational new drug applications, or INDs, that may be required;
- delay or inability to satisfy the requirements for clinical trials conducted in the EU, if applicable, pursuant to Regulation (EU) No 536/2014, or the EU Clinical Trials Regulation;
- negative or inconclusive results from our ongoing non-clinical studies or clinical trials;
- challenges in identifying, recruiting, enrolling and retaining patients to participate in clinical trials;
- challenges in qualifying and activating clinical trial sites, including due to capacity and resource constraints and attrition at sites, and potential delays at clinical trial sites;
- general political and economic conditions, including as a result of future pandemics or other global health crises or bank failures;
- delays in reaching or failing to reach agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites, or failures or problems by CROs or clinical trial sites in executing their activities under such agreements;
- inadequate quantity or quality of supplies of a product candidate or other materials necessary to conduct clinical trials;

- difficulties obtaining Institutional Review Board, or IRB, approval, and equivalent approval for sites outside the U.S., to conduct a clinical trial at a prospective site or sites;
- delays or problems in analyzing data, or the need for additional analysis or data or the need to enroll additional patients;
- the occurrence of serious adverse events or unexpected drug-related side effects experienced by patients in a clinical trial or unexpected results in ongoing non-clinical studies;
- delays in validating endpoints utilized in a clinical trial or the impact of changes in trial design or analysis plans;
- regulatory authorities disagreeing with our clinical trial design and our interpretation of data from clinical trials, or changing the requirements for approval even after the regulatory authority has reviewed and commented on the design for our clinical trials or delays caused by the need or desire for engagement with the applicable regulatory authorities; and
- reports from non-clinical or clinical testing of other therapies that raise safety or efficacy concerns.

In addition, a clinical trial may be suspended or terminated by us, regulatory authorities, the IRB or ethics committee, or EC, at the sites where the IRBs or ECs are overseeing a clinical trial, or recommended for termination or suspension by a data and safety monitoring board overseeing the clinical trial at issue or other regulatory authorities due to a number of factors, including, among others:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities that reveals deficiencies or violations that require us to undertake corrective action, including the imposition of a partial or full clinical hold;
- unforeseen safety issues, including any that could be identified in our ongoing non-clinical studies, or adverse side effects or lack of effectiveness identified in ongoing clinical trials;
- changes in government regulations or administrative actions; and
- problems with clinical supply materials.

Additionally, changes in regulatory requirements, guidance or unanticipated events during our non-clinical studies and clinical trials or other reasons may cause us or our collaborators to amend non-clinical studies and clinical trial protocols or the applicable regulatory authorities may impose additional non-clinical studies and clinical trial requirements. Amendments or changes to clinical trial protocols would require resubmission to the FDA and IRBs for review and approval, which may adversely impact the cost, timing or successful completion of clinical trials. If we or our collaborators experience delays completing, or if we or our collaborators terminate, any of our non-clinical studies or clinical trials, or if we or our collaborators are required to conduct additional non-clinical studies or clinical trials, the development pathway, and ultimately the commercial prospects, for our product candidates may be harmed and our ability to generate product revenue from resulting products, if any, will be delayed.

Finally, if we or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted. For example, in December 2022, with the passage of Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. In June 2024, as mandated by FDORA, the FDA issued draft guidance outlining the general requirements for Diversity Action Plans, or DAPs. Unlike most guidance documents issued by the FDA, the DAP guidance when finalized will have the force of law because FDORA specifically dictates that the form and manner for submission of DAPs are specified in FDA guidance. On January 27, 2025, in response to an Executive Order issued by President Trump on January 21, 2025, on Diversity, Equity and Inclusion programs, the FDA removed this draft guidance from its website. This action raises questions about the applicability of statutory obligations to submit DAPs and the agency's current thinking on best practices for clinical development.

Similarly, the regulatory landscape related to clinical trials in the EU has evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the EU Clinical Trials Directive required a separate clinical trial application to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduced a centralized process and only requires the submission of a single application to all member states concerned. If we or our collaborators are not able to fulfill these new requirements, our ability to conduct clinical trials may be delayed or halted.

We or our collaborators may never seek or receive regulatory approval to market any of our products or product candidates outside of the U.S. or receive pricing and reimbursement outside the U.S. at acceptable levels.

We or our collaborators may not seek, or may seek but never receive, regulatory approval to market our products or product candidates outside of the U.S. or in any particular country or region. In order to market any product outside of the U.S., we or our collaborators must establish and comply with the numerous and varying safety, efficacy and other regulatory requirements of other countries. Approval procedures vary among countries and can involve additional non-clinical studies or clinical trials, additional work related to manufacturing and analytical testing on controls, and additional administrative review periods. The time required to obtain approvals in other countries might differ from that required to obtain FDA approval. Marketing approval in one country does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process in other countries. The marketing approval processes in other countries may implicate all of the risks detailed above regarding FDA approval in the U.S. as well as other risks. In particular, in many countries outside of the U.S., products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval may require additional studies and data, and can result in substantial delays in bringing products to market in such countries and such investment may not be justified from a business standpoint given the market opportunity or level of required investment. Even if we or our collaborators generate the data and information which we or our collaborators believe may be sufficient to file an application for regulatory approval of any of our products or product candidates in a region or country outside the U.S., the relevant regulatory agency may find that we or our collaborators did not meet the requirements for approval, or even if our application is approved, we may have significant post-approval obligations.

We or our collaborators could face heightened risks with respect to seeking marketing approval in the United Kingdom, or UK, as a result of the withdrawal of the UK from the EU, commonly referred to as Brexit. The UK is no longer part of the European Single Market and EU Customs Union. As of January 1, 2021, the MHRA became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland will continue to be subject to EU rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), known as the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law of the body of EU law instruments governing medicinal products that pre-existed prior to the UK's withdrawal from the EU. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us or our collaborators to restrict or delay efforts to seek regulatory approval in the UK for our or their product candidates, which could significantly and materially harm our business.

Even if we or our collaborators are able to successfully develop our product candidates and obtain marketing approval in a country outside the U.S., we or they may not be able to obtain pricing and reimbursement approvals in such country at acceptable levels or at all, and any pricing and reimbursement approval we or they may obtain may be subject to onerous restrictions such as caps, rebates or other hurdles or restrictions on reimbursement. Failure to obtain marketing and pricing approval in countries outside the U.S. without onerous restrictions or limitations related to pricing, or any delay or other setback in obtaining such approval, would impair our ability or that of our collaborators to market our product candidates successfully or at all in such foreign markets. Any such impairment would reduce the size of our potential market or revenue potential, which could have a material adverse impact on our business, results of operations and prospects.

Any setback or delay in obtaining regulatory approval or commencing marketing, if approved, for our product candidates in a country or region outside the U.S. where we or our collaborators have decided it makes business sense to proceed may have a material adverse effect on our business and prospects.

We rely completely on third-party suppliers to manufacture commercial supplies of our products and clinical drug supplies for our product candidates, and we intend to rely on third parties to produce non-clinical, clinical and commercial supplies of our products and product candidates in the future.

We do not currently have, nor do we plan to acquire or develop, the infrastructure or capability internally to manufacture supplies of our products, including ZURZUVAE, for commercial use or any of our other existing or future product candidates, for use in the conduct of our clinical trials and non-clinical studies or for future commercial use, and we rely completely on third-party suppliers for both active drug substances and finished drug products.

We rely on our contract manufacturers to manufacture sufficient quantities of ZURZUVAE active drug substance, finished drug product and packaged and labeled product. We also previously relied on our contract manufacturers for commercial supplies of active drug substance, finished drug product and packaged and labeled product with respect to ZULRESSO until we discontinued ZULRESSO commercial availability in the U.S. as of December 31, 2024. We also rely on our contract manufacturers to manufacture sufficient quantities of our product candidates for ongoing and planned clinical trials and non-clinical studies and expect to rely on them to scale our manufacturing processes for future clinical trials, if our development efforts are successful.

We expect our contract manufacturers to comply with current Good Manufacturing Practices, or cGMPs, in the manufacture of our products. The facilities used by our contract manufacturers to manufacture the active pharmaceutical ingredient and final drug product may be required to complete a pre-approval inspection by the FDA and other comparable foreign regulatory authorities to assess compliance with applicable requirements, including cGMPs, after we submit the relevant NDA or equivalent foreign regulatory submission to the applicable regulatory agency. Contract manufacturers are subject to inspections by the FDA and regulatory authorities outside the U.S. If the FDA or other regulatory authorities were to identify deficiencies in connection with the inspections of our contract manufacturers for our products or any of our product candidates, the FDA could issue a Form 483, and other regulatory authorities could issue equivalent documents, documenting these deficiencies and require that we provide and comply with a corrective action plan, which could impact our ability to supply product or any of our product candidates. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other foreign regulatory authorities, and pass regulatory inspections, on the timelines we expect or at all, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities with respect to our products.

We have no direct control over our contract manufacturers' ability to maintain adequate quality control, quality assurance and qualified personnel. All of our third-party contract manufacturers are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our third-party contract manufacturers to regulatory risks for the production of such materials and products. As a result, failure to satisfy the regulatory requirements for the production of those materials and products may affect the regulatory clearance of our contract manufacturers' facilities generally. If the FDA or an applicable foreign regulatory agency determines now or in the future that these facilities for the manufacture of our products and product candidates are noncompliant, we may need to find alternative manufacturing facilities, which would significantly and adversely delay or impact our commercialization efforts for any approved product and our ability to develop and obtain regulatory approval for our product candidates. Our reliance on contract manufacturers also exposes us to the possibility that they, or third parties with access to their facilities, will have access to and may appropriate our trade secrets or other proprietary information. Also, if a natural disaster, or other events, were to interrupt or halt production of our drug substance or drug product at one of our third-party contract manufacturers, or cause the loss of batches, we could encounter a supply shortage or face significant costs to rebuild our supply.

We have a long-term supply agreement with our contract manufacturer for ZURZUVAE drug product. We have an inventory of ZURZUVAE drug product and drug substance in place to help mitigate any potential supply risks, but there is no guarantee that this inventory will be adequate. We do not have arrangements in place for either long-term supply or redundant supply of drug substance or drug product for our product candidates. Each batch of drug substance and drug product for our product candidates is individually contracted through a purchase order governed by master service and quality agreements.

If our existing contract manufacturing organizations, or CMOs, for our product candidates are unwilling to enter into long-term supply agreements, or are unwilling or unable to supply drug substance or drug product to us, we could be

required to engage new CMOs who would need to scale up the manufacturing process before we would be able to use the drug product or drug substance they manufacture for clinical trials or for future commercialization, if we are successful and gain approval. In addition, any CMO will need to complete validation batches and be approved by regulatory authorities (including passing any required inspections) as our manufacturer before we would be able to use drug product or drug substance they manufacture for commercial purposes, which could result in significant delays or gaps in product availability. We plan to continue to rely upon CMOs to manufacture commercial quantities of ZURZUVAE and of any future products that may be approved. If we are unable to maintain arrangements for third-party manufacturing or are unable to do so on commercially reasonable terms, or are unable to obtain timely regulatory approvals in connection with our CMOs, we may not be able to successfully commercialize any approved product, including ZURZUVAE, or successfully complete development of our current or future product candidates.

Any of our current or future products or product candidates, including ZURZUVAE, may not achieve and maintain broad market acceptance or reimbursement at sufficient levels, which would limit the revenue that we generate from sales.

The commercial success of ZURZUVAE in the U.S. for the treatment of women with PPD, or of any of our current or future products or product candidates, if successfully developed and approved by the FDA or other applicable regulatory authorities, will depend upon the awareness and acceptance among healthcare professionals, patients, policy-makers and healthcare payors, and reimbursement at sufficient levels.

The availability of coverage and adequacy of reimbursement is essential for most patients to be able to access and afford treatments. Patients who are prescribed medications for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Government authorities, including the Centers for Medicare & Medicaid Services, or CMS, an agency within the Department of Health and Human Services, or HHS, in the U.S., and third-party payors, such as private health insurers and health maintenance organizations, or HMOs, decide which medications they will pay for and establish reimbursement levels for those medications. Cost containment is a primary concern in the U.S. healthcare industry and elsewhere. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Payors may adopt restrictions on coverage for any of our products, including ZURZUVAE, such as requiring patients to try other lower cost therapies prior to reimbursing our product, requiring patients to meet certain severity levels on measurement scales or other criteria more restrictive than the approved label for our products, or requiring other onerous and time-consuming forms of utilization management, such as prior authorization procedures. They may limit the amount of reimbursement or restrict access altogether. These restrictions or limitations might impede appropriate use of our products for any approved indications. For example, some payors currently require that healthcare professionals attest that the women with PPD for whom they have prescribed ZURZUVAE have severe symptoms. Restrictions and limitations on reimbursement or delays in obtaining coverage may vary significantly among payors and payor types. As a result, there is uncertainty related to maintaining third-party payor coverage and reimbursement of ZURZUVAE or any of our product candidates, if successfully developed and approved. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is a covered benefit under its health plan; safe, effective and medically necessary; appropriate for the specific patient; cost-effective; and neither experimental nor investigational. Regulatory approvals, pricing and reimbursement for drug products vary widely from country to country.

The inability of us or our collaborators to promptly obtain and maintain coverage and adequate reimbursement rates from both government-funded and private payors for ZURZUVAE for the treatment of women with PPD, and any other approved products that we develop could have a material adverse effect on our operating results, our ability to successfully commercialize our products, our ability to raise capital and our overall financial condition. Even if coverage is provided, we may not be able to realize a sufficient return on our investment, including as a result of restrictions on the type of coverage that is achieved or because we are unable to establish or maintain sufficient pricing.

Obtaining and maintaining coverage and reimbursement approval for a product from a government or other third-party payor can be an expensive and time-consuming process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of our products to the payor. The industry competition to be included in third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement, often leads to downward pricing pressures on pharmaceutical products. In addition, third-party payors

may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors, and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price and best price. Penalties may apply when such metrics are not submitted accurately and on a timely basis. Before granting reimbursement approval, payors may require us to demonstrate, directly or indirectly, that our product candidates, in addition to treating the target indications, also provide incremental health benefits to patients or healthcare costs savings. We cannot be sure that adequate coverage or reimbursement will be available for any of our products and product candidates on reasonable terms or at all.

Market acceptance for any of our approved products and any product candidates that we successfully develop will depend on a number of factors, including, among others:

- the efficacy and safety of our products as demonstrated in clinical trials or in real world use;
- the potential and perceived advantages and limitations of our products over current or future alternative treatment options, including in the case of ZURZUVAE for the treatment of women with PPD, the availability of lower cost antidepressants;
- the incidence and severity of any side effects of the products;
- limitations or warnings contained in the labeling approved for our products by the FDA or other applicable regulatory authorities, such as the boxed warning for ZURZUVAE related to driving impairment and other warnings, precautions and risks identified in the label;
- the clinical indications and size of patient populations for which our products are approved;
- the convenience, risk-benefit profile, ease and availability of alternative treatments already approved or expected to be commercially launched in the near future;
- the willingness of the target patient population to try new therapies and of healthcare professionals to prescribe these therapies, and our ability to increase awareness of our approved products through marketing efforts;
- the strength and effectiveness of our sales, marketing and distribution strategies and support or that of our collaborators;
- publicity concerning our products or competing products and treatments;
- pricing and cost effectiveness; or
- the availability of sufficient third-party coverage or reimbursement, the nature and complexity of restrictions on coverage, and the willingness of patients to pay out-of-pocket in the absence of such coverage or reimbursement.

Our and our collaborators' efforts to change the treatment paradigm for a given disorder or to educate the medical community and third-party payors about the benefits of any current or future products, to the extent permitted, including ZURZUVAE for the treatment of women with PPD, may require significant resources and may never be successful. If any of our current or future products, including ZURZUVAE, does not achieve an adequate level of acceptance by patients, healthcare professionals, and payors, or reimbursement at reasonable levels and without significant or complex restrictions, or if the patient population for which any such product is approved is smaller than we expect, we may not generate sufficient revenue from our products to become or remain profitable or to adequately fund operations or may not do so to the degree or on the timelines we expect.

Even if marketing approval is granted for a product, we may face significant post-marketing obligations and future development and regulatory difficulties.

Regulatory authorities may impose significant and potentially costly post-marketing obligations with respect to approval of any product, including post-marketing studies, additional CMC work and additional pediatric studies. For example, the FDA has imposed post-marketing commitments with respect to approval of ZULRESSO and ZURZUVAE, and we may encounter issues or delays in the conduct of these post-marketing commitments or we may generate unexpected results. For ZURZUVAE, the FDA is requiring two post-marketing studies: a pharmacokinetic and safety study in adolescent females who have completed puberty and an embryofetal toxicity study in a second species.

In the event we or our collaborators elect, or are required, to proceed with pediatric studies of any of our product candidates in any indication, regulatory authorities may also require additional non-clinical studies or clinical trials be completed prior to commencement of such pediatric studies.

As was the case with zuranolone and brexanolone, the FDA may recommend controlled substance scheduling for our current or future product candidates. If products are determined to be controlled substances, the manufacturing, shipping, storing, selling and using of the products will be subject to an additional regulation. Distribution, prescribing and dispensing of these drugs are also regulated. Because of their restrictive nature, these laws and regulations could limit commercialization of our product candidates containing controlled substances. Failure to comply with these laws and regulations could also result in withdrawal of our DEA registrations, disruption in manufacturing and distribution activities, consent decrees, criminal and civil penalties and state actions, among other consequences. The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have no established medicinal use, and may not be marketed or sold in the U.S. A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances. ZURZUVAE (zuranolone) and ZULRESSO (brexanolone) are currently regulated as a Schedule IV controlled substances. Other Schedule IV controlled substances include sedative hypnotics such as benzodiazepines.

ZURZUVAE is, and any future approved products will also be, subject to ongoing FDA requirements governing the labeling, packaging, storage and promotion of the product and record-keeping and submission of safety and other post-market information. The FDA has significant post-marketing authority, including, for example, the authority to require labeling changes based on new safety information and to require post-marketing studies or clinical trials to evaluate serious safety risks, safety and efficacy in pediatric populations or alternate doses or dose regimens.

The FDA also has the authority to require, as part of an NDA or post-approval, the submission of a REMS. For example, the FDA required a REMS for ZULRESSO. Any REMS required by the FDA may lead to increased costs to assure compliance with the REMS and with additional post-approval regulatory requirements and potential requirements or restrictions on the sale of approved products, all of which could lead to lower sales volume and revenue. In addition, if we are unable to comply with any REMS imposed on any of our products, we may face additional restrictions, limitations or substantial penalties, any of which may materially adversely affect our business and results of operations.

We, our collaborators and the third-party manufacturers of our drug substance and drug products and our respective facilities are subject to extensive regulations in the manufacture of our products and product candidates, including GMP, and are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with GMPs and other regulations. If we, our collaborators or a regulatory agency discover problems with our approved products or product candidates such as poor control of production processes or other problems with the facility where our products are manufactured or in the manufacturing process, introduction of contaminants, or adverse events of unanticipated severity or frequency, a regulatory agency may impose restrictions on our products, the manufacturer or us or our collaborators, including requiring withdrawal of such products from the market or suspension of manufacturing. If we, our collaborators, our approved products, our product candidates, or the manufacturers for our products or product candidates fail to comply with applicable regulatory requirements, a regulatory agency may, among other things:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw marketing approval;

- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications submitted by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of products, or require that we initiate a product recall.

In addition, we could be adversely affected by several significant administrative law cases decided by the U.S. Supreme Court in 2024. In *Loper Bright Enterprises v. Raimondo*, for example, the U.S. Supreme Court overruled *Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, which for 40 years required federal courts to defer to permissible agency interpretations of statutes that are silent or ambiguous on a particular topic. The U.S. Supreme Court stripped federal agencies of this presumptive deference and held that courts must exercise their independent judgment when deciding whether an agency such as the FDA acted within its statutory authority under the Administrative Procedure Act, or the APA. Additionally, in *Corner Post, Inc. v. Board of Governors of the Federal Reserve System*, the U.S. Supreme Court held that actions to challenge a federal regulation under the APA can be initiated within six years of the date of injury to the plaintiff, rather than the date the rule is finalized. The decision appears to give prospective plaintiffs a personal statute of limitations to challenge longstanding agency regulations. Another decision, *Securities and Exchange Commission v. Jarkesy*, overturned regulatory agencies' ability to impose civil penalties in administrative proceedings. These decisions introduce additional uncertainty into the regulatory process and may result in additional legal challenges to actions taken by federal regulatory agencies, including the FDA and CMS, that we rely on. In addition to potential changes to regulations as a result of legal challenges, these decisions may result in increased regulatory uncertainty and delays and other impacts, any of which could adversely impact our business and operations.

Further, our ability to develop and market new drug products may be impacted by litigation challenging the FDA's approval of another company's drug product. In April 2023, the U.S. District Court for the Northern District of Texas invalidated the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various measures adopted under a REMS. The U.S. Court of Appeals for the Fifth Circuit declined to order the removal of mifepristone from the market but did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone, which the FDA authorized in 2016 and 2021 were arbitrary and capricious. In June 2024, the U.S. Supreme Court reversed that decision after unanimously finding that the plaintiffs (anti-abortion doctors and organizations) did not have standing to bring this legal action against the FDA. On October 11, 2024, the attorneys general of three states (Missouri, Idaho and Kansas) filed an amended complaint in the district court in Texas challenging the FDA's actions. Depending on the outcome of this litigation, our ability to develop new drug product candidates and to maintain approval of existing drug products could be delayed, undermined or subject to protracted litigation.

Finally, with the change in presidential administrations in 2025, there is substantial uncertainty as to how, if at all, the new administration will seek to modify or revise the requirements and policies of the FDA and other regulatory agencies with jurisdiction over our product candidates. The impending uncertainty could present new challenges or potential opportunities as we navigate the clinical development and approval process for our product candidates.

Competing therapies may exist or could be approved that adversely affect the amount of revenue we are able to generate from the sale of ZURZUVAE or any of our other current or future product candidates, if successfully developed and approved.

The biopharmaceuticals industry is highly competitive. There are many public and private companies, universities, governmental agencies and other research organizations actively engaged in the research and development of products that may be similar to our products or product candidates or address similar markets. It is probable that the number of companies seeking to develop products and therapies similar to our products or targeting similar indications will increase. Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and human resources than we do, and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and the commercialization of those treatments. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. We expect competition in the indications we are pursuing will focus on efficacy, safety, convenience, availability, and price. Our commercial opportunity could be reduced or eliminated if our

competitors develop and commercialize products that are perceived to be safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop.

Our competitors also may 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.

Currently, the only pharmacological therapies specifically approved for the treatment of PPD are ZURZUVAE and ZULRESSO. We discontinued commercial availability of ZULRESSO in the U.S. as of December 31, 2024. ZURZUVAE currently competes with the current standard of care for PPD, which commonly consists of psychotherapy; however, patients with moderate or severe symptoms of PPD are often prescribed antidepressant medications such as selective serotonin reuptake inhibitors, or SSRIs, and serotonin and norepinephrine reuptake inhibitors, or SNRIs. ZURZUVAE may also face competition from drugs currently in development, if successfully developed and approved in the future for the treatment of PPD, including potentially LPCN 1154, an oral formulation of the neuroactive steroid brexanolone under development by Lipocine, Inc. under the streamlined 505(b)(2) regulatory pathway, which allows for potential approval of an abbreviated NDA by the FDA, and BRII-296, an intramuscular formulation of brexanolone being developed by Brii Biosciences.

In the field of neuroactive steroids focused specifically on modulation of $GABA_A$ receptors, we also face competition from a number of companies, including Marinus Pharmaceuticals, Inc. (acquired by Immedica Pharma AB), which received FDA approval of ganaxolone, a known $GABA_A$ positive allosteric modulator neuroactive steroid, to treat seizures associated with CDKL5 deficiency disorder, a rare, genetic epilepsy. Other $GABA_A$ competitors include darigabat, which is being developed by Cerevel Therapeutics, Inc. (acquired by AbbVie Inc.) for the treatment of epilepsy and panic disorder.

Our existing collaborations with Biogen and Shionogi, and any future collaborations, may not lead to the successful development or regulatory approval of product candidates or commercialization of products. Our collaborators may have competing priorities, conflicting incentives, or different views than us on key decisions, including regulatory, development or commercialization strategy or appropriate program spending, that may hamper or delay our development and commercialization efforts or increase our costs. Our business may be adversely affected and we may be subject to delays, disputes, or litigation if we and any of our collaborators disagree significantly, if any of our collaborators fails to perform its obligations or terminates our collaboration, or if we are not able to establish future collaborations that we believe to be important to our business on commercially reasonable terms.

Our drug development programs, the commercialization of ZURZUVAE for the treatment of women with PPD, and any potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates in some or all markets.

We and our collaboration partner Biogen achieved regulatory approval in the U.S. of ZURZUVAE for the treatment of adults with PPD, and launched ZURZUVAE for that indication. Our collaboration with Biogen may not lead to successful commercialization of ZURZUVAE in the U.S. or successful development of zuranolone in Biogen's ex-U.S. territory. In the third quarter of 2023, our collaboration partner, Shionogi, filed an NDA in Japan for zuranolone for the treatment of MDD; however, Shionogi may not be successful in obtaining regulatory approval for zuranolone for the treatment of MDD, or if approved, may not be successful in commercializing zuranolone in Japan. Our existing and future collaborations, if any, may also not lead to the successful development and commercialization of ZURZUVAE in other indications or territories or of any other products. Our collaborators face both the same challenges and hurdles that we would face in the development and commercialization of product candidates if we were engaged in the activities solely ourselves, as well as additional challenges related to operating under a collaboration. The efforts under our existing collaborations may not be successful and we may never meet applicable milestones or actually receive any additional milestone payments, profit-share revenue or royalty payments from Biogen or Shionogi. For example, while ZURZUVAE was approved for the treatment of adults with PPD in the U.S., the FDA issued a CRL to the NDA for zuranolone for the treatment of MDD in the U.S. Because we and Biogen have agreed not to pursue further development for zuranolone for the treatment of MDD in the U.S., we will not receive the $150.0 million milestone payment for the first commercial sale of ZURZUVAE for the treatment of MDD in the U.S. Our collaborators may decide to terminate their collaboration with us. For example, in September 2024, after we and Biogen decided to discontinue development of SAGE-324 in essential

tremor, Biogen notified us of its termination of our collaboration agreement solely with respect to SAGE-324 on a worldwide basis, effective February 17, 2025. We are evaluating next steps, if any, for other potential indications of SAGE-324, including seizures in DEEs. We may choose not to further develop SAGE-324 in this or any other indication. Additional risks and uncertainties relating to our collaboration with Biogen are set forth in the Risk Factor above captioned "*Our plans to explore strategic alternatives and our rejection of an unsolicited, non-binding acquisition proposal from Biogen to acquire all of our outstanding shares not owned by Biogen may have a material adverse effect on our business*."

In addition, under most collaborations, including our existing collaborations, a certain degree of control in decision-making is transferred to or shared with our collaborators. Our collaborators may use their decision-making authority to make decisions that could delay, decrease the potential of, or otherwise adversely impact, development of our product candidates or commercialization of approved products. Similarly, where we share decision-making authority, the need to gain alignment on decisions may slow or impede advancement of or appropriate investment in our programs or commercialization of an approved product, and cause us not to be able to meet our timelines or achieve our goals. Our collaborators may have competing priorities or different incentives that cause them to divert resources away from our collaboration, or we may not agree on appropriate spending levels or regulatory, development or commercialization strategy, which could hamper or delay our overall development and commercialization efforts or increase our overall spending. Our collaborators may independently develop, or develop with a competitor, competitive products or may believe that product candidates being evaluated in the collaboration could be competitive with the collaborator's own products. In the case of the collaboration with Biogen, both companies have agreed to certain exclusivity provisions for certain products in specified indications which may limit certain development opportunities outside the collaboration. In addition, if we depend on collaborators for capabilities and funding for major product development efforts or commercialization globally or in key territories then our business may be adversely affected if our collaborator fails to perform its obligations under the agreement or the collaboration terminates. Disputes may also arise with respect to the ownership of rights to technology or products developed with collaborators, which could have an adverse effect on our ability to develop and commercialize any affected product candidate.

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all.

We may not be successful in our efforts to identify or discover additional product candidates beyond our existing product candidates or to file IND applications for clinical development of new compounds at the rate we expect, or we may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

The success of our business depends upon our and our collaborators' ability not only to successfully commercialize existing approved products but also to develop, gain approval of and commercialize products based on our current product candidates and to generate new compounds for development in the future and to successfully complete the non-clinical work necessary to file INDs to pursue clinical development of such new compounds. Our research programs may fail to generate new compounds that meet the standards for non-clinical development. Even if we are successful in generating such compounds, we may not be able to produce the non-clinical and other data necessary to support IND applications for clinical development, in each case in the number or at the rate we expect or at all for a number of reasons. For example, we may not be able to identify a sufficient number of new targets in areas of interest to us. Our research methodology may be unsuccessful in generating a sufficient number of new compounds appropriate for non-clinical testing in the target areas we identify. Even if we generate new compounds in areas of interest to us, we may determine that those compounds are not appropriate for non-clinical development, or we may generate data in non-clinical development that do not support IND filings for clinical development. We may not have, or devote, sufficient technical, financial, and human resources to our research efforts at the various stages needed to identify targets, generate compounds, conduct non-clinical studies and prepare INDs. Additional potential product candidates may be shown to have harmful side effects or may not have a positive risk/benefit profile or may have other characteristics that may make the product candidates not appropriate for further development or unlikely to receive marketing approval. Further, even if we generate new compounds in areas of interest, we may determine that those compounds are not worth pursuing for strategic reasons, including new legislation that may impact the viability of commercializing such compounds, if approved.

Because we have limited financial and management resources, we focus on a limited number of clinical and research programs and product candidates and are currently focused on certain brain health disorders. As a result, we may forego or delay pursuit of opportunities with certain product candidates or for other indications that later prove to have greater commercial potential. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful and may not yield any commercially viable drugs. For example, we recently discontinued development of dalzanemdor and are considering whether to continue development of SAGE-324 in other indications, after our clinical trials for both programs failed to meet their primary endpoints. Our resource allocation decisions may cause us to fail to capitalize on other viable opportunities. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights through future collaborations, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain such sole development and commercialization rights. If any of these events occur, it may have a material adverse effect on our business.

We rely, and expect that we will continue to rely, on third parties to conduct any clinical trials for our product candidates. If these third parties do not successfully carry out their contractual duties, comply with applicable standards and meet expected deadlines, we may not be able to successfully develop and obtain regulatory approval for our product candidates, and our business could be substantially harmed.

We do not have the ability to independently conduct clinical trials. We rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct clinical trials of our product candidates. We enter into agreements with third-party CROs to provide monitors for and to manage data for our ongoing clinical trials. We rely heavily on these parties for execution of clinical trials for our product candidates and control only certain aspects of their activities. As a result, we have less direct control over the conduct, timing and completion of these clinical trials and the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties and shortages, attrition of experienced staff, and other resource constraints;
- fail to comply with contractual obligations;
- fail to comply with current Good Clinical Practices, or GCPs, or experience other regulatory compliance issues;
- undergo changes in priorities or become financially distressed;
- misappropriate our intellectual property;
- form relationships with other entities, some of which may be our competitors; or
- be impacted by changes to the macroeconomic and geopolitical environment or disruptions arising from pandemics or other global heath crises, and the downstream effects of these changes or disruptions.

These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials, and may subject us to unexpected cost increases that are beyond our control. In addition, certain Chinese CROs that supply us with medicinal chemistry and drug metabolism research may become subject to trade restrictions, sanctions, and other regulatory requirements by the U.S. government, including the proposed BIOSECURE Act, any of which could restrict or even prohibit our ability to work with such entities, thereby potentially disrupting our research activities. Such disruption could have adverse effects on the development of our product candidates and our business operations.

Nevertheless, we and our collaborators are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements, and scientific standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. We and our collaborators, clinical investigators, and our CROs are required to comply with regulations and guidelines, including GCPs, for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, or EEA, and comparable foreign regulatory authorities for any product candidates in clinical development or where clinical trials are being

conducted. If we or our CROs or CMOs fail to comply with these regulations or if the quality or accuracy of the clinical data obtained is compromised due to the failure to adhere to our clinical protocols or other regulatory requirements or for other reasons, and we and our collaborators are unable to rely on clinical data collected, we and our collaborators may be required to repeat clinical trials or extend the duration of, or increase the size of, our clinical trials, or we may not be able to rely on the results of our clinical trials. This would delay the regulatory approval process, and could also subject us to enforcement action up to and including civil and criminal penalties. If any of our relationships with third-party CROs terminate or if a CRO needs to be replaced, we may not be able to enter into arrangements with alternative CROs in a timely manner or at all. Any of these issues could significantly delay or prevent regulatory approval of our product candidates and require significantly greater expenditures. In such an event, we believe that our financial results might be harmed, our costs could increase and our ability to generate revenue from products beyond ZURZUVAE could be delayed.

Our future success depends on our ability to attract, retain and motivate qualified personnel.

To accomplish our objectives, we require a strong management team with expertise in research and development, clinical development and commercialization. Although we have entered into employment agreements with each of our executive officers, each of them is employed "at will" and may terminate his or her employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. Recruiting and retaining qualified personnel is critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific personnel from universities and research institutions. Failure to succeed in commercializing approved products or in conducting clinical trials or in obtaining regulatory approval may make it more challenging to recruit and retain qualified personnel. If we are unable to continue to attract and retain high quality personnel, our development efforts, commercialization activities, business, financial condition, results of operations and growth prospects could be adversely affected.

We face potential product liability exposure, and, if claims are brought against us, we may incur substantial liability.

The sale of ZURZUVAE and any future approved products, and the use of our product candidates in clinical trials expose us to the risk of product liability claims. In addition, product liability claims related to ZULRESSO may arise and/or be brought even though we discontinued commercial availability of the product as of December 31, 2024. Product liability claims might be brought against us by patients, healthcare professionals or others using, prescribing, selling or otherwise coming into contact with our products and product candidates. For example, we may be sued if any product or product candidate allegedly causes injury or is found to be otherwise unsuitable during clinical trials, manufacturing, marketing, sale or commercial use. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, including as a result of interactions with alcohol or other drugs, knowledge of risks, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection laws. If we become subject to product liability claims and cannot successfully defend ourselves against them, we could incur substantial liabilities. Regardless of merit or eventual outcome, product liability claims may result in, among other things:

- withdrawal of patients from our clinical trials, or difficulty in enrolling clinical trials;
- substantial monetary awards to patients or other claimants;
- decreased demand for our approved products;
- damage to our reputation and exposure to adverse publicity;
- increased FDA warnings on product labels;
- litigation costs;
- distraction of management's attention from our primary business;
- loss of revenue; and
- withdrawal of products from the market or our inability to successfully gain approval of product candidates.

Although we maintain product liability insurance coverage, our insurance coverage may be insufficient to reimburse us for any expenses or losses we may suffer. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses, including if insurance coverage becomes increasingly expensive. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. The cost of any product liability litigation or other proceedings, even if resolved in our favor, could be substantial, particularly in light of the size of our business and financial resources. A product liability claim or series of claims brought against us could cause our stock price to decline and, if we are unsuccessful in defending such a claim or claims and the resulting judgments or settlements exceed our insurance coverage, our financial condition, business and prospects could be materially adversely affected.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

The Medicaid Drug Rebate Program, which we participate in, and other governmental programs impose obligations to report pricing figures to the federal government, require us to pay rebates and participate in discount programs. Other programs impose limits on the price we or our collaborators are permitted to charge certain entities for ZURZUVAE or for any future products for which we receive regulatory approval. Statutory and regulatory changes or binding guidance regarding these programs and their requirements could negatively affect the coverage and reimbursement by these programs of ZURZUVAE or any future products for which we receive regulatory approval and could negatively impact our results of operations. Our failure to comply with these price reporting and rebate payment obligations could negatively impact our financial results. The Patient Protection and Affordable Care Act, as amended, referred to herein as the ACA, and regulations promulgated thereunder could affect our obligations in ways we cannot anticipate.

Pricing and rebate calculations vary among products and programs. The calculations are complex and are often subject to interpretation by us, governmental or regulatory authorities and the courts. If we become obligated to restate or recalculate the amounts we report under these programs, our costs for complying with the laws and regulations governing the Medicaid Drug Rebate Program and our price discounts and rebates could be increased. Additionally, we could be held liable for errors associated with our submission of pricing data under the Medicaid Drug Rebate Program and other federal or state drug pricing programs, including retroactive rebates and program refunds, and if we are found to have knowingly submitted false average manufacturer price or best price information to the government, we could be subject to civil monetary penalties per item of false information. Certain failures to submit required data could result in a civil monetary penalty for each day the information is late beyond the due date and be grounds for CMS to terminate our Medicaid drug rebate agreement, pursuant to which we participate in the Medicaid program, or, if we fail to comply with 340B program requirements, the Health Resources and Services Administration, or HRSA, could decide to terminate our 340B program participation agreement. In the event that CMS terminates our rebate agreement or HRSA terminates our 340B program participation agreement, no federal payments would be available under Medicaid or Medicare Part B for our covered outpatient drugs. We are also subject to civil monetary and other penalties applicable to the drug pricing negotiation program and Part B and Part D inflation rebate programs, as discussed further below under the risk factor entitled "*Healthcare regulations aimed at reducing healthcare costs may have a material adverse effect on our business or results of operation*."

We are subject to other laws and regulations, which could expose us to investigation, criminal sanctions, civil penalties, administrative penalties, contractual damages, reputational harm and diminished profits and future earnings.

We are subject to a number of healthcare and other statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in the countries in which we currently or may in the future conduct our business.

Our current or future interactions and arrangements with third-party payors, healthcare professionals, patients, healthcare settings, and others who play a role in the recommendation, prescription, reimbursement and administration of ZURZUVAE, and will play a similar role with respect to any of our current or future product candidates, if successfully developed and approved, are governed in part by 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 ZURZUVAE, or expect to market, sell and distribute any future approved products. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- The federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly (including any kickback, bribe or certain rebates), 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 healthcare programs such as Medicare and Medicaid. This statute has been interpreted to apply to arrangements between pharmaceutical companies on the one hand, and prescribers, purchasers and formulary managers, among others, on the other.
- The federal False Claims Act imposes criminal and civil penalties, including those from 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, with potential liability including mandatory treble damages and significant per-claim penalties. Pharmaceutical companies have faced enforcement actions under the False Claims Act in connection with their alleged off-label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes, and allegedly providing free product to customers with the expectation that the customers would bill federal healthcare programs for the product, among other activities. In addition, the government may assert that a claim, including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes privacy, security and breach reporting obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information upon covered entities subject to the rule.
- The federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services.
- The federal transparency requirements, sometimes referred to as the “Sunshine Act”, under the ACA require manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children’s Health Insurance Program to report to CMS information related to physician payments and other transfers of value made to physicians, certain non-physician providers, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.
- Analogous state laws and regulations, such as state anti-kickback and false claims laws and transparency laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare professionals or marketing expenditures and drug pricing.
- Various federal and state health information and data protection laws and regulations, and similar types of laws outside the U.S., govern the collection, use, disclosure and protection of health-related and other personal information by us and our collaborators.

Ensuring that our future practices and business arrangements comply with applicable healthcare laws and regulations is costly. It is possible that governmental authorities will conclude that our business practices and arrangements do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our practices or operations, including activities conducted by our commercial team or other of our employees, consultants or vendors, were 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 and exclusion from government-funded healthcare programs, such as Medicare and Medicaid, any of which could substantially disrupt our operations and materially adversely affect our business and financial condition. We may also be substantially negatively impacted if governmental authorities conclude that the business practices of one of our collaborators does not comply with applicable laws or regulations. If any of the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws or regulations, they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs.

We and our employees are also subject to other statutes and regulations related to our business, including: regulations imposed by the FDA and applicable non-U.S. regulators, as previously discussed; anti-bribery and anti-corruption laws and regulations applicable to activities outside the U.S.; rules on reporting financial and other information or data timely and accurately; and rules related to insider trading.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to regulatory authorities. Regulatory authorities may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected the interpretation of the study. Regulatory authorities may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by regulatory authorities, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

Although we have adopted a code of conduct and have an active compliance program, it is not always possible to identify and deter employee, consultant, vendor or collaborator misconduct, and the precautions we take to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure by such persons to comply with these laws or regulations.

Data collection is governed by restrictive regulations governing the use, processing, and cross-border transfer of personal information. Compliance with these regulations can be time-consuming and onerous. If we are found to have improperly handled personal information, we may become subject to fines and penalties, litigation and reputational harm.

We must comply with numerous federal, state and non-U.S. laws which govern the privacy and security of health and other personal information. As described above, to the extent applicable to our business activities, HIPAA imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. In addition, when we conduct clinical trials in the U.S., any personal information that is collected in connection with these trials also is regulated by the Federal Policy for the Protection of Human Subjects (the Common Rule) which creates obligations for our company when conducting these trials.

We may enroll subjects in our future clinical trials in the EU or other countries. When we do so, we may be subject to additional privacy restrictions, including restrictions relating to the collection, use, storage, transfer, and other processing of personal data, including personal health data, regarding these individuals. Clinical trial activities in the EEA, for example, are governed by the General Data Protection Regulation, or GDPR, in relation to the processing of personal data. The GDPR imposes several requirements on companies that process personal data, strict rules on the transfer of personal data out of the EEA, including to the U.S., and fines and penalties for failure to comply with the requirements of the GDPR and the related national data protection laws of the EU Member States. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR in some situations. The obligations under the GDPR may be onerous and adversely affect our business, financial condition, results of operations and prospects. Compliance with the GDPR is a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with any European activities, including processing of personal data originating from the EU. The issues related to the transfer of personal data are subject to substantial uncertainty at this time, and there can be no reasonable level of confidence that any such data transfers will be found to be consistent with EU law if they are challenged. The exit of the UK from the EU, often referred to as Brexit, has created

uncertainty with regard to future data protection regulation in the UK. The European Commission has adopted an adequacy decision concerning the level of data protection in the UK. Personal data may now flow freely from the EEA to the UK; however, the European Commission may suspend the adequacy decision if it decides that the UK no longer provides for an adequate level of data protection. Similar laws exist in many other countries around the world, and these laws (which are evolving and expanding) create complicated and potentially inconsistent obligations that may impact our business.

We are also subject to the California Consumer Privacy Act, as amended by the California Privacy Rights Act, or the CCPA, which creates individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. While there is currently an exception for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact our business activities. Failure to comply with the CCPA may result in, among other things, significant civil penalties and injunctive relief, or statutory or actual damages. In addition, California consumers have the right to bring a private right of action in connection with certain types of incidents. These claims may result in significant liability and damages.

In addition to California, several other states have passed comprehensive privacy laws similar to the CCPA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data, which includes health data in some cases. Some of the provisions of these laws may apply to our business activities. Other states will be considering similar laws in the future. There are also states that are specifically regulating health information that may affect our business. For example, Washington state passed a health privacy law that will regulate the collection and sharing of health information, and the law also has a private right of action. Connecticut and Nevada have also passed similar health-specific consumer privacy laws. These laws and regulations are constantly evolving and may impose limitations on our business activities.

Plaintiffs' lawyers are also increasingly using privacy-related statutes at both the state and federal level to bring lawsuits against companies for their data-related practices. In particular, there have been a significant number of cases filed against companies for their use of pixels and other web trackers. These cases often allege violations of the California Invasion of Privacy Act and other state laws regulating wiretapping, as well as the federal Video Privacy Protection Act. The rise in these types of lawsuits creates potential risk for our business.

In addition, there are substantial efforts at the federal level to pass a national data privacy law that may impact our business activities. The uncertainty, ambiguity, complexity and potential inconsistency surrounding the implementation and interpretation of laws at the state and federal levels exemplify the vulnerability of our business to the evolving regulatory environment related to the privacy, security and confidentiality of personal data and consumer health information. We may be subject to fines, penalties, or private actions in the event of non-compliance with such laws. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products. We have implemented processes to manage compliance with applicable laws and continue to assess their impact on our business as additional information and guidance becomes available.

In addition to the foregoing, any breach of privacy laws or data security laws, particularly resulting in a significant security incident or breach involving the misappropriation, loss or other unauthorized use or disclosure of sensitive or confidential patient or consumer information, could have a material adverse effect on our business, reputation and financial condition. As a data controller, we will be accountable for any third-party service providers we engage to process personal data on our behalf, including our CROs. There is no assurance that privacy and security-related safeguards we implement will protect us from all risks associated with the third-party processing, storage and transmission of such information. In certain situations, both in the U.S. and in other countries, we also may be obligated as a result of a security breach to notify individuals and/or government entities about these breaches.

The FDA and other regulatory and enforcement agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found to have improperly promoted off-label uses, we may become subject to significant liability.

The FDA and other regulatory and enforcement authorities strictly regulate the promotional claims that may be made about prescription products, and enforce laws and regulations prohibiting the promotion of unapproved, or "off-label" uses. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory authorities as reflected in the approved labeling of the product. For example, ZURZUVAE is approved in the U.S. for the treatment of adults with PPD only and may not be promoted for any uses that are not approved by the FDA, including MDD. If we are found to have promoted off-label uses for any product, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has taken steps to restrict promotional activities of those companies. Pharmaceutical companies have also been prosecuted and incurred significant civil, criminal and administrative penalties, damages, and fines under the False Claims Act in connection with their alleged off-label promotion of drugs. Any promotion of the off-label use of ZURZUVAE or any of our other products by us or any of our employees could subject us to significant liability, which would materially adversely affect our business and financial condition.

We will need to carefully navigate the FDA's various regulations, guidance and policies, along with recently enacted legislation, to ensure compliance with restrictions governing promotion of our products. In September 2021, the FDA published final regulations which describe the types of evidence that the Agency will consider in determining the intended use of a drug or biologic. Moreover, with passage of the Pre-Approval Information Exchange Act in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. In addition, in January 2025, the FDA published final guidance outlining its policies governing the distribution of scientific information to healthcare providers about unapproved uses of approved products. The final guidance calls for such communications to be truthful, non-misleading and scientifically sound and to include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use of the approved product. If a company engages in such communications consistent with the guidance's recommendations, the FDA indicated that it will not treat such communications as evidence of unlawful promotion of a new intended use for the approved product. While this guidance only applies to communications about unapproved uses of approved products, it may be helpful in understanding the FDA's approach to communications about unapproved products.

Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens, price controls, reimbursement issues and other risks and uncertainties, and could negatively impact our U.S. business.

Our future profitability may depend, in part, on our ability, ourselves or through our collaborators, to commercialize our products and product candidates in foreign markets.

The pricing of prescription pharmaceuticals in foreign markets is subject to foreign governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of regulatory approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our or our collaborators' ability to generate revenues and become profitable could be impaired. In addition, these factors could impact our or our collaborators' decision on whether to commercialize a product candidate, even if successfully developed and approved.

In some countries, including Member States of the EU, the pricing of prescription drugs is subject to governmental control. Additional countries may adopt similar approaches to the pricing of prescription drugs. There can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various countries and parallel distribution, or arbitrage between low-priced and high-priced countries, can further reduce prices. In the U.S., recent legislative and administrative policies and proposals signal a desire to lower drug prices in the U.S. As a result, we or our collaborators outside the U.S. in the future may be limited in the prices we are able to charge for our

products in the U.S. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales by us or our collaborators and the potential profitability of our products in those countries would be negatively affected.

Commercializing our products and product candidates in foreign markets would subject us to additional risks and uncertainties, including:

- our inability to directly control commercial activities to the extent we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements, including the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- reduced protection of intellectual property rights, and the existence of additional potentially relevant third-party intellectual property rights, in some foreign countries; and
- foreign currency exchange rate fluctuations.

Foreign sales of our product candidates could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs. For example, Brexit has already and may continue to adversely affect European and/or worldwide regulatory conditions. Brexit could continue to lead to legal uncertainty and potentially divergent national laws and regulations in the EU and the UK, including those related to the pricing of prescription pharmaceuticals, as the UK determines which EU laws to replicate or replace, which could impair our ability to transact business in the EU and the UK in the future, if we elect to seek to commercialize any of our products there.

Risks Related to Our Intellectual Property Rights

If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents that are sufficient to protect our product candidates, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.

We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking patents intended to cover our products and compositions, their methods of use and any other inventions that are important to the development of our business. We may also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents, should they issue; preserve the confidentiality of our trade secrets; and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain the proprietary position of our product candidates.

We cannot provide any assurances that any of our pending patent applications will mature into issued patents. For example, the U.S. Patent and Trademark Office, or U.S. PTO, has issued a final rejection against one of our patent applications claiming one of our proprietary $GABA_A$ positive allosteric modulator compounds, asserting a lack of novelty and non-obviousness. We are in the process of appealing the rejection, and may not be successful in overturning the rejection.

We may be unable to obtain issued patents covering our proprietary compounds. We cannot provide any assurances that any of our issued patents will be enforceable, or include claims with a scope sufficient to protect our product

candidates or otherwise provide any competitive advantage. For example, the issued patent and patent applications that provide coverage for ZULRESSO only cover particular formulations and particular methods of using such formulations to treat depressive disorders such as PPD and MDD. As a result, such issued patent and any patent that may issue from such patent applications, would not prevent third-party competitors from creating, making and marketing alternative formulations of brexanolone that fall outside the scope of the patent claims or from practicing alternative methods. Moreover, other parties have developed technologies that may be related or competitive to our approach, and may have filed or may file patent applications and may have received or may receive patents that may overlap or conflict with our patent applications, either by claiming the same methods or formulations or by claiming subject matter that could dominate our patent position. Such third-party patent positions may limit or even eliminate our ability to obtain patent protection for certain inventions.

The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, and, therefore, the issuance, scope, validity and enforceability of any patent claims that we may obtain cannot be predicted with certainty. Patents, if issued, may be challenged, deemed unenforceable, invalidated, or circumvented. U.S. patents and patent applications may also be subject to interference proceedings, derivation proceedings, *ex parte* reexamination, or *inter partes* review proceedings, post-grant review proceedings, supplemental examination and challenges in district court. Patents may be subjected to opposition, post-grant review, or comparable proceedings lodged in various foreign, both national and regional, patent offices. These proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such proceedings may be costly. For example, certain of our granted patents have, in the past, been opposed by third parties, and further such proceedings in the future could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. Thus, any patents, should they issue, that we may own or exclusively license may not provide any protection against competitors. Furthermore, an adverse decision in an interference proceeding or a derivation proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize our product candidates. Furthermore, though a patent, if it were to issue, is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability, and it may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Even if a patent issues, and is held to be valid and enforceable, competitors may be able to design around our patents, such as using pre-existing or newly developed technology. Other parties may develop and obtain patent protection for more effective technologies, designs or methods.

We also may not be able to prevent the unauthorized disclosure or use of our technical knowledge or trade secrets by consultants, vendors, former employees and current employees. The laws of some foreign countries do not protect our proprietary rights to the same extent as the laws of the U.S., and we may encounter significant problems in protecting our proprietary rights in these countries. If these developments were to occur, they could have a material adverse effect on our sales if any of our product candidates are approved in those countries. Our ability to enforce our patent rights depends on our ability to detect infringement. It is difficult to detect infringers who do not advertise the components that are used in their products. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product. Any litigation to enforce or defend our patent rights, even if we were to prevail, could be costly and time-consuming, and would divert the attention of our management and key personnel from our business operations. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

In addition, proceedings to enforce or defend our patents, if and when issued, could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any of our patents, if and when issued, covering our product or product candidates is invalidated or found unenforceable, our financial position and results of operations may be materially and adversely impacted. In addition, if a court found that valid, enforceable patents held by third parties covered our product candidates, our financial position and results of operations may also be materially and adversely impacted.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our pending patent applications, if issued as a patent, will include claims having a scope sufficient to protect our current product candidates or any other products or product candidates;
- any of our pending patent applications will issue as patents at all;
- we will be able to generate significant revenue from sales of ZURZUVAE or any of our product candidates, if successfully developed and approved, before our relevant patents expire;
- we were the first to make the inventions covered by each of our pending patent applications and any patents that may issue in the future;
- we were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe any patents that have been or may be issued to us;
- others will not use pre-existing technology to effectively compete against us;
- any of our patents, if issued or as issued, will provide us with a competitive advantage and be found ultimately to be valid and enforceable;
- any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies or product candidates that are separately patentable; or
- that our commercial activities or products will not infringe upon the patents or proprietary rights of others.

We may rely upon unpatented trade secrets and depend on unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our CROs, collaborators and consultants. It is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees and consultants who are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could otherwise become known or be independently discovered by our competitors.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing ZURZUVAE or any of our product candidates that we may successfully develop.

Our success will depend in part on our ability to operate without infringing the intellectual property and proprietary rights of third parties. We cannot assure you that our business, products and methods do not or will not infringe the patents or other intellectual property rights of third parties. The pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that our products or product candidates or the use of our technologies infringes patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization. As we continue to develop our current product candidates and commercialize ZURZUVAE and any future products, competitors may claim that our technology infringes their intellectual property rights as part of business strategies designed to impede our successful commercialization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, third parties may have currently pending patent applications which may later result in issued patents that our products or product candidates may infringe, or which such third parties claim are infringed by our technologies. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a

material adverse effect on us. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. Patent litigation is costly and time-consuming. Any claim relating to intellectual property infringement that is successfully asserted against us may require us to pay substantial damages, including treble damages and attorney's fees if we are found to be willfully infringing another party's patents, for past use of the asserted intellectual property and royalties and other consideration going forward if we are forced to take a license. In addition, if any such claim were successfully asserted against us and we could not obtain such a license, we may be forced to stop or delay developing, manufacturing, selling or otherwise commercializing our product or product candidates. In the case of trademark claims, if we are found to be infringing, we may be required to redesign, or rename, some or all of our product candidates to avoid infringing the intellectual property rights of third parties, which may not be possible and, even if possible, could be costly and time-consuming. Even if we are successful in these proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us.

Any of these risks coming to fruition could have a material adverse effect on our business, results of operations, financial condition and prospects.

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

We enter into confidentiality and intellectual property assignment agreements with our employees, consultants, CROs, outside scientific collaborators, and other advisors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and/or may not effectively assign intellectual property rights to us. For example, even if we have a consulting agreement in place with an academic advisor pursuant to which such academic advisor is required to assign to us any inventions developed in connection with providing services to us, such academic advisor may not have the right to assign such inventions to us, as it may conflict with his or her obligations to assign all such intellectual property to his or her employing institution or another party.

Most of our employees have also been previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We also engage advisors and consultants who are concurrently employed at universities or who perform services for other entities. We may be subject to claims that an employee, advisor or consultant performed work for us that conflicts with that person's obligations to a third party, such as an employer, and thus, that the third party has an ownership interest in the intellectual property arising out of work performed for us.

Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees, which could have a material adverse effect on our business.

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

The U.S. PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other formalities and provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming, and unsuccessful.

Even if the patent applications we own or license are issued, competitors may infringe these patents. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable and/or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents should be interpreted narrowly and do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings or derivation proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the U.S.

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

Issued patents covering our products or any of our product candidates could be found invalid or unenforceable if challenged in court.

If we or one of our collaborators or licensors initiated legal proceedings against a third party to enforce a patent, if and when issued, covering our products or any of our product candidates, the defendant could counterclaim that the patent covering our products or any of our product candidates is invalid and/or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory and non-statutory requirements, including lack of novelty, obviousness, non-statutory obviousness type double patenting, lack of written description, or non-enablement. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld relevant information from the U.S. PTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the U.S. or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *ex parte* reexamination, *inter partes* review, derivation proceedings or interferences and equivalent proceedings in foreign jurisdictions, e.g., opposition or revocation proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. Certain of our granted patents have, in the past, been opposed by third parties, and further such proceedings in the future could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on the applicable product or product candidates. Such a loss of patent protection could have a material adverse impact on our business.

We will not seek to protect our intellectual property rights in all jurisdictions throughout the world, and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing patent applications and prosecuting and defending patents on products and product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. could be less extensive than those in the U.S., assuming that rights are obtained in the U.S. In

addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the 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. The statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority date of each of our patent applications.

Competitors may use our technologies in jurisdictions where we do not pursue patent protection. They may pursue and obtain their own patent protection to develop their own products. Further, they 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. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the U.S. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biotechnology and pharmaceuticals. For example, a 2024 report from the Office of the U.S. Trade Representative identified a number of countries, including India and China, where challenges to the procurement and enforcement of patent rights have been reported. Several countries, including India and China, have been listed in the report every year since 1989. This could make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of our other intellectual property rights in such jurisdictions. Many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

Furthermore, proceedings to enforce our patent rights in foreign jurisdictions could, among other things, 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 rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

For certain of our products and product candidates, we are dependent on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing certain of our products or product candidates, if approved. If we breach any of the agreements under which we license the use, development and commercialization rights to our products, product candidates or technology from third parties or, in certain cases, we fail to meet certain development deadlines, we could lose license rights that are important to our business.

We are a party to a number of license agreements under which we are granted rights to intellectual property that are important to our business and we expect that we may need to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose on us, various development, regulatory and/or commercial diligence obligations, payment of milestones and/or royalties and other obligations. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license. Our business could suffer, for example, if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms.

As we have done previously, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we cannot provide any assurances that third-party patents do not exist that might be enforced against our current product candidates or future products in the absence of such a license. We may

fail to obtain any of these licenses on commercially reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. If we fail to obtain a license, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under licenses or collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully commercialize the relevant product or to successfully develop and commercialize the affected product candidates.

We have entered into several licenses to support our various programs. We may enter into additional licenses to third-party intellectual property that are necessary or useful to our business. Our current licenses and any future licenses that we may enter into impose various royalty payment, milestone, and other obligations on us. For example, the licensor may retain control over patent prosecution and maintenance under a license agreement, in which case, we may not be able to adequately influence patent prosecution or prevent inadvertent lapses of coverage due to failure to pay maintenance fees. If we fail to comply with any of our obligations under a current or future license agreement, the licensor may allege that we have breached our license agreement, and may accordingly seek to terminate our license. In addition, future licensors may decide to terminate their licenses with us at will. Termination of any of our current or future licenses could result in our loss of the right to use the licensed intellectual property, which could materially adversely affect our ability to develop a product candidate or commercialize a product, as well as harm our competitive business position and our business prospects.

In addition, if our licensors fail to abide by the terms of the license, if the licensors fail to prevent infringement by third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms, our business could materially suffer.

Some intellectual property which we have licensed, or may in the future license, may have been discovered through government-funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements, and a preference for U.S. industry. Compliance with such regulations may limit our exclusive rights, subject us to expenditure of resources with respect to reporting requirements, and limit our ability to contract with non-U.S. manufacturers.

Some of the intellectual property rights we have licensed, or may in the future license, may have been generated through the use of U.S. government funding and may therefore be subject to certain federal regulations. For example, some of the intellectual property rights licensed to us under the license agreement with The Regents of the University of California may have been generated using U.S. government funds. As a result, the U.S. government may have certain rights to intellectual property embodied in our current product or current or future product candidates pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act. These U.S. government rights in certain inventions developed under a

government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if the government determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if we fail, or the applicable licensor fails, to disclose the invention to the government and/or file an application to register the intellectual property within specified time limits. In addition, the U.S. government may acquire title to these inventions in any country in which a patent application is not filed within specified time limits. Intellectual property generated under a government-funded program is also subject to certain reporting requirements, compliance with which may require us, or the applicable licensor, to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the U.S. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the U.S. or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property.

If we enter into future arrangements involving government funding, and we discover compounds or product candidates as a result of such funding, intellectual property rights to such discoveries may be subject to the applicable provisions of the Bayh-Dole Act.

If we do not obtain new chemical entity or other types of marketing and data exclusivity for our product candidates and if we do not obtain additional protection under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act, and similar foreign legislation by extending the patent terms of our product candidates, our business may be materially harmed.

Marketing exclusivity provisions under the Federal Food, Drug, and Cosmetic Act, or FDCA, can delay the submission or the approval of certain marketing applications by other companies for a product with the same active moiety as a product we sell or may in the future sell. The FDCA provides a five-year period of non-patent marketing exclusivity within the U.S. to the first applicant to obtain approval of an NDA for a new chemical entity, or NCE. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for a full NDA, or supplement to an existing NDA, if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application (e.g., new indications, dosages or strengths of an existing drug). This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. We have obtained NCE exclusivity for brexanolone and zuranolone and plan to seek NCE exclusivity for our current and future product candidates. The NCE exclusivity for brexanolone expired in June 2024, five years following approval of ZULRESSO. Lipocine, Inc. is currently developing LPCN 1154, an oral formulation of brexanolone, under the streamlined 505(b)(2) regulatory pathway, which allows for potential approval of an abbreviated NDA by the FDA. There is no guarantee that our product candidates will qualify for marketing or data exclusivity under these provisions or that such exclusivity for any of our products will alone be sufficient for our business. The applicable five-year and three-year exclusivity periods of NCE or data exclusivity under the FDCA will not delay the submission or approval of a full NDA.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of the U.S. patents we own or license may be eligible for limited patent term restoration in the future under the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. Even if, at the relevant time, we have a valid issued patent covering our product, we may not be granted an extension if we were to fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less

than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, and we do not have any other exclusivity, our competitors may obtain approval of competing products following our patent expiration and our business, financial condition or results of operations could be adversely affected.

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

Our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involves both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the U.S. has recently enacted wide-ranging patent reform legislation: the Leahy-Smith America Invents Act, referred to as the America Invents Act. The America Invents Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. It is not yet clear what, if any, impact the America Invents Act will have on the operation of our business. However, 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 any patents that may issue from our patent applications, all of which could have a material adverse effect on our business and financial condition.

In addition, 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. For example, in March 2012, in *Mayo Collaborative Services, DBA Mayo Medical Laboratories, et al. v. Prometheus Laboratories, Inc.*, the U.S. Supreme Court held that several claims drawn to measuring drug metabolite levels from patient samples and correlating them to drug doses were not patentable subject matter. The decision appears to impact diagnostics patents that merely apply a law of nature via a series of routine steps and it has created uncertainty around the ability to obtain patent protection for certain inventions. Additionally, in June 2013, in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, the U.S. Supreme Court held that claims to isolated genomic DNA are not patentable, but claims to complementary DNA molecules are patent eligible because they are not a natural product. In June 2014, in *Alice Corporation Pty. Ltd. v. CLS Bank International, et al.*, a case involving patent claims directed to a method for mitigating settlement risk, the U.S. Supreme Court held that the patent eligibility of claims directed to abstract ideas, products of nature, and laws of nature should be determined using the same framework set forth in *Prometheus*. The U.S. PTO has issued a set of guidelines setting forth procedures for determining subject matter eligibility of claims directed to abstract ideas, products of nature, and laws of nature in line with the *Prometheus*, *Myriad*, and *Alice* decisions. The guidance does not limit the application of *Myriad* to DNA but, rather, applies the decision to other natural products. The full impact of these decisions on our business is not yet known.

In May 2023, the Supreme Court, in *Amgen Inc. v. Sanofi, et al.*, held that claims to a functionally-defined genus of monoclonal antibodies were invalid due to a lack of enablement, as they failed to provide adequate guidance for making and using the claimed antibodies. The Supreme Court noted that the general principle remains that all claims must be enabled to their "full scope" and that broader claims require more enablement.

In addition to increasing uncertainty with regard to our ability to obtain future patents, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on these and other decisions by the U.S. Congress, the federal courts and the U.S. PTO, the laws and regulations governing patents, including patent terms, could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce any patents that may issue in the future.

With passage of the CREATES Act, we are exposed to possible litigation and damages by competitors. In addition, existing statutes, including the CREATES Act, and proposed legislation in Congress, if passed into law, could limit the patent exclusivity on our products or facilitate earlier entry of generic competition.

Under the CREATES Act, legislation intended to facilitate the development of generic and biosimilar products, we are exposed to possible litigation and damages by competitors who may claim that we are not providing sufficient quantities of our approved products on commercially reasonable, market-based terms for testing in support of their ANDAs and 505(b)(2) applications. Such litigation would subject us to litigation costs, damages and reputational harm, which could lead to lower revenues. Increased risk of generic competition with ZURZUVAE and any of our product candidates, if approved, including as a result of the CREATES Act, could impact our ability to maximize product revenue.

In addition, members of Congress have proposed numerous legislative initiatives aimed at limiting the patent exclusivity on drug products or facilitating earlier entry of generic versions of approved drugs. Examples of bills that have been proposed include a bill that, if passed, would create a presumption of invalidity for patents beyond the first patent covering a drug product thus shifting the burden to the innovator to prove that these subsequent patents are separately patentable inventions, distinct from the first patent; a bill that, if passed, would empower the Federal Trade Commission to investigate whether large patent portfolios covering a drug product constitute an anti-competitive practice and to file antitrust lawsuits in such instances; and a bill that, if passed, would limit the availability of a 30-month stay on approval by the FDA of a generic version of a drug to only those instances where the ANDA litigation involves a composition of matter patent claiming the drug substance. Such legislation, if passed into law, could adversely affect ZURZUVAE or any future products or product candidates or result in earlier entry into the market of generic versions of our drugs.

Risks Related to our Industry

Healthcare regulations aimed at reducing healthcare costs may have a material adverse effect on our business or results of operations.

There have been, and likely will continue to be, legislation and legislative, administrative and regulatory proposals in the U.S., both at the federal and state level, and in many foreign jurisdictions, aimed at reducing healthcare costs. The implementation of cost containment measures, drug pricing controls or other reforms could have an adverse effect on our revenue from ZURZUVAE or from the sales of any other future products that are successfully developed and approved, and may limit our ability to achieve profitability.

For example, the ACA substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry. The ACA, among other things, subjects biological products to potential competition by lower-cost biosimilars, provided a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% (pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D (subsequently modified by the Inflation Reduction Act of 2022, or IRA, as discussed below).

The Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031. Pursuant to the Coronavirus Aid, Relief and Economic Security Act and subsequent legislation, these Medicare sequester reductions were reduced and suspended, with the current 2% rate of sequestration resuming in July 2022. The rate of sequestration is currently set at 2%, will increase to 2.25% for the first half of fiscal year 2030, to 3% for the second half of fiscal year 2030, and to 4% for the remainder of the sequestration period that lasts through the first six months of fiscal year 2031. These and other laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our products or product candidates for which we may obtain regulatory approval or the frequency with which any such product is prescribed or used.

Certain provisions of the ACA have been subject to judicial challenges as well as efforts to modify them or to alter their interpretation or implementation. For example, the U.S. Tax Cuts and Jobs Act of 2017 included a provision repealing the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." We expect that the ACA, its implementation, efforts to challenge or modify the ACA or its implementing regulations, or portions thereof, and other healthcare reform measures that may be adopted in the future, could have a material adverse effect on our industry generally and on our ability to commercialize our products and product candidates, if approved.

There has been increasing legislative and enforcement interest in the U.S. with respect to drug pricing practices. Specifically, there have been several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing; reduce the cost of prescription drugs, including under Medicare and Medicaid, which may potentially impact negotiations on pricing and discounts with commercial payors; review the relationship between pricing and manufacturer patient programs; and reform government program reimbursement methodologies for drugs. There have been multiple Congressional and administrative efforts to address drug pricing, including the IRA. It is unclear whether any other legislation or public policy will come to pass, and if so, what effect it could have on our business.

The IRA has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for certain outpatient prescription drug coverage, as well as Medicare Part B. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare, with negotiated prices subject to a cap and first set to take effect in 2026; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (the first Part B inflation rebate period was in the first quarter of 2023; the first Part D inflation rebate period was the fourth quarter of 2022 through the third quarter of 2023); and replaces the Part D coverage gap discount program with a new Part D discounting program, which began in 2025. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years of these programs. Manufacturers may be subject to civil monetary penalties for certain violations of the negotiation and inflation rebate provisions and an excise tax during a noncompliance period under the negotiation program.

Specifically, with respect to price negotiations, Congress authorized CMS to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. Drugs may be selected for negotiation only once they are at least seven years post-approval (such that they will be nine years post-approval when first subject to the maximum negotiated price) and biologics may be selected for negotiation 11 years post approval (such that they will be 13 years post-approval when first subject to the maximum negotiated price). It does not apply to drugs and biologics that have orphan drug designation and have been approved for a single rare disease or condition. We could be at risk of government action for any noncompliance with the price negotiation program if, in the future, any of our products are the subject of Medicare price negotiations. In that event, the outcome of the Medicare price negotiations, which will be made publicly available, may also impact negotiations on pricing and discounts with commercial payors.

The first cycle of negotiations for the Medicare Drug Price Negotiation Program commenced in the summer of 2023. On August 15, 2024, HHS published the results of the first Medicare drug price negotiations for ten selected drugs that treat a range of conditions, including diabetes, chronic kidney disease, and rheumatoid arthritis. The prices of these ten drugs are scheduled to become effective January 1, 2026. On January 17, 2025, CMS announced its selection of 15 additional drugs covered by Part D for the second cycle of negotiations by February 1, 2025. While there had been some questions about the Trump Administration's position on this program, CMS issued a public statement on January 29, 2025, declaring that lowering the cost of prescription drugs is a top priority of the new administration and CMS is committed to considering opportunities to bring greater transparency in the negotiation program. The second cycle of negotiations with participating drug companies will occur during 2025, and any negotiated prices for this second set of drugs will be effective starting January 1, 2027.

These risks as to pricing may further heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if the pricing of any of our products are the subject of Medicare price negotiations. As a result, these risks may also impact the development decisions we make with respect to our products and product candidates, including zuranolone.

Further, the IRA subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the IRA by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law. The IRA also requires manufacturers to pay rebates for drugs reimbursed under Medicare Part B or Part D whose price increases exceed inflation and caps Medicare Part D out-of-pocket drug costs beginning in 2025, at $2,000 a year, subject to an adjustment for inflation thereafter. Drug manufacturers may also be subject to civil monetary penalties with respect to their compliance with these programs.

It is unclear how the IRA will be implemented. Several pharmaceutical companies, as well as the U.S. Chamber of Commerce, and the Pharmaceutical Research and Manufacturers of America, or PhRMA, have filed lawsuits against HHS and CMS asserting that, among other things, the IRA's drug price negotiation program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the U.S. Constitution and is otherwise unlawful. HHS has generally won the substantive disputes in these cases, and various federal district court judges have expressed skepticism regarding the merits of the legal arguments being pursued by the pharmaceutical industry. Certain of these cases are now on appeal and, on October 30, 2024, the U.S. Court of Appeals for the Third Circuit heard oral argument in three of these cases. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results. We further cannot predict with certainty what impact the IRA or any other federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition. There may be additional Congressional and administrative efforts to address drug pricing.

At the state level, legislatures have increasingly passed legislation and agencies have implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and price transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Additionally, some individual states have begun establishing Prescription Drug Affordability Boards, or PDABs, to conduct affordability reviews for certain drugs, including high-cost drugs and drugs with qualifying price increases. In some states, the PDAB has authority to set upper payment limits on what certain purchasers and payers may pay or reimburse for drugs that are found to pose an affordability challenge in the state. If one of our products is selected for an affordability review and subject to an upper payment limit by a PDAB, it could have a material adverse effect on our ability to commercialize the product and achieve the full value of our patents.

In addition, in October 2020, the HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program to import certain prescription drugs from Canada into the U.S. That regulation was challenged in a lawsuit by PhRMA, but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue the HHS. Seven states (Colorado, Florida, Maine, New Hampshire, New Mexico, Texas and Vermont) have passed laws allowing for the importation of drugs from Canada. North Dakota and Virginia have passed legislation establishing workgroups to examine the impact of a state importation program. As of October 2024, five states (Colorado, Florida, Maine, New Hampshire and New Mexico) had submitted Section 804 Importation Program proposals to the FDA. Vermont has submitted a concept letter to the HHS. On January 5, 2024, the FDA approved Florida's plan for Canadian drug importation. Florida now has authority to import certain drugs from Canada for a period of two years once certain conditions are met. Florida will first need to submit a pre-import request for each drug selected for importation, which must be approved by the FDA. The state will also need to relabel the drugs and perform quality testing of the products to meet FDA standards.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at containing or lowering the cost of healthcare or limiting exclusivity periods for pharmaceutical products. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for ZURZUVAE or any of our product candidates, if approved;
- our ability to receive or set a price that we believe is fair for our products;
- our ability to generate revenue and achieve or maintain profitability;
- the amount of taxes that we are required to pay; and
- the availability of capital.

We expect that the measures discussed above, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, lower reimbursement, and new payment methodologies. This could lower the price that we receive for any approved product. Any denial in coverage or reduction in reimbursement from Medicare or other government-funded programs may result in a similar denial or reduction in payments from private payors, which may prevent us from being able to generate

sufficient revenue from sales of ZURZUVAE, successfully commercialize any other products if approved in the future, and achieve profitability.

Our internal computer systems or networks or cloud platforms, or those of our collaborators, our third-party CROs or our other contractors, consultants or service providers, may fail or suffer security breaches, which could result in a material disruption of our development programs, compromise personal or sensitive information related to our business, or cause us to incur significant liabilities which could adversely impact our business.

We are increasingly dependent upon information technology systems, infrastructure and data to operate our business. Despite the implementation of security measures, our internal computer systems and those of our collaborators, our third-party CROs and our other contractors, consultants and service providers are vulnerable to cyber security threats, including damage from unauthorized access, theft, natural disasters, terrorism, war, telecommunication and electrical failures, and system malfunction, or from cyber-attacks by malicious third parties (including the deployment of harmful malware, ransomware, viruses, worms, denial-of-service attacks, supply chain attacks, social engineering schemes and other means to affect service reliability and threaten the confidentiality, integrity and availability of information). In addition, cyber-attacks against us or against third parties we do business with could also utilize phishing attempts, email fraud, or attempts to cause payments, confidential or sensitive information, or other data to be transmitted to an unintended recipient, and could include the use of artificial intelligence, or AI, and machine learning to launch more automated, targeted and coordinated attacks. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs or cause us to have liability for disclosure of personal information of our customers. For example, the loss of clinical trial data for our product candidates could result in delays in our regulatory submission and approval efforts and significantly increase our costs to recover or reproduce the data, if possible. To the extent that any disruption, disaster or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed or prevented.

Moreover, as AI and machine learning technologies evolve and their use increases, we will need to invest in resources to ensure appropriate development and use of any generative AI, or similar technologies, and to develop internal compliance policies and procedures addressing this use, including in response to laws and regulations that may be adopted or interpreted to address these technologies, such as the EU AI Act. Our potential future use and/or development of AI, if applicable, could place us under increased regulatory oversight, exacerbate our risks related to litigation and intellectual property, and augment our existing obligations regarding information security.

We could be required to expend significant amounts of money and other resources to respond to these threats or breaches and to repair or replace information systems or networks or cloud platforms. We also could suffer financial loss or the loss of valuable confidential information. In addition, we could be subject to regulatory actions and/or claims made by individuals and groups in private litigation involving privacy issues related to data collection and use practices and other data privacy laws and regulations, including claims for misuse or inappropriate disclosure of data, as well as unfair or deceptive acts or practices in violation of Section 5(a) of the Federal Trade Commission Act, or the FTC Act. The Federal Trade Commission, or the FTC, expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards. The guidance of the FTC for appropriately securing consumers' personal information is similar to what is required by the HIPAA Security Rule, which establishes national standards for covered entities to protect individuals' electronic personal health information. The HIPAA Security Rule requires covered entities to have appropriate administrative, physical and technical safeguards to help ensure the confidentiality, integrity, and security of electronic protected health information. With respect to privacy, the FTC also sets expectations that companies honor the privacy promises made to individuals about how the company handles consumers' personal information. Any failure to honor promises, such as the statements made in a privacy policy or on a website, may also constitute unfair or deceptive acts or practices in violation of the FTC Act. The FTC is also actively expanding its authority under the "unfairness" prong of Section 5 of the FTC Act through its recent enforcement actions and is especially focused on health data. While we do not intend to engage in unfair or deceptive acts or practices, the FTC has the power to enforce promises as it interprets them, and events that we cannot fully control, such as data breaches, may result in FTC enforcement. Enforcement by the FTC under the FTC Act can result in civil penalties or enforcement actions.

Although we develop and maintain systems and controls designed to prevent these events from occurring and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes are costly and require ongoing monitoring and updating as technologies change and efforts to overcome security measures become increasingly sophisticated. Moreover, we cannot guarantee that our, or our third-party CROs' or our other contractors', consultants' or service providers' security measures will be sufficient to prevent data loss and other security breaches. Despite our efforts, the possibility of these events occurring cannot be eliminated entirely and there can be no assurance that any measures we take will prevent cyber-attacks or security breaches that could adversely affect our business, including security breaches that may remain undetected for extended periods of time, which can substantially increase the potential for a material adverse impact resulting from the breach.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shutdowns, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the Agency have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may delay the availability or responsiveness of regulators throughout the development process, which could negatively impact our ability to advance our programs. For example, such disruptions could 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 and unpredictable.

In addition, disruptions may result from events similar to the COVID-19 pandemic. During the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. In the event of a similar public health emergency in the future, the FDA may not be able to continue its current pace and review timelines could be extended. Regulatory authorities outside the U.S. facing similar circumstances may adopt similar restrictions or other policy measures in response to a similar public health emergency and may also experience delays in their regulatory activities.

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. For example, over the last several 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 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.

Our employees, independent contractors, consultants, collaborators and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and/or requirements and insider trading, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, consultants, collaborators and vendors. Misconduct by these partners could include intentional, reckless and/or negligent conduct or unauthorized activities that violate FDA regulations or similar regulations of comparable foreign regulatory authorities; provide inaccurate information to the FDA or comparable foreign regulatory authorities; fail to comply with manufacturing standards, federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities; fail to comply with state drug pricing transparency filing requirements; fail to report financial information or data accurately; or fail to disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of

clinical trials, which could result in regulatory sanctions and serious harm to our reputation. This could include violations of HIPAA, other U.S. federal and state laws, and requirements of foreign jurisdictions, including the GDPR. We are also exposed to risks in connection with any insider trading violations by employees or others affiliated with us. It is not always possible to identify and deter employee or third-party misconduct, and the precautions we take to detect and prevent these activities may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from significant penalties, governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards, regulations, guidance or codes of conduct. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

Risks Related to Our Financial Position and Need for Capital

We are a biopharmaceutical company that has not generated significant revenue to date. We have incurred significant operating losses since our inception and anticipate that we will incur losses for the foreseeable future.

We are a biopharmaceutical company with only one approved product being commercialized, and we only began generating revenue from product sales in the second quarter of 2019. Biopharmaceutical product development and commercialization are highly speculative undertakings and involve a substantial degree of risk.

We have funded our operations to date primarily through proceeds from sales of common stock, including the sale of stock to Biogen MA Inc., or BIMA; redeemable convertible preferred stock prior to our initial public offering and, to a lesser extent, the issuance of convertible notes. From our inception through December 31, 2024, we had received aggregate net proceeds of $2.8 billion from such transactions. We also received $1.0 billion in upfront payments under our collaborations with Biogen and Shionogi and received a milestone payment under the collaboration agreement with Biogen totaling $75.0 million for the first commercial sale of ZURZUVAE for the treatment of women with PPD. As of December 31, 2024, our cash, cash equivalents and marketable securities were $504.4 million. We have incurred net losses in each year since our inception, except for net income of $606.1 million for the year ended December 31, 2020, reflecting revenue recognized under a collaboration and license agreement with Biogen. Our net loss was $400.7 million for the year ended December 31, 2024, and our accumulated deficit was $3.0 billion as of December 31, 2024.

Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from selling, general and administrative costs associated with our operations. We expect to continue to incur operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. Although we expect that our operating expenses will decrease in 2025 as compared to 2024 as a result of our pipeline prioritization and anticipated cost savings from the October 2024 corporate reorganization, we expect to continue to incur significant operating expenses, particularly as we and our collaboration partner Biogen continue to commercialize ZURZUVAE in the U.S. for the treatment of women with PPD and as we continue work to advance ongoing and future product candidates. We expect these costs will include the costs and expenses associated with: our sales and marketing activities; conducting clinical trials of current and future product candidates; continuing certain research activities; outsourced manufacturing; pursuing potential business development activities; and the impact of future decisions and activities. If we receive marketing approval of any current or future product candidate beyond ZURZUVAE and ZULRESSO for the treatment of PPD, we will incur significant additional sales, marketing and manufacturing expenses. We incur significant legal and accounting costs associated with operating as a public company. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

Our ability to become profitable depends upon our ability to generate product revenue and/or revenue from our collaborations on a sustained basis. We began to generate revenue from product sales in the second quarter of 2019 in conjunction with launch of our product ZULRESSO, which commenced in June 2019. We discontinued commercial availability of ZULRESSO in the U.S. as of December 31, 2024, and as a result will no longer generate additional revenue from ZULRESSO. We began to generate revenue from sales of ZURZUVAE in December 2023. Our ability to generate

significant product and collaboration revenues from our current products and any future approved product depends on a number of factors, including, but not limited to:

- our ability to successfully commercialize, with Biogen, ZURZUVAE for the treatment of women with PPD in the U.S., including our ability to achieve and maintain satisfactory coverage and reimbursement and market acceptance among healthcare providers, patients and third-party payors;
- our ability to successfully complete all ongoing and future clinical trials and non-clinical studies required to file for, and obtain, U.S. and foreign marketing approval for our current or future product candidates; and our ability to file for and receive marketing approval to commercialize our product candidates, if successfully developed; and
- with respect to any product candidate potentially approved in the future, our ability, alone or with collaborators, to commercialize the product by developing and effectively deploying a sales force, and to achieve market acceptance and satisfactory coverage and reimbursement of such product among healthcare providers, patients and third-party payors.

If we are unable to generate significant product revenue and/or revenue from our current collaborations on a sustained basis, we will not become profitable, and may be unable to continue operations without continued funding.

We will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or in light of other strategic considerations. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, the ownership interest of our stockholders in our company will be diluted.

We are currently commercializing ZURZUVAE for the treatment of women with PPD in the U.S. We are also advancing our prioritized pipeline of product candidates through non-clinical and clinical development. Commercializing products and developing additional small molecule products are expensive. In October 2024 and August 2023, we implemented strategic corporate reorganizations to support our goal of long-term business growth. Although we expect that our operating expenses will decrease in 2025 as compared to 2024 as a result of our pipeline prioritization and anticipated cost savings from the October 2024 corporate reorganization, we expect to continue to incur significant operating expenses, particularly as we and our collaboration partner Biogen continue commercialization of ZURZUVAE in the U.S. for the treatment of women with PPD. Our anticipated operating expenses include costs associated with: sales and marketing activities; manufacturing; clinical trials of our current and future product candidates; pursuing potential business development activities; continuation of certain research activities; and the impact of future decisions and activities. We will need to raise additional capital in the future to fund operating needs. Our cash needs will increase further if we choose to pursue additional indications and/or geographies for our product candidates, conduct additional clinical trials for indications we are already pursuing beyond the anticipated trials, identify new potential opportunities or otherwise expand our activities more rapidly than we presently anticipate.

As of December 31, 2024, our cash, cash equivalents and marketable securities were $504.4 million. Based upon our current operating plan, we anticipate that our existing cash, cash equivalents and marketable securities as of December 31, 2024, together with anticipated funding from our ongoing collaborations and estimated revenues, excluding any potential milestone payments we may receive under our collaboration agreements, will support our operations to mid-2027. We have based this estimate on assumptions that may prove to be wrong, such as the revenue that we expect to realize from our collaboration agreement for the continued commercialization of ZURZUVAE. To the extent estimated revenue levels are not realized, we may adjust our operating plan accordingly, including the deferral or reduction of planned operating expenses, as needed. Our current operating plan does not contemplate other development activities we may pursue or that all of the currently planned activities will proceed at the same pace, or that all of the activities will be fully initiated or completed during that time. We may not achieve milestones tied to cash payments to us from our collaboration partners on the timelines we expect or at all, or generate anticipated revenues from sales of ZURZUVAE for the treatment of women with PPD at the levels or on the timelines we expect. We may use available capital resources sooner than we expect under our current operating plan, including as a result of unexpected events or changes in plans. We also may not achieve cost savings from our October 2024 corporate reorganization at the levels we expect. In addition, our operating

plan may change. We may choose to seek additional funds through equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances, licensing or royalty arrangements and arrangements involving other rights or a combination of these or other approaches. In any event, we anticipate we will require additional capital to fund our operations. If current or future economic conditions impact capital markets for an extended period, or if our business prospects are impaired or the capital markets disrupted for any other reason, additional capital may not be available to us on acceptable terms, or at all. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if we believe market conditions are favorable or in light of other strategic considerations.

We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Any time we encounter a major setback in our development or regulatory activities, such as the CRL issued by the FDA related to our NDA for zuranolone for the treatment of MDD, or in our commercialization efforts, or receive negative data from a key clinical program, such as the announcement of negative results from the DIMENSION Study in November 2024, the LIGHTWAVE Study in October 2024, the PRECEDENT Study in April 2024, and the KINETIC 2 Study in July 2024, our stock price is likely to decline, as it did in those instances, which would make a future financing more difficult and potentially more dilutive to our existing stockholders. In addition, future global economic uncertainty, reduced liquidity, capital market disruptions, and other macroeconomic or geopolitical conditions, including future banking crises, or pandemics and other health crises, may potentially make it more difficult for us to raise additional funds on favorable terms. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders. The issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. Failure to obtain capital if and when needed may force us to delay, limit or terminate our product development efforts or other operations, including the commercialization of any approved product.

We could also be required to seek funds through arrangements with collaboration partners or otherwise at an earlier stage than otherwise would be desirable, and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which could have a material adverse effect on our business, operating results and prospects.

To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, the ownership interest of our stockholders in our company will be diluted. For example, in September, 2024, we entered into a Sales Agreement, or the ATM Sales Agreement, with TD Securities (USA) LLC, as sales agent, or TD Cowen, with respect to an "at the market offering" program pursuant to which we may offer and sell shares of our common stock having an aggregate offering price of up to $250.0 million, from time to time through TD Cowen. Any significant sales of shares of our common stock pursuant to the ATM Sales Agreement would result in dilution to our current stockholders.

Debt financing, if available, would increase our fixed payment obligations and 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. The incurrence of indebtedness would result in increased fixed payment obligations, and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through collaborations, strategic partnerships and licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates, our intellectual property, future revenue streams or grant licenses on terms that are not favorable to us.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any approved product, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

Risks Related to Our Common Stock

Market volatility may cause our stock price, and the value of an investment in our stock, to fluctuate.

The market price for our common stock, similar to that of other biopharmaceutical companies, is volatile. The market price of our common stock may fluctuate significantly in response to a number of factors, most of which we cannot control, including, among others:

- the results of our commercialization efforts with respect to ZURZUVAE in the U.S. as a treatment for women with PPD, and our ability to attain and maintain commercial success;
- developments related to the state of our collaborations, Biogen's unsolicited, non-binding acquisition proposal, and our strategic review process;
- plans for, progress of, timing of, changes to, delays in or the results from clinical trials or non-clinical studies of any of our products or product candidates, serious adverse events arising in the course of development or post-marketing, or any delays or major announcements related to such studies or trials;
- the success or failure of any regulatory activities with respect to our existing or future product candidates;
- announcements of new products, technologies, commercial relationships, acquisitions, collaborations or other events by us or our competitors;
- the success or failure of our therapies;
- other developments with respect to our pipeline, including initiation of clinical trials of existing products in additional indications or key decisions of the FDA;
- regulatory or legal developments in the U.S. and other countries;
- adverse developments with respect to our intellectual property portfolio or failure to obtain or loss of exclusivity;
- failure of our future product candidates, if successfully developed and approved, to achieve commercial success;
- fluctuations in stock market prices and trading volumes of similar companies;
- the state of the U.S. and world economies, general market conditions and overall fluctuations in U.S. equity markets, including as a result of U.S. or world events;
- changes in healthcare laws affecting pricing, reimbursement or access;
- variations in our quarterly operating results, including as a result of events beyond our control, such as natural disasters, regional economic downturns, pandemics or other global health crises, social unrest, political instability, terrorism, or acts of war;
- changes in our financial guidance or securities analysts' estimates of our financial performance;
- changes in accounting principles;
- our ability to raise additional capital and the terms on which we can raise it;
- the impact of macroeconomic and geopolitical conditions;
- sales of large blocks of our common stock, including sales by our executive officers, directors and significant stockholders;
- additions or departures of key personnel;
- discussion of us or our stock price by the press and by online investor communities; and
- other risks and uncertainties described in these risk factors.

We are currently subject to legal actions and proceedings, which could distract our management and could result in substantial costs or large judgments against us.

In August 2024, a plaintiff filed a purported federal securities class action lawsuit in the Southern District of New York, or the Securities Class Action, against us and certain of our executive officers alleging violations of U.S. securities laws under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder and seeking an as-yet unspecified amount of damages allegedly sustained by parties who purchased our stock between April 12, 2021 and July 23, 2024, as well as applicable attorneys' fees and costs. In addition, we received a subpoena from the Enforcement Division of the U.S. Securities and Exchange Commission, or the SEC, in October 2024, requesting documents and information related to our NDA for zuranolone for the treatment of MDD, including communications with the FDA and any communications containing material nonpublic information.

At this time, we are unable to predict the outcome of the Securities Class Action or the SEC investigation or reasonably estimate a range of possible losses. If either of these matters were concluded in a manner adverse to us and for which we incur substantial costs or damages not covered by our directors' and officers' liability insurance, such a conclusion could have a material adverse effect on our financial condition and business. In addition, either of these matters could adversely impact our reputation and divert management's attention and resources from other priorities, including the execution of business plans and strategies that are important to our ability to grow our business, any of which could have a material adverse effect on our business.

We have broad discretion in how we use our existing cash and the proceeds from potential future follow-on public offerings, and may not use such cash and proceeds effectively, which could affect our results of operations and cause our stock price to decline.

We have considerable discretion in the use of our cash and the application of the net proceeds from potential future follow-on public offerings. We may use cash and net proceeds for purposes that do not yield a significant return or any return at all for our stockholders. In addition, pending their use, we may invest the net proceeds from any potential future follow-on offerings in a manner that does not produce income or that loses value.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, even one that may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders and the ability of our board of directors to issue preferred stock without stockholder approval. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirers to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

Future sales of our common stock may cause our stock price to decline.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur could significantly reduce the market price of our common stock, and impair our ability to raise adequate capital through the sale of additional equity securities. For example, the 6,241,473 shares of our common stock purchased by BIMA are no longer subject to contractually-agreed lockup periods and volume limitations, the last of which expired on December 31, 2023, and accordingly, BIMA is able to sell these shares without contractual limitations.

Item 1B. Unresolved Staff Comments

None.

Item 1C. Cybersecurity

Risk Management and Strategy

As is the case for similar companies of our size and industry, we may be the target of cyber attacks and other cyber incidents and, therefore, cybersecurity is an important element of our overall enterprise risk management program. We have certain processes to systematically evaluate, identify, address, and manage cybersecurity risks, which are built into our overall risk management program and are designed to help safeguard our information assets and operational integrity from internal and external cyber threats, protect employee information from unauthorized access or attack, as well as secure our networks and systems. Such processes include physical, procedural, and technical safeguards, response plans, and continuity exercises on our systems. We also routinely review our policies and procedures to identify risks and refine our practices. By prioritizing cyber risk comprehension and management, we aim to enhance business resiliency, protect information from unauthorized access or attacks, and secure our digital footprint.

We engage certain external parties, including cybersecurity and privacy firms, to enhance our cybersecurity oversight and risk reduction abilities. We also perform an annual cybersecurity assessment designed to help align our cybersecurity program with industry best practices. In addition, we regularly consult with industry groups, peer organizations, and external executives to assess the cybersecurity threat landscape throughout the year.

Our cybersecurity policies, standards, and procedures include cyber and data breach response plans benchmarked against multiple cybersecurity risk frameworks. Our incident response plan is designed to help coordinate the response to and recovery from cybersecurity incidents and includes processes to identify, investigate, triage, assess the severity of, escalate, contain, and remediate incidents and comply with applicable legal or regulatory obligations. We also regularly perform technical reviews of our systems to help secure our digital environment and confirm software patches are appropriately up-to-date.

To oversee and identify risks from cybersecurity threats associated with our use of third-party service providers, we have implemented a third-party risk management program designed to help protect against information misuse and assess the information technology security measures of potential third parties and business partners. We perform a third-party risk assessment before starting a relationship with certain service providers and utilize a third-party risk intelligence program to monitor the activity of critical vendors following engagement. In addition, we maintain cyber insurance coverage as part of our overall risk mitigation strategy. This cyber insurance coverage may not be sufficient to cover against all claims.

We do not believe that there are currently any risks from cybersecurity threats that are reasonably likely to materially affect us or our business strategy, results of operations or financial condition.

Governance

Our Audit Committee of the Board of Directors provides direct oversight over cybersecurity risk. The Audit Committee receives annual updates from management regarding cybersecurity matters and is notified between such updates regarding significant new cybersecurity threats or incidents, if applicable.

We also have a cybersecurity steering committee responsible for assisting with our overall day-to-day cybersecurity responsibilities and implementing our cybersecurity programs. The cybersecurity steering committee is currently comprised of members of our digital and enterprise capabilities team and is chaired by our executive director of cybersecurity. Among other things, the cybersecurity steering committee:

- reviews our internal controls to help protect our information assets;
- assists with developing practices, procedures, and controls designed to identify, assess, and manage critical cybersecurity programs and risks; and
- works to align our risk governance structure, including policies and procedures, with our business objectives.

The chair of the cybersecurity steering committee, our executive director of cybersecurity, has over 25 years of information technology industry experience, including 20 years focused on cybersecurity, and master's degrees in a cybersecurity discipline and in business administration, in addition to multiple certifications related to information technology and cybersecurity.

In addition, to help prevent and detect cybersecurity threats, we provide all employees, including part-time and temporary employees, with monthly cybersecurity and privacy training, which covers timely and relevant cybersecurity topics, including social engineering, phishing, password protection, confidential data protection, asset use, and mobile security.

Item 2. Properties

Our corporate headquarters are located in Cambridge, Massachusetts. We lease 30,567 square feet of office space in a multi-tenant building pursuant to a lease dated as of January 2024, that will expire on February 28, 2030.

We have entered into other non-material leases and may lease additional space prior to the expiration of our leases to meet the needs of the business.

Item 3. Legal Proceedings

On August 28, 2024, named plaintiff Darren Korver filed a purported federal securities class action lawsuit in the Southern District of New York against us and individuals, Barry E. Greene and Kimi Iguchi, or the Securities Class Action. The complaint in the Securities Class Action alleges violations of U.S. securities laws under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder and seeks an as-yet unspecified amount of damages allegedly sustained by parties who purchased Sage stock between April 12, 2021 and July 23, 2024, as well as applicable attorneys' fees and costs. We deny any allegations of wrongdoing and intend to vigorously defend against the Securities Class Action.

On October 16, 2024, we received a subpoena from the Enforcement Division of the U.S. Securities and Exchange Commission, or the SEC, requesting documents and information related to our new drug application for zuranolone for the treatment of MDD, including communications with the FDA and any communications containing material nonpublic information. We are cooperating with the SEC and intend to continue to provide information responsive to the SEC's requests.

At this time, we are unable to predict the outcome of the Securities Class Action or the SEC investigation or reasonably estimate a range of possible losses.

On January 16, 2025, we commenced litigation against Biogen Inc. and Biogen MA Inc., or together with Biogen Inc., Biogen, in the Delaware Court of Chancery seeking declaratory, injunctive and other relief. The action is captioned Sage Therapeutics, Inc. v. Biogen Inc., et al., C.A. No. 2025-0054-BWD (Del. Ch.). In our complaint, we allege that Biogen breached the standstill provision in the stock purchase agreement we entered into with Biogen on November 27, 2020, or the Biogen Stock Purchase Agreement, by making an unsolicited acquisition proposal and related public disclosures. On this basis, we also sought a temporary restraining order enjoining Biogen from future breaches of the standstill provision. At a hearing held on January 28, 2025, the Court granted our motion for a temporary restraining order against Biogen MA Inc., and entered an implementing order on January 30, 2025, or the TRO Order. Pursuant to the TRO Order, unless consented to by Sage in writing or otherwise ordered by the court, Biogen MA Inc. and its directors, officers, agents, employees, attorneys, representatives, persons in active concert or participation with it, and anyone acting under its direction or control are enjoined from taking any action inconsistent with the Biogen Stock Purchase Agreement's contractual prohibitions against (i) making a public acquisition proposal, (ii) making a private acquisition proposal that is reasonably expected to require public disclosure, or (iii) publicly encouraging any acquisition proposal. Various motions and related items (whether procedural, discovery-related and/or substantive in nature) occur from time to time with respect to this matter. We intend to continue to vigorously pursue our claims against Biogen, but we are unable to predict the outcome of the litigation at this time.

We may from time to time become involved in other legal proceedings relating to claims arising from our ordinary course of business, including claims related to contracts, employment arrangements, operating activities, intellectual property or other matters.

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

On July 18, 2014, our common stock began trading on the Nasdaq Global Market under the symbol "SAGE". Prior to that time, there was no public market for our common stock.

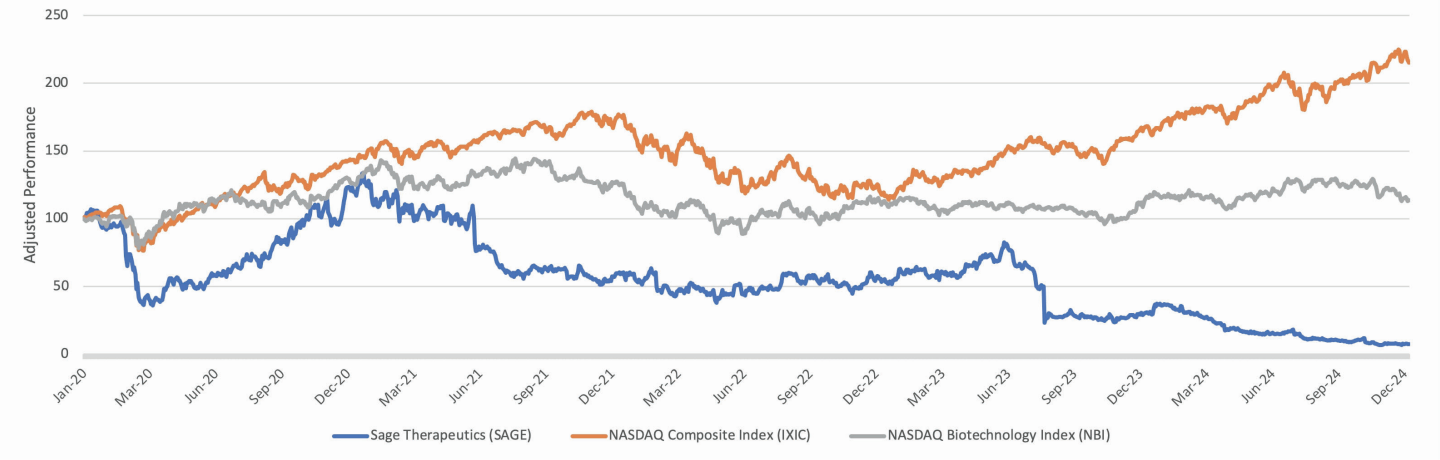
Stockholders

As of February 4, 2025, there were seven stockholders of record of our common stock. The actual number of holders of our common stock 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 or held by other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return for our common stock since January 1, 2020 through December 31, 2024, to two indices: the Nasdaq Composite Index and the Nasdaq Biotechnology Index. The graph assumes an initial investment of $100 on December 31, 2019 in our common stock, the stocks comprising the Nasdaq Composite Index, and the stocks comprising the Nasdaq Biotechnology Index. Historical stockholder return is not necessarily indicative of the performance to be expected for any future periods.

Comparison of Cumulative Total Return*
Among Sage Therapeutics, Inc., the Nasdaq Composite Index and the Nasdaq Biotechnology Index



* $100 invested on December 31, 2019 in stock or index.

The performance graph shall not be deemed to be incorporated by reference by means of any general statement incorporating by reference this Annual Report into any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except to the extent that we specifically incorporate such information by reference, and shall not otherwise be deemed filed under such acts.

Dividend Policy

We have never paid or declared any cash dividends on our common stock, and we do not anticipate paying any cash dividends on our common stock in the foreseeable future. We intend to retain all available funds and any future earnings to fund the development and expansion of our business. Any future determination to pay dividends will be at the discretion of our board of directors and will depend upon a number of factors, including our results of operations, financial condition, future prospects, contractual restrictions, restrictions imposed by applicable law and other factors that our board of directors deems relevant.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report.

Item 6. [Reserved]

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K, for the year ended December 31, 2024, or Annual Report. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. We caution you that forward-looking statements are not guarantees of future performance, and that our actual results of operations, financial condition and liquidity, and the developments in our business and the industry in which we operate, may differ materially from the results discussed or projected in the forward-looking statements contained in this Annual Report. We discuss risks and other factors that we believe could cause or contribute to these potential differences elsewhere in this Annual Report, including under Part I, Item 1A, "Risk Factors" and under "Cautionary Note Regarding Forward-Looking Statements" in this Annual Report. In addition, even if our results of operations, financial condition and liquidity, and the developments in our business and the industry in which we operate are consistent with the forward-looking statements contained in this Annual Report, they may not be predictive of results or developments in future periods. We caution readers not to place undue reliance on any forward-looking statements made by us, as such statements speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the Securities and Exchange Commission, or SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

Information pertaining to fiscal year 2022 was included in the Company's Annual Report on Form 10-K for the year-ended December 31, 2023, on pages 92 through 113, under Part II, Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations," which was filed with the SEC on February 14, 2024.

Overview

We are a biopharmaceutical company with a mission to pioneer solutions to deliver life-changing brain health medicines, so every person can thrive. Alongside our commercial product for the treatment of postpartum depression, we are advancing a portfolio of internally discovered novel chemical entities with the potential to become differentiated treatments designed to improve brain health by primarily targeting two critical central nervous system, or CNS, receptor systems, GABA and NMDA. The GABA receptor family, which is recognized as the major inhibitory neurotransmitter in the CNS, mediates downstream neurologic and bodily function via activation of $GABA_A$ receptors. The NMDA-type receptors of the glutamate receptor system are a major excitatory receptor system in the CNS. Dysfunction in these systems is thought to be at the core of numerous neuropsychiatric and neurodevelopmental disorders.

Our product ZURZUVAE® (zuranolone) was approved by the U.S. Food and Drug Administration, or FDA, on August 4, 2023 for the treatment of postpartum depression, or PPD, in adults. ZURZUVAE is a neuroactive steroid that is a positive allosteric modulator of $GABA_A$ receptors, targeting both synaptic and extrasynaptic $GABA_A$ receptors, and is the first oral, once-daily, 14-day treatment specifically indicated for adults with PPD. ZURZUVAE became commercially available in the U.S. in December 2023 as a treatment option for women with PPD. We and our collaboration partner, Biogen MA Inc., or BIMA, and Biogen International GmbH, or, together with BIMA, Biogen, are jointly commercializing ZURZUVAE in the U.S. under our collaboration and license agreement, or the Biogen Collaboration Agreement, that became effective in December 2020. We and Biogen equally share in all operating profits and losses arising from sales of ZURZUVAE in the U.S., with Biogen recording such product sales.

We jointly commercialize ZURZUVAE with Biogen in the U.S. and have the right to jointly commercialize any additional products containing zuranolone, which, along with ZURZUVAE, we refer to as Licensed 217 Products, if our ongoing and any future development efforts are successful. In addition, we have granted Biogen sole rights to develop and commercialize the Licensed 217 Products outside the U.S., other than in Japan, Taiwan and South Korea, or the Shionogi Territory, with respect to zuranolone, where we have granted such rights to Shionogi & Co., Ltd., or Shionogi. We refer to the territories outside the U.S. to which Biogen has rights under the Biogen Collaboration Agreement with respect to the Licensed 217 Products as the Biogen Territory.

We also have a collaboration agreement with Shionogi for the development of zuranolone in the Shionogi Territory. Shionogi is currently developing zuranolone for the treatment of major depressive disorder, or MDD, in Japan. In the third quarter of 2024, Shionogi reported that it submitted a new drug application, or NDA, in Japan for zuranolone for the treatment of MDD.

Under the Biogen Collaboration Agreement, we and Biogen also previously agreed to jointly develop and commercialize products containing SAGE-324, which we refer to as the Licensed 324 Products.

Following announcement of topline results from the KINETIC 2 Phase 2b clinical trial, which failed to meet its primary endpoint, in September 2024, Biogen notified us of its termination of the Biogen Collaboration Agreement solely with respect to the Licensed 324 Products on a worldwide basis, effective February 17, 2025, or the SAGE-324 Termination. As a result of the SAGE-324 Termination, as of February 17, 2025, all licenses granted by us to Biogen or by Biogen to us regarding the Licensed 324 Products shall expire with respect to the Licensed 324 Products on a worldwide basis. Biogen shall grant to us an irrevocable, perpetual license for any Biogen background technology, Biogen collaboration technology or joint collaboration technology that exists as of February 17, 2025 with respect to the Licensed 324 Products on a worldwide basis, in each case in accordance with the terms of the Biogen Collaboration Agreement. We and Biogen continue to be responsible for our respective share of costs for ongoing activities related to the Licensed 324 Products in accordance with the terms of the Biogen Collaboration Agreement until February 17, 2025.

We are evaluating other potential indications for SAGE-324, including seizures in developmental and epileptic encephalopathies, or DEEs, and expect to provide an update on next steps, if any, in mid-2025.

Our other area of focus is SAGE-319, an extrasynaptic-preferring $GABA_A$ receptor positive allosteric modulator, or $GABA_A$ PAM, designed to have a novel pharmacology and a differentiated clinical profile from other $GABA_A$ PAMs in our portfolio. We are currently investigating SAGE-319 as a potential treatment for behavioral symptoms associated with certain neurodevelopmental disorders. We expect to announce data from a Phase 1 multiple ascending dose study of SAGE-319 for behavioral symptoms associated with certain neurodevelopmental disorders by late 2025, and will evaluate next steps, if any, based on these data.

We previously commercialized ZULRESSO® (brexanolone) CIV injection for the treatment of PPD. ZULRESSO is approved in the U.S. for the treatment of PPD in individuals 15 years old and older. ZULRESSO was administered as a continuous intravenous infusion for two and a half days and could only be administered in qualified medically-supervised healthcare settings. Given the complexities and challenges associated with administration of ZULRESSO, use of the product was limited and further reduced as a result of the availability of ZURZUVAE for the treatment of women with PPD. For that reason, we discontinued commercial availability of ZULRESSO in the U.S. as of December 31, 2024.

Additionally, we previously evaluated dalzanemdor in certain cognitive disorders associated with NMDA receptor dysfunction. In November 2024, based on the results of our Phase 2 DIMENSION, LIGHTWAVE, and PRECEDENT Studies, which failed to meet their primary endpoints, we announced that we do not plan to pursue any further development of dalzanemdor.

We expect to continue to focus on the development of product candidates for the treatment of both acute and chronic brain health disorders, including work on allosteric modulation of the $GABA_A$ and NMDA receptor systems in the brain, and are continuing to explore targeted work within our NMDA receptor negative allosteric modulator, or NMDAR NAMs, platform with SAGE-817 and SAGE-039. The $GABA_A$ and NMDA receptor systems are broadly accepted as impacting many neuropsychiatric and neurodevelopmental disorders, spanning disorders of mood, seizure, cognition, anxiety, sleep, pain, and movement, among others. We believe that we may have the opportunity to develop molecules from our internal portfolio with the goal of addressing a number of these disorders in the future, and also believe that we may have opportunity to use our scientific approach to explore targets beyond the $GABA_A$ and NMDA receptor systems and to develop compounds in areas of unmet need outside of brain health.

On January 10, 2025, we received an unsolicited, non-binding acquisition proposal from Biogen to acquire all of our outstanding shares not owned by Biogen for $7.22 per share, or the Biogen Proposal. On January 27, 2025, we announced that our Board of Directors has initiated a process to explore strategic alternatives, and further announced that our Board of Directors unanimously rejected the Biogen Proposal. On January 16, 2025, we commenced litigation against Biogen in the Delaware Court of Chancery seeking to enforce the standstill provision in the stock purchase agreement we entered into with Biogen on November 27, 2020. Our rejection of the Biogen Proposal, our efforts to enforce the terms of the

stock purchase agreement and our strategic review process may adversely impact our relationship with Biogen, including our efforts to commercialize ZURZUVAE for the treatment of women with PPD. We cannot be certain that our efforts to date with Biogen, including regarding sales force coordination, engagement with payors, and education efforts related to PPD, will not be adversely impacted or that Biogen will continue to make investments related to ZURZUVAE. Any disruption of our relationship with Biogen under our collaboration agreement with Biogen may have an adverse impact on sales of ZURZUVAE, which could in turn materially adversely affect our business, results of operations, financial condition and prospects. We have not set a timetable for the strategic review process, nor have we made any decisions related to any potential strategic alternatives at this time. There can be no assurance that our strategic review process will result in any transaction or other strategic outcome. We do not intend to disclose further developments on this strategic review process unless and until we determine that such disclosure is appropriate or necessary. If we determine to engage in a transaction as a result of our exploration and evaluation of strategic alternatives, our future business, prospects, financial position and operating results could be significantly different than those in historical periods or projected by our management.

We began to generate revenue from product sales in the second quarter of 2019 in conjunction with the launch of our product ZULRESSO in June 2019. In the fourth quarter of 2020, we recorded revenue from the strategic collaboration with and stock purchase by Biogen. In addition, we record as "collaboration revenue - related party" our share of Biogen's sales of ZURZUVAE, which became commercially available in December 2023. We also achieved and recognized a milestone totaling $75.0 million for the first commercial sale of ZURZUVAE for the treatment of women with PPD in the U.S. in the fourth quarter of 2023, as a result of the first sale of ZURZUVAE to a distributor, and received the milestone payment in January 2024.

We have incurred net losses in each year since our inception, except for net income of $606.1 million for the year ended December 31, 2020, reflecting revenue recognized under the Biogen Collaboration Agreement, and we had an accumulated deficit of $3.0 billion as of December 31, 2024. Our net losses were $400.7 million, $541.5 million, and $532.8 million for the years ended December 31, 2024, 2023 and 2022, respectively. These losses have resulted principally from costs incurred in connection with research and development activities and selling, general and administrative costs associated with our operations and expansion of our commercial operations. We expect to incur significant expenses and continued operating losses for the foreseeable future.

In October 2024, we implemented a strategic reorganization of our business operations intended to strengthen our balance sheet and focus investment on the ongoing launch of ZURZUVAE for the treatment of women with PPD and our prioritized pipeline development efforts, or the 2024 Restructuring. As part of the 2024 Restructuring, we implemented a reduction of approximately 33% of our total workforce and approximately 55% of our research and development workforce. We anticipate that the implementation of the 2024 Restructuring and our pipeline prioritization will result in a reduction of our operating expenses in 2025 relative to 2024. Based upon our current operating plan, we anticipate that our existing cash, cash equivalents and marketable securities as of December 31, 2024, together with anticipated funding from our ongoing collaborations and estimated revenues, excluding any potential milestone payments we may receive under our collaboration agreements, will support our operations to mid-2027. We have based this estimate on assumptions that may prove to be wrong, such as the revenue that we expect to realize from our collaboration agreement for the continued commercialization of ZURZUVAE for the treatment of women with PPD. To the extent estimated revenue levels are not realized, we may adjust our operating plan accordingly, including the deferral or reduction of planned operating expenses, as needed. See "—Liquidity and Capital Resources".

Although we expect that our operating expenses will decrease in 2025 as compared to 2024 as a result of our pipeline prioritization and the anticipated cost savings from the 2024 Restructuring, we expect to continue to incur significant costs in connection with our ongoing activities, including if and as we pursue key elements of our strategy to:

- successfully commercialize ZURZUVAE, along with our collaboration partner, Biogen, for the treatment of women with PPD in the U.S., including our goals to establish ZURZUVAE as the standard of care for women with PPD, expand market growth in PPD, accelerate topline revenue growth, and ultimately help more women with PPD;
- investigate SAGE-319 as a potential treatment for behavioral symptoms associated with certain neurodevelopmental disorders;

- evaluate potential further indications for SAGE-324;
- support our collaboration with Biogen with respect to zuranolone in the U.S., and support Biogen's development of zuranolone in the Biogen Territory and Shionogi's development of zuranolone in the Shionogi Territory;
- continue work on our prioritized pipeline focused on neurodevelopmental disorders and neuropsychiatry, including to explore targeted work within our NMDAR NAMs platform with SAGE-817 and SAGE-039;
- focus on maintaining a strong balance sheet while reducing operating expenses;
- continue to explore business development opportunities, including opportunities to establish licenses, collaborations, or other agreements or alliances with other biotechnology and pharmaceutical companies, at the appropriate time, where we believe a collaboration may add significant value to our efforts, including through capabilities, infrastructure, speed or financial contributions, or to acquire new compounds, product candidates or products if we believe such opportunities will help us achieve our goals or meet other strategic objectives;
- prepare and file NDAs with the FDA, and conduct permitted pre-launch activities with respect to any of our product candidates that we believe have been successfully developed;
- commercialize any product candidates for which we obtain regulatory approval, including the manufacture of commercial supplies;
- evaluate the market potential and regulatory pathways for our product candidates beyond zuranolone in the European Union, or EU, and other jurisdictions outside the U.S., and determine how best to move forward where and when it may make business and strategic sense; and
- continue to build, maintain, defend, leverage, and expand our intellectual property portfolio, including by utilizing the strengths of our proprietary chemistry platform and scientific know-how to expand our portfolio of new chemical entities with the goals of lessening our long-term reliance on the success of any one program and facilitating long-term growth.

Until such time that we can generate significant revenue on a sustained basis from product sales and/or from collaborations, if ever, we expect to finance our operations primarily through a combination of revenue, equity or debt financings and other sources of financing, including our collaborations with Biogen and Shionogi and potential future collaborations. We may not be successful in our ongoing commercialization of ZURZUVAE or any other product and may not generate meaningful revenue or revenue at the levels or on the timing necessary to support our investment and goals. We may never successfully complete development of any of our current or future product candidates, successfully file for or obtain necessary regulatory approval for such product candidates or achieve commercial viability for any resulting approved product. We may not obtain or maintain adequate patent protection or other exclusivity for our products or product candidates. Adequate additional financing may not be available to us on acceptable terms, or at all. Our inability to raise capital if and when needed would have a negative impact on our financial condition and on our ability to pursue our business strategy. Arrangements with our existing collaborators have required us to relinquish rights to certain of our technologies or product candidates, and any future collaborations, licenses, or similar arrangements may require us to relinquish additional rights. We will need to generate significant revenue to achieve profitability, and we may never do so.

Financial Operations Overview

Revenue

We began to generate revenue from product sales in the second quarter of 2019 in conjunction with the launch of our product ZULRESSO as a treatment for PPD. In addition, in late 2023, we began to generate collaboration revenue - related party from our share of Biogen's sales of ZURZUVAE in the U.S.

ZURZUVAE became commercially available in the U.S. in December 2023 as the first and only oral product approved by the FDA specifically for the treatment of adults with PPD. We and Biogen are jointly commercializing ZURZUVAE in the U.S. for the treatment of women with PPD under the Biogen Collaboration Agreement. We and

Biogen equally share in all operating profits and losses arising from sales of ZURZUVAE in the U.S., with Biogen recording such product sales.

We and Biogen are utilizing a specialty pharmacy distribution model by which ZURZUVAE is shipped directly to women with PPD who are prescribed the treatment. We and Biogen have active field sales forces supported by experienced sales leadership teams and professionals in marketing, access and reimbursement, managed markets, market research, commercial operations, and sales force planning and management. We and Biogen are continuing to engage in discussions with national, regional and government payors to advocate for broad and equitable access to ZURZUVAE for women with PPD with minimal restrictions. Payor coverage for ZURZUVAE for the treatment of women with PPD is currently in place for a majority of commercial and Medicaid covered lives without step therapy or complex prior authorizations, including coverage from all three national Pharmacy Benefit Managers. We expect formulary discussions to continue over the course of 2025.

In the fourth quarter ending December 31, 2024, nearly 2,500 prescriptions for ZURZUVAE were shipped and delivered to women with PPD, an approximately 21% increase from the prior quarter. For the year ended December 31, 2024, the first full year of shipments, more than 6,600 prescriptions were shipped and delivered. To help enable broad and equitable access, we also maintain a patient support program, ZURZUVAE For You, which provides educational resources, help with understanding insurance coverage, and assistance navigating the prescription fulfillment process for women with PPD who are prescribed treatment. This program also includes financial assistance for women with PPD, such as the potential for copay assistance for those with commercial insurance and the potential to be provided product at no cost for other eligible patients

We will not generate revenue from other products unless and until we or any of our collaborators successfully develop, obtain regulatory approval of, and commercialize one of our current or future product candidates. If we enter into additional collaboration agreements with third parties for our product candidates, we may generate revenue from those collaborations. We expect that revenue, if any, that we may generate under our existing or future collaboration agreements will fluctuate from quarter to quarter as a result of the timing and amount of license fees, payments for clinical materials or manufacturing services, milestone payments, royalties paid to us and our share of collaboration revenues resulting from sales of any commercialized products, and other payments.

In June 2018, we entered into a strategic collaboration with Shionogi for the clinical development and commercialization of zuranolone for the treatment of MDD and other potential indications in the Shionogi Territory. Under the terms of the agreement, Shionogi is responsible for all clinical development, regulatory filings and commercialization and drug product manufacturing of zuranolone for the treatment of MDD, and potentially other indications, in the Shionogi Territory. In October 2018, we also entered into a clinical supply agreement with Shionogi under which we supply Shionogi with zuranolone material for clinical and development purposes. To date, revenue from our collaboration with Shionogi has come from an initial, upfront license fee upon execution of the collaboration agreement of $90.0 million in the year ended December 31, 2018, and from the supply of materials under the clinical supply agreement. In the third quarter of 2024, Shionogi announced that it had submitted an NDA in Japan for zuranolone for the treatment of MDD.

In November 2020, we entered into the Biogen Collaboration Agreement with Biogen for the development, manufacture and commercialization of the Licensed 217 Products and the Licensed 324 Products. In connection with the execution of the Biogen Collaboration Agreement, we also entered into a stock purchase agreement for the sale and issuance to BIMA of 6,241,473 shares of our common stock for aggregate consideration of $650.0 million. The Biogen Collaboration Agreement became effective in December 2020, and the sale of the common stock under the stock purchase agreement closed on December 31, 2020. In September 2024, Biogen notified us of the SAGE-324 Termination.

Under the terms of the Biogen Collaboration Agreement, we will jointly develop and, if successful, jointly commercialize the Licensed 217 Products in the U.S. and Biogen solely will develop and commercialize the Licensed 217 Products in the Biogen Territory. We and Biogen have agreed to share equally all costs for activities, as well as the profits and losses, upon FDA approval of the Licensed 217 Products solely for the U.S. Under the Biogen Collaboration Agreement, Biogen is solely responsible for all costs for activities in the Biogen Territory. Biogen is the principal and records sales of ZURZUVAE in the U.S. and will be the principal and record sales of Licensed 217 Products globally.

In the year ended December 31, 2020, we recorded license and milestone revenue – related party of $1.1 billion, consisting of an upfront payment of $875.0 million plus $232.5 million in excess proceeds from the equity investment

under the stock purchase agreement, when measured at fair value. We also achieved a milestone under the Biogen Collaboration Agreement totaling $75.0 million and recorded license and milestone revenue - related party in the fourth quarter of 2023 for the first commercial sale of ZURZUVAE for the treatment of women with PPD in the U.S., as a result of the first sale of ZURZUVAE to a distributor, and received the milestone payment in January 2024. As a result of the SAGE-324 Termination, we will not receive any milestone payments for Licensed 324 Products under the Biogen Collaboration Agreement. For further discussion regarding the accounting for the Biogen Collaboration Agreement, refer to Note 7, *Collaboration Agreements,* in the accompanying Notes to Consolidated Financial Statements appearing elsewhere in this Annual Report.

Collaborative Arrangements

We analyze our collaboration arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities and therefore within the scope of Accounting Standards Codification, or ASC, Topic 808, *Collaborative Arrangements*, or Topic 808. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of Topic 808 that contain multiple elements, we first determine which elements of the collaboration are deemed to be within the scope of Topic 808 and which elements of the collaboration are more reflective of a vendor-customer relationship and therefore within the scope of ASC Topic 606, *Revenue from Contracts with Customers*, or Topic 606. For elements of collaboration arrangements that are accounted for pursuant to Topic 808, an appropriate recognition method is determined and applied consistently, either by analogy to authoritative accounting literature or by applying a reasonable and rational policy election. For those elements of the arrangement that are accounted for pursuant to Topic 606, we apply the five-step revenue recognition model and present the arrangement as license and milestone revenue or other collaboration revenue in the consolidated statements of operations and comprehensive loss.

For collaboration arrangements that are within the scope of Topic 808, we evaluate the income statement classification for presentation of amounts due from or owed to other participants associated with multiple activities in a collaboration arrangement based on the nature of each separate activity. Payments or reimbursements that are the result of a collaborative relationship, instead of a customer relationship, are recorded as an increase to collaboration revenue, an increase to or reduction of cost of revenues, research and development expense or selling, general and administrative expense, depending on the nature of the activity. For further discussion regarding the accounting for collaborative arrangements, refer to Note 7, *Collaboration Agreements*, in the accompanying Notes to Consolidated Financial Statements appearing elsewhere in this Annual Report.

We expect that revenue, if any, that we may generate under our collaboration agreements will fluctuate from quarter to quarter as a result of the timing and amount of license fees, payments for clinical materials or manufacturing services, milestone payments, royalties paid to us and our share of collaboration revenues from sales of any commercialized products, and other payments. We expect that our collaboration revenue will increase due to the commercial launch of ZURZUVAE for the treatment of women with PPD that commenced in December 2023. For further discussion regarding our collaboration agreements with Shionogi and Biogen and the accounting for revenue from collaboration agreements, refer to Note 2, *Summary of Significant Accounting Policies* and Note 7, *Collaboration Agreements,* in the accompanying Notes to Consolidated Financial Statements appearing elsewhere in this Annual Report.

Cost of Revenues

Cost of revenues included direct and indirect costs related to the manufacturing and distribution of ZULRESSO, including third-party manufacturing costs, packaging services, freight, third-party royalties payable on our net product revenue of ZULRESSO and amortization of intangible assets associated with ZULRESSO. Cost of revenues also includes our proportionate share of ZURZUVAE manufacturing costs under the Biogen Collaboration Agreement, (for further discussion regarding our collaboration agreement with Biogen and the accounting from collaboration agreements, refer to Note 2, *Summary of Significant Accounting Policies* and Note 7, *Collaboration Agreements,* in the accompanying Notes to Consolidated Financial Statements appearing in Part IV, Item 15 of this Annual Report). Cost of revenues may also include period costs, related to certain inventory manufacturing services and inventory adjustment charges. We expect to

utilize zero-cost inventory for ZURZUVAE for an extended period of time. We expect that our overall cost of revenues will increase over time due to sales of ZURZUVAE and the recording of our proportionate share of product costs in the U.S. under the Biogen Collaboration Agreement.

Operating Expenses

Our operating expenses consist primarily of costs associated with research and development activities and selling, general and administrative activities.

Research and Development Expenses

Research and development expenses, which consist primarily of costs associated with our product research and development efforts, are expensed as incurred. Research and development expenses consist primarily of:

- personnel costs, including salaries, benefits, stock-based compensation and travel expenses, for employees engaged in research and development functions;
- expenses incurred under agreements with contract research organizations, or CROs, and sites that conduct our non-clinical studies and clinical trials;
- expenses associated with manufacturing materials for use in non-clinical studies and clinical trials and developing external manufacturing capabilities;
- costs of outside consultants engaged in research and development activities, including their fees and travel expenses;
- other expenses related to our non-clinical studies and clinical trials and expenses related to our regulatory activities;
- payments made under our third-party license agreements; and
- a portion of our information technology, facilities and other related expenses, including rent, depreciation, maintenance of facilities, insurance and supplies.

We consider the collaborative activities associated with the co-development, co-commercialization, and co-manufacturing of the Licensed 217 Products and, through the SAGE-324 Termination effective date, the Licensed 324 Products in the U.S. to be separate units of account within the scope of Topic 808 as we and Biogen are both active participants in the development and commercialization activities and are exposed to significant risks and rewards that are dependent on the development and commercial success of the activities in the arrangement. In periods prior to commercialization, payments to or reimbursements from Biogen related to the co-development and co-manufacturing activities are accounted for as an increase to or reduction of research and development expense. Following commercialization in the U.S., payments to or reimbursements from Biogen related to commercial co-manufacturing activities in the U.S. are accounted for as an increase to or reduction of cost of revenues. During the years ended December 31, 2024, 2023, and 2022, we recorded net reimbursement of $15.7 million, $76.2 million, and $73.2 million, respectively, from Biogen that was deducted from our research and development expenses because we incurred a greater amount of these expenses than Biogen.

Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites.

We have been developing our product candidates and focusing on other research and development programs, including exploratory efforts to identify new compounds, target validation for identified compounds and lead optimization for our earlier-validated programs. Our direct research and development expenses are tracked on a program-by-program basis, and consist primarily of external costs, such as fees paid to investigators, central laboratories, CROs and contract manufacturing organizations in connection with our non-clinical studies and clinical trials; third-party license fees related to our product candidates; and fees paid to outside consultants who perform work on our programs. We do not allocate employee-related costs and other indirect costs to specific research and development programs because these costs are deployed across multiple product programs under research and development and, as such, are separately classified as unallocated or stock-based compensation in research and development expenses.

Research and development activities are central to our business. Even though we have post-approval obligations for ZURZUVAE, we expect that our research and development spending will decrease as a result of the reprioritization of our pipeline development efforts and the anticipated cost savings from the 2024 Restructuring.

We cannot determine with certainty the duration and costs of the current or future clinical trials of our product candidates. The duration, costs, and timing of clinical trials and development of our product candidates will depend on a variety of factors, including:

- the scope, size, rate of progress, and expense of our ongoing as well as any additional clinical trials, non-clinical studies, and other research and development activities;
- future results of ongoing, planned or future clinical trials and non-clinical studies;
- decisions by regulatory authorities related to our product candidates;
- uncertainties in clinical trial enrollment rate or design;
- significant and changing government regulation; and
- the receipt and timing of regulatory approvals, if any.

In addition, healthcare and vendor staffing shortages and disruption to the U.S. healthcare system, and/or the impact of other macroeconomic and geopolitical conditions, may also negatively impact our ongoing and planned development activities and increase our research and development costs. Concerns, precautions and restrictions related to future pandemics or other events, staffing shortages, or other changes to the macroeconomic environment may substantially slow clinical site identification and activation and enrollment in our clinical trials, may impair or delay the conduct, auditing, monitoring, or completion of our trials, may impair or impede the timeliness and completion of our data collection and analysis efforts or the integrity of our data, or may cause us to pause trials, in each case which may significantly impact our ability to meet our expected timelines or cause us to change our plans and may significantly increase our research and development costs.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development of a product candidate or for regulatory approval, or if we experience significant delays in enrollment in any of our clinical trials or need to enroll additional patients, we could be required to expend significant additional financial resources and time on the completion of clinical development.

Any failure to complete any stage of the development of any potential product candidates in a timely manner could have a material adverse effect on our operations, financial position and liquidity. A discussion of some of the risks and uncertainties associated with not completing our programs on schedule, or at all, and the potential consequences of failing to do so, are set forth in Part I, Item 1A of this Annual Report under the heading “Risk Factors”.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of personnel costs, including those personnel costs associated with the direct sales and marketing force and our patient support program for ZURZUVAE, as well as salaries, benefits and travel expenses for our executive, finance, business, commercial, corporate development and other administrative functions, and stock-based compensation expense. Selling, general and administrative expenses also include professional fees for expenses incurred under agreements with third parties relating to the commercialization of ZURZUVAE; ongoing launch activities related to ZURZUVAE; public relations, audit, tax and legal services, including legal expenses to pursue patent protection of our intellectual property; and a portion of our information technology, facilities and other related expenses, including rent, depreciation, maintenance of facilities, insurance and supplies.

We have an active field sales force supported by experienced sales leadership teams and professionals in marketing, access and reimbursement, managed markets, market research, commercial operations, and sales force planning, and management dedicated to commercialization of ZURZUVAE. We expect to continue to incur significant commercialization expenses, including payroll and related expenses, to support ongoing commercialization activities associated with ZURZUVAE.

As a result of the 2024 Restructuring, we expect that our selling, general and administrative expenses will decrease in 2025 as compared to 2024. However, we expect to continue to incur significant selling, general and administrative expenses as we and our collaboration partner, Biogen, continue to commercialize ZURZUVAE in the U.S. for the treatment of women with PPD. These expenses include the personnel costs associated with the direct sales and marketing force for ZURZUVAE and our patient support program for ZURZUVAE. For example, we recently completed a strategic expansion of our sales force, where we believe additional resources will help accelerate demand for ZURZUVAE for the treatment of women with PPD. In addition, our current commercialization investment plan includes joint sales force expansions and planned digital marketing campaigns to help expand market growth in PPD, along with increased disease state awareness efforts to support improved PPD screening and diagnosis. Additionally, we expect to incur significant expenses from the progression of our development efforts for our current or future product candidates and commercialization of those products, if successfully developed and approved. We also expect to continue to incur significant expenses associated with general operations, including costs related to accounting and legal services, director and officer insurance premiums, facilities and other corporate infrastructure and office-related costs, such as information technology costs.

We consider the collaborative activities associated with the co-development, co-commercialization, and co-manufacturing of the Licensed 217 Products and, through the SAGE-324 Termination effective date, the Licensed 324 Products in the U.S. to be separate units of account within the scope of Topic 808 as we and Biogen are both active participants in the development and commercialization activities and are exposed to significant risks and rewards that are dependent on the development and commercial success of the activities in the arrangement. Payments to or reimbursements from Biogen related to the co-commercialization activities are accounted for as an increase to or reduction of selling, general and administrative expense. During the years ended December 31, 2024 and 2023, we recorded net reimbursement from us to Biogen of $10.9 million and $16.5 million, respectively, that was added to our selling, general and administrative expenses. During the year ended December 31, 2022, we recorded net reimbursement from Biogen to us of $2.2 million that was deducted from our selling, general and administrative expenses.

2023 Restructuring

In August 2023, we implemented a strategic corporate reorganization and reprioritization of our pipeline, or the 2023 Restructuring. The reorganization included a reduction of our workforce by approximately 40%, designed to right-size the organization as we worked to achieve sustained growth and support the goal of successful commercialization of ZURZUVAE for the treatment of women with PPD. As of December 31, 2024, we recorded a total of $32.9 million of expense related to the 2023 Restructuring, primarily for one-time termination benefits to the affected employees and, primarily consisting of cash payments of severance, healthcare benefits and outplacement assistance. Substantially all of the accrued restructuring charges incurred in connection with the 2023 Restructuring have been paid in cash as of December 31, 2024.

2024 Restructuring

In October 2024, we implemented the 2024 Restructuring to focus investment on the ongoing launch of ZURZUVAE for the treatment of women with PPD and prioritized pipeline development efforts. The reorganization included a reduction of approximately 33% of our total workforce and approximately 55% of our research and development workforce. As a result, we expect that our operating expenses will decrease in 2025 as compared to 2024. During the year ended December 31, 2024, we recorded a total of $22.3 million of expense related to the 2024 Restructuring, primarily for one-time termination benefits to the affected employees, primarily consisting of cash payments of severance, healthcare benefits and outplacement assistance. We expect to incur an additional $1.3 million of expense related to the 2024 Restructuring in future periods. We expect that substantially all of the accrued restructuring charges incurred for the year ended December 31, 2024 will be paid in cash as of June 30, 2025.

Critical Accounting Policies and Significant Judgments and Estimates

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles in the U.S. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amount of assets, liabilities, revenue, costs and expenses, and related disclosures. We believe that the estimates and assumptions involved in the accounting policies described below may have the greatest potential impact on our consolidated financial statements and, therefore, consider these to be our critical accounting policies. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions and conditions. While our significant accounting policies are described in more detail in the Notes to our Consolidated Financial Statements appearing elsewhere in this Annual Report, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Revenue Recognition

Under ASC Topic 606, *Revenue from Contracts with Customers*, or Topic 606, an entity recognizes revenue when or as performance obligations are satisfied by transferring control of promised goods or services to a customer, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. We assess if these options provide a material right to the customer and if so, they are considered performance obligations. The exercise of a material right may be accounted for as a contract modification or as a continuation of the contract for accounting purposes.

For contracts determined to be within the scope of Topic 606, we assess whether the goods or services promised within each contract are distinct to identify those that are performance obligations. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract.

We allocate the transaction price (the amount of consideration we expect to be entitled to from a customer in exchange for the promised goods or services) to each performance obligation and recognize the associated revenue when (or as) each performance obligation is satisfied. Our estimate of the transaction price for each contract includes all variable consideration to which we expect to be entitled.

Product Revenue, Net

In 2024, we generated product revenue from the sale of ZULRESSO to a limited number of specialty distributors and specialty pharmacy providers. We recognized product revenue, net of variable consideration related to certain allowances and accruals that are determined using the expected value method, in our consolidated financial statements at the point in time when control transfers to the customer, which is typically when the product was delivered to the customer's location. The amount included in the transaction price was constrained to the amount for which it was probable that a significant reversal of cumulative revenue recognized would not occur. Our only performance obligation identified for ZULRESSO was to deliver the product to the location specified by the customer's order. We recorded shipping and handling costs associated with delivery of product to our customers within selling, general and administrative expenses on our consolidated statements of operations and comprehensive loss. We expensed incremental costs of obtaining a contract as incurred if the expected amortization period of the asset would be less than one year. If we had incurred incremental costs with an amortization period greater than a year, such costs would have been capitalized as contract assets, as they are expected to be recovered, and would be expensed by amortizing on a systematic basis that is consistent with the transfer to the customer of the goods or services to which the asset relates. We did not have any contract assets (unbilled receivables) at December 31, 2024, as customer invoicing generally occurred before or at the time of revenue recognition. The Company did not have any contract liabilities at December 31, 2024, as we did not receive any payments in advance of satisfying our performance obligations to our customers. Amounts billed or invoiced that are considered trade accounts receivable are included in prepaid expenses and other current assets on the consolidated balance sheets.

As of December 31, 2024 and 2023, we had not provided any allowance for bad debts against the trade accounts receivable, and the amount of trade accounts receivable was not significant.

We recorded reserves, based on contractual terms, for the following components of variable consideration related to product sold during the reporting period, as well as our estimate of product that remains in the distribution channel inventory of our customers at the end of the reporting period. On a quarterly basis, we updated our estimates, if necessary, and recorded any material adjustments in the period they were identified.

Chargebacks: We estimated chargebacks from our customers who directly purchased the product from us for discounts resulting from contractual commitments to sell products to eligible healthcare settings at prices lower than the list prices charged to our customers. Customers charged us for the difference between what they paid to us for the product and the selling price to the eligible healthcare settings. Reserves for chargebacks consist of credits that we expected to issue for units that remained in the distribution channel inventories at the end of each reporting period that we expected would be sold to eligible healthcare settings, and chargebacks that customers have claimed, but for which we have not yet issued a credit.

Government Rebates: We are subject to discount obligations under government programs, including Medicaid. We recorded reserves for rebates in the same period the related product revenue was recognized, resulting in a reduction of ZULRESSO product revenue and a current liability that is included in accrued expenses on our consolidated balance sheets. Our liability for these rebates consisted of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimates of future claims that will be made for product that has been recognized as revenue, but which remained in the distribution channel at the end of each reporting period.

Trade Discounts and Allowances: We generally provided customary invoice discounts on ZULRESSO sales to our customers for prompt payment and we paid fees for sales order management, data, and distribution services. We estimated our customers will earn these discounts and fees and deducted these discounts and fees in full from gross ZULRESSO revenue and accounts receivable at the time we recognized the related revenue.

Financial Assistance: We provide voluntary financial assistance programs to patients with commercial insurance that have coverage and reside in states that allow financial assistance. We estimated the financial assistance amounts for ZULRESSO and recorded any such amounts within accrued expenses on the consolidated balance sheets. The calculation of the accrual for financial assistance was based on an estimate of claims and the cost per claim that we expected to receive using demographics for patients who had registered and been approved for assistance. Any adjustments were recorded in the same period the related revenue was recognized, resulting in a

reduction of product revenue and the establishment of a current liability, which was included as a component of accrued expenses on the consolidated balance sheets.

Product Returns: Consistent with industry practice, we offer product return rights to customers for damaged, defective or expiring product, provided it is within a specified period around the product expiration date as set forth in our return goods policy. We estimated the amount of our product sales that may be returned by our customers and recorded this estimate as a reduction of revenue in the period the related product revenue was recognized, as well as a reserve within accrued expenses on our consolidated balance sheets. Product returns have not been significant to date and are not expected to be significant in the future.

License, Milestone, and Collaboration Revenue

In assessing whether a promised good or service is distinct in the evaluation of a collaboration or license arrangement subject to Topic 606, we consider factors such as the research, manufacturing and commercialization capabilities of the collaboration partner, and the availability of the associated expertise in the general marketplace. We also consider the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, we are required to combine that good or service with other promised goods or services until we identify a bundle of goods or services that is distinct.

The transaction price is then determined and allocated to the identified performance obligations in proportion to their standalone selling prices, or SSP, on a relative SSP basis. SSP is determined at contract inception and is not updated to reflect changes between contract inception and when the performance obligations are satisfied. Determining the SSP for performance obligations requires significant judgment. In developing the SSP for a performance obligation, we consider applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. In certain circumstances, we may apply the residual method to determine the SSP of a good or service if the standalone selling price is considered highly variable or uncertain. We validate the SSP for performance obligations by evaluating whether changes in the key assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, we estimate the amount of consideration to which we will be entitled in exchange for transferring the promised goods or services to a customer. We determine the amount of variable consideration by using the expected value method or the most likely amount method. We include the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, we re-evaluate the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

If an arrangement includes development and regulatory milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received.

In determining the transaction price, we adjust consideration for the effects of the time value of money if the timing of payments provides us with a significant benefit of financing. We do not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. We assessed our arrangements with Shionogi and Biogen and concluded that a significant financing component does not exist for either arrangement. For arrangements with licenses of intellectual property that include sales-based royalties or milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties or milestone payments relate, we recognize royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty or milestone payment has been allocated has been satisfied.

We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time this is based on the use of an output or input method. For additional information, see Collaborative Arrangements section below and refer to Note 7, *Collaboration Agreements*, to our Consolidated Financial Statements appearing elsewhere in this Annual Report.

Collaborative Arrangements

We analyze our collaboration arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities and therefore within the scope of Topic 808. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of Topic 808 that contain multiple elements, we first determine which elements of the collaboration are deemed to be within the scope of Topic 808 and which elements of the collaboration are more reflective of a vendor-customer relationship and therefore within the scope of Topic 606. For elements of collaboration arrangements that are accounted for pursuant to Topic 808, an appropriate recognition method is determined and applied consistently, either by analogy to authoritative accounting literature or by applying a reasonable and rational policy election. For those elements of the arrangement that are accounted for pursuant to Topic 606, we apply the five-step model described above and presents the arrangement as license and milestone revenue or other collaboration revenue in the consolidated statements of operations and comprehensive loss.

For collaboration arrangements that are within the scope of Topic 808, we evaluate the income statement classification for presentation of amounts due from or owed to other participants associated with multiple activities in a collaboration arrangement based on the nature of each separate activity. Payments or reimbursements that are the result of a collaborative relationship, instead of a customer relationship are recorded as an increase to collaboration revenue, an increase to or reduction of research and development expense or selling, general and administrative expense, depending on the nature of the activity.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel and vendors to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to:

- CROs in connection with performing research and development services on our behalf;
- other providers in connection with clinical trials;
- vendors in connection with non-clinical development activities; and
- vendors related to product manufacturing, development and distribution of clinical supplies.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs that conduct and manage clinical trials on our behalf. The financial terms of these agreements vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. When determining accruals, we estimate the time period over which services will be performed, enrollment of patients, number of sites activated and level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred,

our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting expenses that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of accrued research and development expenses.

Stock-Based Compensation

We recognize compensation expense for stock-based awards, including grants of stock options and restricted stock units, granted to employees, non-employee directors and non-employee consultants based on the estimated fair value on the date of grant, over the requisite service period. We recognize stock-based compensation expense for only the portion of awards that are expected to vest.

For awards that vest upon achievement of a performance condition, we recognize compensation expense when achievement of the performance condition is met or during the period from which meeting the condition is deemed probable until the expected date of meeting the performance condition, using management's best estimates, which consider the inherent risk and uncertainty regarding the future outcomes of the milestones.

The fair value of each stock option grant is estimated using the Black-Scholes option-pricing model. We use the historical volatility of only our common stock, as there is adequate historical data for the duration of the expected term.

The expected term of the stock options granted to employees, non-employee directors and non-employee consultants by us has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" stock options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the date of grant for time periods approximately equal to the expected term of the award. The expected dividend yield is zero, based on the fact that we have never paid cash dividends and do not expect to pay any cash dividends in the foreseeable future.

We also apply a forfeiture rate in order to calculate stock-based compensation expense. Expected forfeitures are based on our historical experience and management's expectations of future forfeitures. To the extent actual forfeitures differ from the estimates, the difference is recorded as a cumulative adjustment in the period in which the estimates are revised.

The fair value of each stock option granted under our equity plans has been calculated on the date of grant using the following weighted average assumptions:

	Year Ended December 31,		
	2024	2023	2022
Expected dividend yield	0%	0%	0%
Expected volatility	76%	72%	73%
Risk-free interest rate	4.24%	3.85%	2.49%
Expected term	6.01 years	6.01 years	6.03 years

These assumptions represented our best estimates, but the estimates involve inherent uncertainties and the application of our judgment. As a result, if factors change and we use significantly different assumptions or estimates when valuing our stock options, our stock-based compensation expense could be materially different. In developing a forfeiture rate estimate for pre-vesting forfeitures, we have considered our historical experience of actual forfeitures. In the future, if our actual forfeiture rate is materially different from our estimate, then our stock-based compensation expense could be significantly different from what we have recognized in the current period.

As of December 31, 2024, we had unrecognized stock-based compensation expense related to our outstanding and unvested time-based stock option awards of $24.1 million, which is expected to be recognized over the remaining weighted average vesting period of 3.18 years.

As of December 31, 2024, 455,000 performance-based stock options were both outstanding and unvested, the total unrecognized stock-based compensation expense related to these awards was $24.9 million and the timing of recognition of this stock-based compensation expense is subject to our judgment as to when the performance conditions are considered probable of being achieved.

As of December 31, 2024, 1,788,137 time-based restricted stock units were both outstanding and unvested, and the total unrecognized stock-based compensation expense related to these awards was $13.8 million.

As of December 31, 2024, 1,212,253 performance restricted stock units were both outstanding and unvested, and the total unrecognized stock-based compensation expense related to these awards was $42.9 million.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is set forth in Note 2, *Summary of Significant Accounting Policies*, to the Consolidated Financial Statements appearing elsewhere in this Annual Report.

Results of Operations

Comparison of the Years Ended December 31, 2024 and 2023

The following table summarizes our results of operations for the years ended December 31, 2024 and 2023:

	Year Ended December 31,		Increase (Decrease)
	2024	2023	
		(in thousands)	
Product revenue, net	$ 3,574	$ 10,454	$ (6,880)
License and milestone revenue - related party	—	75,000	(75,000)
Collaboration revenue - related party	36,087	824	35,263
Other collaboration revenue	1,582	177	1,405
Total revenues	41,243	86,455	(45,212)
Operating costs and expenses:			
Cost of revenues	9,444	2,159	7,285
Research and development	225,895	356,235	(130,340)
Selling, general and administrative	216,420	274,524	(58,104)
Restructuring	21,854	33,386	(11,532)
Total operating costs and expenses	473,613	666,304	(192,691)
Loss from operations	(432,370)	(579,849)	147,479
Interest income, net	31,675	38,743	(7,068)
Other income (expense), net	29	(383)	412
Net loss	$ (400,666)	$ (541,489)	$ 140,823

Product Revenue, Net

During the years ended December 31, 2024 and 2023, we recognized $3.6 million and $10.5 million, respectively, of net product revenue related to sales of ZULRESSO. Sales allowances and accruals consisted of chargebacks, discounts, distribution fees and patient financial assistance, and were not significant during either year.

License and Milestone Revenue - Related Party

During the year ended December 31, 2024, we recognized no license and milestone revenue - related party under the Biogen Collaboration Agreement.

During the year ended December 31, 2023, we recognized $75.0 million of license and milestone revenue - related party for the achievement of a milestone under the Biogen Collaboration Agreement for the first commercial sale of ZURZUVAE for the treatment of women with PPD in the U.S.

Collaboration Revenue - Related Party

During the years ended December 31, 2024 and 2023, we recognized $36.1 million and $0.8 million, respectively, of collaboration revenue - related party for our share of Biogen's net ZURZUVAE sales to customers in the U.S. under the Biogen Collaboration Agreement. To record our share of collaboration revenue – related party from the sales of ZURZUVAE, we utilize certain information from Biogen, including revenue from the sale of the product and associated reserves. Reported collaboration revenue - related party is 50% of the net sales Biogen reports for ZURZUVAE.

Other Collaboration Revenue

During the years ended December 31, 2024 and 2023, we recognized $0.6 million and $0.2 million, respectively, of other collaboration revenue related to the supply of zuranolone active pharmaceutical ingredients under our agreement with Shionogi.

During the year ended December 31, 2024, we recognized $0.9 million of other collaboration revenue related to providing development and regulatory support to Biogen in the Biogen Territory under the Biogen Collaboration Agreement. During the year ended December 31, 2023, we did not recognize any other collaboration revenue under the Biogen Collaboration Agreement.

We expect that further revenue, if any, that we may generate under our collaboration agreements will fluctuate from quarter to quarter as a result of the timing and amount of our share of collaboration revenues resulting from Biogen's sales of any commercialized products, license fees, payments for clinical materials or manufacturing services, milestone payments, royalties paid to us, and other payments. For further discussion regarding our collaboration agreements with Shionogi and Biogen and the accounting for revenue from collaboration agreements, refer to Note 2, *Summary of Significant Accounting Policies*; and Note 7, *Collaboration Agreements* in the Notes to Consolidated Financial Statements appearing elsewhere in this Annual Report.

Cost of Revenues

During the years ended December 31, 2024 and 2023, cost of revenues was $9.4 million and $2.2 million, respectively, and is made up of direct and indirect costs related to the manufacturing and distribution of ZULRESSO including third-party manufacturing costs, packaging services, freight, third-party royalties payable on our net product revenue of ZULRESSO and amortization of intangible assets associated with ZULRESSO. During the year ended December 31, 2024, we incurred $3.6 million of one-time charges related to the write-off of excess inventory and impairment of intangible assets related to ZULRESSO as a result of the decision to discontinue commercial availability in the U.S. as of December 31, 2024. Cost of revenues may also include period costs related to certain inventory manufacturing services and inventory adjustment charges. Cost of revenues also includes our proportionate share of ZURZUVAE manufacturing costs under the Biogen Collaboration Agreement (for further discussion regarding our collaboration agreement with Biogen and the accounting for collaboration agreements, refer to Note 2, *Summary of*

Significant Accounting Policies; and Note 7, *Collaboration Agreements* in the Notes to Consolidated Financial Statements appearing elsewhere in this Annual Report).

Prior to receiving FDA approval for ZULRESSO in March 2019, we manufactured ZULRESSO inventory to be sold upon commercialization and recorded $8.9 million related to this inventory build-up as research and development expense. As a result, the manufacturing costs related to the ZULRESSO inventory build-up incurred before FDA approval were already expensed in a prior period and therefore a portion of such costs are excluded from the cost of revenues for the years ended December 31, 2024 and 2023. Our cost of revenues for ZULRESSO as a percentage of net product revenue remained in the high-single digit to low-double digits percentage range for the duration of ZULRESSO's commercial availability. We utilized zero-cost inventory with respect to ZULRESSO during this period.

Research and Development Expenses

The following table summarizes our research and development expenses for the years ended December 31, 2024 and 2023:

	Year Ended December 31,		Increase (Decrease)
	2024	2023	
	(in thousands)		
zuranolone (ZURZUVAE)	$ 3,129	$ 104,937	$ (101,808)
SAGE-324	21,093	33,211	(12,118)
dalzanemdor (SAGE-718)	57,256	54,994	2,262
Other research and development programs	45,586	72,997	(27,411)
Unallocated expenses	95,626	141,491	(45,865)
Stock-based compensation	18,885	24,813	(5,928)
Net reimbursement from Biogen	(15,680)	(76,208)	60,528
	$ 225,895	$ 356,235	$ (130,340)

Research and development expenses for the year ended December 31, 2024 were $225.9 million, compared to $356.2 million for the year ended December 31, 2023. The decrease of $130.3 million was primarily due to the following:

- a decrease of $101.8 million in expenses for development of zuranolone, primarily due to expenses incurred during the year ended December 31, 2023 related to ongoing clinical trial costs that did not occur in 2024, and cost savings in 2024 resulting from the cancelation of excess purchase commitments for manufacturing as a result of the CRL received from the FDA related to the NDA for zuranolone for the treatment of MDD;
- a decrease of $12.1 million in expenses for development of SAGE-324, primarily due to activities directed towards the conduct of two Phase 2 clinical trials which were initiated in late 2022, conducted throughout the year ended December 31, 2023, and were concluded during the year ended December 31, 2024, resulting in lower expense in 2024;
- a decrease of $27.4 million in expenses for other research and development programs, primarily due to the pipeline prioritization cost saving initiatives of the 2024 Restructuring and 2023 Restructuring;
- a decrease of $45.9 million in unallocated expenses, primarily due to the effects of a decreased headcount in 2024 and overhead cost savings initiatives resulting from the 2023 Restructuring;
- a decrease of $5.9 million in stock-based compensation expenses, primarily due to the recognition of $2.5 million of expense for the achievement of one performance-based vesting criteria and probable achievement of another performance-based vesting criteria during the year ended December 31, 2024, as compared to $6.9 million of expense for the vesting of three performance-based vesting criteria during the year ended December 31, 2023 and decreased expense for time-based stock options and restricted stock units during the year ended December 31, 2024, as compared to the year ended December 31, 2023 as a result of lower headcount after the 2024 Restructuring; and
- a decrease of $60.5 million in the net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement. For the year ended December 31, 2024, the amount of net reimbursement was $1.3 million for

zuranolone, $10.6 million for SAGE-324 and $3.8 million for costs that are reimbursable and included in unallocated expenses. For the year ended December 31, 2023, the amount of net reimbursement was $51.1 million for zuranolone, $16.3 million for SAGE-324 and $8.8 million for costs that are reimbursable and included in unallocated expenses. The primary reason for the decrease in net reimbursement in 2024 compared to 2023 was the decrease in spending for zuranolone, primarily due to expenses related to the completion of ongoing clinical trials during the year ended December 31, 2023, and canceling excess purchase commitments for manufacturing as a result of the CRL received from the FDA related to the NDA for zuranolone for the treatment of MDD.

Selling, General and Administrative Expenses

The following table summarizes our selling, general and administrative expenses for the years ended December 31, 2024 and 2023:

	Year Ended December 31,		Increase (Decrease)
	2024	2023	
		(in thousands)	
Personnel-related	$ 88,325	$ 108,201	$ (19,876)
Stock-based compensation	35,587	47,716	(12,129)
Professional fees	46,838	51,436	(4,598)
Other	34,789	50,675	(15,886)
Net reimbursement to Biogen	10,881	16,496	(5,615)
	$ 216,420	$ 274,524	$ (58,104)

Selling, general and administrative expenses for the year ended December 31, 2024, were $216.4 million, compared to $274.5 million for the year ended December 31, 2023. The decrease of $58.1 million was primarily due to the following:

- a decrease of $19.9 million in personnel-related costs, primarily due to the effects of a decreased headcount in 2024 resulting from the 2023 Restructuring;
- a decrease of $12.1 million in non-cash stock-based compensation expense, primarily due to the recognition of $5.1 million of expense for the achievement of one performance-based vesting criteria and probable achievement of another performance-based vesting criteria during the year ended December 31, 2024, as compared to $18.1 million of expense for the vesting of three performance-based vesting criteria during the year ended December 31, 2023 for a decrease of $13.0 million. The decrease in performance-based stock-compensation expense was partially offset by a $0.9 million increase to time-based grants of stock options and restricted stock units during the year ended December 31, 2024 as compared to the year ended December 31, 2023;

- a decrease of $4.6 million in professional fees, primarily due to a reduction in pre-launch readiness spend and decreased investment in commercial spend following the CRL received from the FDA related to the NDA for zuranolone for the treatment of MDD;
- a decrease of $15.9 million in other fees, primarily due to the implementation of cost saving initiatives as part of the 2023 Restructuring; and
- a decrease of $5.6 million in the net reimbursement to Biogen pursuant to the Biogen Collaboration Agreement. For the year ended December 31, 2024, the amount of net reimbursement from us to Biogen was $10.7 million for external costs and $0.2 million for personnel-related costs. For the year ended December 31, 2023, the amount of net reimbursement from us to Biogen was $16.4 million for external costs and $0.1 million for personnel-related costs. The primary reason for the decrease in net reimbursement was a decrease in the collaboration costs incurred by Biogen following the CRL received from the FDA related to the NDA for zuranolone for the treatment of MDD.

Restructuring

Restructuring expense for the years ended December 31, 2024 and 2023, was $21.9 and $33.4 million, respectively. The primary reason for the decrease in 2024 as compared to 2023 was the headcount reduction resulting from the 2024 Restructuring during the year ended December 31, 2024 was smaller as compared to the 2023 Restructuring during the year ended December 31, 2023.

Interest Income, Net and Other Income, Net

Interest income, net, and other income, net, for the years ended December 31, 2024 and 2023, were $31.7 million and $38.4 million, respectively. The primary reason for the decrease in 2024 as compared to 2023 was the decrease in total balance of marketable securities during the year ended December 31, 2024 as compared to the year ended December 31, 2023.

Liquidity and Capital Resources

We began to generate revenue from product sales in the second quarter of 2019 in conjunction with the commercial launch of our first product, ZULRESSO, in June 2019 for the treatment of PPD in the U.S. We began to generate collaboration revenue from product sales of ZURZUVAE for the treatment of women with PPD in the U.S. in December 2023. We have incurred net losses in each year since our inception, except for net income of $606.1 million for the year ended December 31, 2020, reflecting revenue recognized under the Biogen Collaboration Agreement. As of December 31, 2024, we had an accumulated deficit of $3.0 billion. On December 31, 2020, we completed the sale of 6,241,473 shares of our common stock in a private placement to BIMA at a price of approximately $104.14 per share, resulting in aggregate gross proceeds of $650.0 million. In January 2024, we received a $75.0 million milestone payment from Biogen as a result of the first commercial sale of ZURZUVAE for the treatment of women with PPD in the U.S. in the fourth quarter of 2023. From our inception through December 31, 2024, we have received aggregate net proceeds of $2.8 billion from the sales of redeemable convertible preferred stock prior to our initial public offering, the issuance of convertible notes, and the sales of common stock in our initial public offering in July 2014, follow-on offerings and in the sale of shares of our common stock to Biogen in connection with the Biogen Collaboration Agreement, which we refer to as the Biogen Equity Purchase. We also received $1.0 billion in upfront payments under our collaborations with Biogen and Shionogi.

In September 2024, we entered into a Sales Agreement, or the ATM Sales Agreement, with TD Securities (USA) LLC, as sales agent, or TD Cowen, with respect to an "at the market offering" program pursuant to which we may offer and sell shares of our common stock having an aggregate offering price of up to $250.0 million, from time to time through TD Cowen. Upon our entry into the ATM Sales Agreement, we terminated our prior sales agreement with Cowen and Company, LLC, an affiliate of TD Cowen, dated November 7, 2023, or the Original Sales Agreement. At the time of such termination, $241.7 million out of an aggregate of $250.0 million of shares remained unsold under the Original Sales Agreement. During the year ended December 31, 2024, we did not sell any shares under the ATM Sales Agreement. During the year ended December 31, 2024, we sold an aggregate of 700,000 shares under the Original Sales Agreement at an average price per share of $11.90 and received gross proceeds of approximately $8.3 million, before deducting commissions, underwriting discounts, and offering costs of $0.3 million. As of December 31, 2024, $250.0 million of shares remained available for issuance and sale under the ATM Sales Agreement.

As of December 31, 2024, our primary sources of liquidity were our cash, cash equivalents and marketable securities, which totaled $504.4 million. We invest our cash in money market funds, U.S. government securities, corporate bonds, commercial paper, certificates of deposit and municipal securities, and our primary objectives are to preserve principal, provide liquidity and maximize income without significantly increasing risk.

The following table summarizes the primary sources and uses of cash for the years ended December 31, 2024 and 2023:

	Year Ended December 31,	
	2024	2023
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$ (267,194)	$ (540,585)
Investing activities	266,678	442,913
Financing activities	10,663	6,027
	$ 10,147	$ (91,645)

Operating Activities

During the year ended December 31, 2024, net cash used in operating activities primarily resulted from our net loss of $400.7 million, which was primarily attributable to our research and development activities and our selling, general and administrative expenses, partially offset by changes in our operating assets and liabilities of $84.8 million and $48.7 million of non-cash items.

During the year ended December 31, 2023, net cash used in operating activities primarily resulted from our net loss of $541.5 million, which was primarily attributable to our research and development activities and our selling, general and administrative expenses, along with changes in our operating assets and liabilities of $67.4 million, partially offset by $68.3 million of non-cash items.

Investing Activities

During the years ended December 31, 2024 and 2023, net cash provided by investing activities was $266.7 million and $442.9 million, respectively. During the years ended December 31, 2024 and 2023, we purchased marketable securities and had sales and maturities of our marketable securities as part of managing our cash and investments portfolio.

Financing Activities

During the years ended December 31, 2024 and 2023, net cash provided by financing activities was $10.7 million and $6.0 million, respectively. The increase was primarily due to proceeds from the sale of shares of our common stock pursuant to the Original Sales Agreement in 2024, partially offset by a decrease in proceeds from purchases made under our employee stock purchase plan.

Operating Capital Requirements

We anticipate that we will continue to generate losses for the foreseeable future as we commercialize ZURZUVAE, along with our collaboration partner Biogen, for the treatment of women with PPD in the U.S.; continue the development of our current and future product candidates, and seek regulatory approvals for those product candidates that are successfully developed; prepare for potential commercialization of any product candidates that are successfully developed and approved; and continue our efforts to identify and develop new product candidates beyond our current portfolio. We also expect to incur significant costs associated with general operations. In addition, we expect to incur significant commercialization expenses for product sales, marketing and outsourced manufacturing with respect to ZURZUVAE and any other future products that are successfully developed and approved. Accordingly, we anticipate that we will need substantial additional funding in connection with our continuing operations.

Based upon our current operating plan, we anticipate that our existing cash, cash equivalents and marketable securities as of December 31, 2024, together with anticipated funding from our ongoing collaborations and estimated revenues, excluding any potential milestone payments we may receive under our collaboration agreements, will support our operations to mid-2027. We have based this estimate on assumptions that may prove to be wrong, such as the revenue that we expect to realize from our collaboration agreement for the continued commercialization of ZURZUVAE. To the extent estimated revenue levels are not realized, we may adjust our operating plan accordingly, including the deferral or reduction of planned operating expenses, as needed.

Although we expect an overall decrease in our operating expenses in 2025 as compared to 2024 as a result of our pipeline prioritization and the anticipated cost savings from the 2024 Restructuring, we still expect to incur significant operating expenses, including in connection with our efforts to commercialize ZURZUVAE in the U.S. for the treatment of women with PPD. We expect these costs will include the expenses associated with: ongoing co-commercialization activities; conducting clinical trials of our other current and future product candidates; continuing certain research activities; pursuing potential business development activities; and pursuing our strategic plan.

Our current operating plan does not contemplate other activities that we may pursue or that all of our currently planned activities will proceed at the same pace, or that all of these activities will be fully initiated or completed during that time. We have based our estimates on assumptions that could change, such as the revenue that we expect to generate, or the clinical development costs we expect to incur, particularly as the process of testing drug candidates in clinical trials is costly and the timing of progress in these trials is uncertain. As a result, we may use our available capital resources sooner than we currently expect and may need to adjust our plans accordingly. We may also choose to change or increase our development, commercialization or other efforts or incur significant unanticipated expenses. Because of the numerous risks and uncertainties associated with the development and commercialization of any product or product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures necessary to complete development of our current or future product candidates or to commercialize any approved product.

Our future capital requirements will depend on many factors, including:

- our ability, with our collaborator Biogen, to successfully commercialize ZURZUVAE for the treatment of women with PPD in the U.S., and the timing and amount of costs associated with commercialization; the timing and amount of revenues from sales of ZURZUVAE; the level of reimbursement for ZURZUVAE both by commercial and government payors, and the nature of any potential limitations on coverage and reimbursement; and the degree of market acceptance of ZURZUVAE by healthcare professionals and women with PPD;
- the impact of the 2024 Restructuring;
- the impact of our decision to discontinue commercial availability of ZULRESSO in the U.S. as of December 31, 2024;
- the initiation, progress, completion, timing, costs, and results of ongoing, planned and future non-clinical studies and clinical trials for our existing and future product candidates; the number and length of clinical trials required by regulatory authorities to support regulatory approval; and the costs of preparing, submitting and supporting regulatory filings for our product candidates, if our development efforts are successful;

- general macroeconomic and geopolitical conditions, including any capacity and resource constraints at our vendors and clinical trial sites on initiation and conduct of our clinical trials or on our supply chain;
- the ability of our product candidates to progress through development successfully and on the timelines we expect; the outcome of discussions with regulatory authorities on regulatory pathways with respect to our product candidates, including the number and length of clinical trials required to support regulatory approval; the timing, scope and outcome of regulatory filings and reviews and approvals of such product candidates, if we are successful in our development efforts; the scope and cost of any clinical trials or other commitments required post-approval for any approved products resulting from such development efforts, if successful; and the level, timing and amount of costs associated with permitted prelaunch activities and preparing for a potential future commercial launch of any such product candidate that is successfully developed and approved;
- the impact of current and future products developed by third parties that may compete with our current or future marketed products;
- the amounts we are entitled to receive, if any, from Biogen and Shionogi under our collaborations for profit-sharing, cost-sharing, development, regulatory, and sales milestones, and royalty payments;
- the size of the markets for which our products are approved and in the indications we are pursuing or plan to study with our product candidates; the portion of the population in the approved indications for our products that are actually prescribed; and the rate and degree of market acceptance, pricing, and availability and level of reimbursement for our products and product candidates, if successfully developed and approved;
- the number and characteristics of the product candidates we pursue in development and the nature and scope of our discovery and development programs;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other products and technologies; and
- our ability to establish any future collaboration arrangements on favorable terms, if at all.

Until such time, if ever, as we can generate substantial product revenue and/or collaboration revenue and achieve sustained profitability, we will need additional financing. We expect to finance our additional cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, licensing or royalty arrangements and other sources of funding. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or in light of other strategic considerations. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, 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 and may require the issuance of warrants, which could potentially dilute the ownership interest of our stockholders. If we raise additional funds through collaborations, strategic alliances, licensing or royalty arrangements or other agreements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or research programs or to grant licenses on terms that may not be favorable to us. Raising funds may present challenges. Markets may experience volatility or become disrupted in the future for any number of reasons, including as a result of macroeconomic or geopolitical conditions, result in an economic recession, a decrease in corporate and consumer expenditures, prolonged unemployment, or other circumstances that could negatively impact general economic conditions. If we are unable to raise additional funds through equity or debt financings or other means when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations at December 31, 2024 and the effect such obligations are expected to have on our liquidity and cash flow in future periods:

	Payments Due by Period				
	Total	Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years
			(in thousands)		
Operating lease commitments[1]	$ 15,414	$ 2,461	$ 6,035	$ 6,376	$ 542
Total[1][2]	$ 15,414	$ 2,461	$ 6,035	$ 6,376	$ 542

Amounts related to contingent milestone payments are not considered contractual obligations as they are contingent on the successful achievement of certain milestones. These contingent milestones may not be achieved. We have not included any of these amounts in the table as we cannot estimate or predict when, or if, these amounts will become due. We do not include amounts related to milestones for indications that we are no longer pursuing.

(1) We lease office space in one multi-tenant building in Cambridge, Massachusetts, consisting, as of December 31, 2024, of 30,567 square feet, under an operating lease which commenced in August 2024 and which will expire on February 28, 2030. The minimum lease payments in the table do not include related common area maintenance costs or real estate taxes, because those costs are variable.

(2) We enter into contracts in the normal course of business with CROs for clinical trials, non-clinical research studies and testing, manufacturing and other services and products as part of general operations. These contracts generally provide for termination upon notice, and we believe that our non-cancelable obligations under these agreements are not material.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

We had cash, cash equivalents and marketable securities of $504.4 million as of December 31, 2024. The primary objectives of our investment activities are to preserve principal, provide liquidity and maximize income without significantly increasing risk. Our primary exposure to market risk relates to fluctuations in interest rates, which are affected by changes in the general level of U.S. interest rates. Given the short-term nature of our cash, cash equivalents and marketable securities, we do not expect that a sudden change in market interest rates would have a material impact on our financial condition and/or results of operations. We do not own any derivative financial instruments.

We contract with vendors in foreign countries and have subsidiaries in Europe, Canada, and Bermuda. As such, we have exposure to adverse changes in exchange rates of foreign currencies associated with our foreign transactions. We believe this exposure to be immaterial. We do not hedge against this exposure to fluctuations in exchange rates.

We do not believe that our cash, cash equivalents and marketable securities have significant risk of default or illiquidity. While we believe our cash, cash equivalents and marketable securities do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash, cash equivalents and marketable securities that are in excess of federally insured limits at one or more financial institutions.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our results of operations during the year ended December 31, 2024.

Item 8. Financial Statements and Supplementary Data

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report. An index of those financial statements is found in Item 15.

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

We maintain disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Securities Exchange Act of 1934) that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities Exchange Act of 1934 is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our President and Chief Executive Officer, who is our principal executive officer, and our Chief Operating Officer, who is our principal financial and accounting officer, as appropriate, to allow timely decisions regarding required disclosure.

As of December 31, 2024, our management, with the participation of our principal executive officer and principal financial and accounting officer, evaluated the effectiveness of our disclosure controls and procedures. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial and accounting officer have concluded, based upon the evaluation described above, that, as of December 31, 2024, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) under the Securities Exchange Act of 1934). Our internal control over financial reporting is a process designed under the supervision of our principal executive officer and principal financial officer to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our financial statements for external purposes in accordance with generally accepted accounting principles. Management evaluated the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in *Internal Control—Integrated Framework* (the 2013 Framework). Management, under the supervision and with the participation of the principal executive officer and principal financial officer, assessed the effectiveness of our internal control over financial reporting as of December 31, 2024 and concluded that it was effective based on those criteria.

The effectiveness of our internal control over financial reporting as of December 31, 2024 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in its report, which is included in this Annual Report.

Changes in Internal Control over Financial Reporting

There were no changes to our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934) that occurred during the quarter ended December 31, 2024 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

Director and Officer Trading Arrangements

In connection with Gregory Shiferman's appointment as an executive officer on November 1, 2024, Mr. Shiferman's durable sale instruction pertaining to eligible sell-to-cover transactions (as described in Rule 10b5-1(c)(1)(ii)(D)(3) under the Exchange Act) in connection with his restricted stock unit ("RSU") and performance restricted stock unit ("PSU") awards terminated automatically in accordance with its terms, and his RSU and PSU award agreements were amended to replace their sell-to-cover provisions with share-withholding provisions in accordance with our standard practice to require share withholding for all RSUs and PSUs held by our executive officers.

Other than as set forth above, none of our directors or officers adopted or terminated a Rule 10b5-1 trading arrangement or a non-Rule 10b5-1 trading arrangement (as defined in Item 408(c) of Regulation S-K) during the fourth quarter of 2024.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item is incorporated herein by reference to the information that will be contained in "Election of Directors" and "Corporate Governance" in our proxy statement related to the 2025 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Code of Business Conduct and Ethics. We have adopted a Code of Business Conduct and Ethics, which we call Our Values Code, that applies to all of our employees, officers and directors, including those officers responsible for financial reporting. The current version of Our Values Code, as may be amended from time to time, is available on our website at http://investor.sagerx.com/corporate-governance. A copy of Our Values Code may also be obtained, free of charge, upon a request directed to: Sage Therapeutics, Inc., 55 Cambridge Parkway, Cambridge, Massachusetts 02142, Attention: SVP, General Counsel. We intend to disclose any amendment or waiver of a provision of Our Values Code that applies to our principal executive officer, principal financial officer, or principal accounting officer, or persons performing similar functions, by posting such information on our website (available at www.sagerx.com) and/or in our public filings with the Securities and Exchange Commission.

Insider Trading Policy. We have adopted an Insider Trading Policy, as amended and restated on June 15, 2023, or the Insider Trading Policy, governing the purchase, sale and/or other dispositions of our securities by directors, officers, and employees. We believe the Insider Trading Policy is reasonably designed to promote compliance with insider trading laws, rules and regulations, and applicable Nasdaq listing standards. A copy of the Insider Trading Policy is filed as Exhibit 19.1 to this Annual Report.

Item 11. Executive Compensation

The information required by this Item is incorporated herein by reference to the information that will be contained in "Executive Officer and Director Compensation," "Compensation Committee Interlocks and Insider Participation" and "Compensation Committee Report," but exclusive of any information contained under the heading "Pay Versus Performance" in our proxy statement related to the 2025 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

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

The information required by this Item is incorporated herein by reference to the information that will be contained in "Securities Authorized for Issuance Under Equity Compensation Plans" and "Security Ownership of Certain Beneficial Owners and Management" in our proxy statement related to the 2025 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

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

The information required by this Item is incorporated herein by reference to the information that will be contained in "Corporate Governance" and "Certain Relationships and Related Party Transactions" in our proxy statement related to the 2025 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Item 14. Principal Accounting Fees and Services

The information required by this Item is incorporated herein by reference to the information that will be contained in "Ratification of Appointment of Auditors" in our proxy statement related to the 2025 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) The following documents are filed as part of this report:

(1) Financial Statements:

(2) Financial Statement Schedules:

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(3) Exhibits. The exhibits filed as part of this Annual Report are set forth on the Exhibit Index immediately following our consolidated financial statements. The Exhibit Index is incorporated herein by reference.

Item 16. Form 10-K Summary

Not applicable.

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Sage Therapeutics, Inc.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of Sage Therapeutics, Inc. and its subsidiaries (the "Company") as of December 31, 2024 and 2023, and the related consolidated statements of operations and comprehensive loss, of changes in stockholders' equity and of cash flows for each of the three years in the period ended December 31, 2024, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2024, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2024 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2024, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated 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 consolidated 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 consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

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 (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) 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 (iii) 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.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that (i) relates to accounts or disclosures that are material to the consolidated financial statements and (ii) 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 matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Accrued Research and Development Costs

As described in Notes 2 and 5 to the consolidated financial statements, the Company has entered into various research and development contracts with research institutions and other companies. When billing terms under these contracts do not coincide with the timing of when the work is performed, management is required to make estimates of outstanding obligations to those third parties as of the end of the reporting period. Within accrued expenses, total accrued research and development costs amounted to $19.8 million as of December 31, 2024, which include accruals for these estimated ongoing research and development costs. Any accrual estimates are based on a number of factors, including management's knowledge of the progress towards completion of the research and development activities, invoicing to date under the contracts, communication from the research institution or other companies of any actual costs incurred during the period that have not yet been invoiced, and the costs included in the contracts. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period.

The principal considerations for our determination that performing procedures relating to accrued research and development costs is a critical audit matter are the significant judgment by management in determining the accrued costs which in turn led to a high degree of auditor judgment, subjectivity and effort in performing procedures and evaluating audit evidence for these accrued costs and the factors related to progress towards completion of the research and development activities, invoicing to date under the contracts, and communication from the research institution or other companies of any actual costs incurred during the period that have not yet been invoiced.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of controls relating to accrued research and development costs, including controls over the review of contracts, accumulating information on actual costs incurred during the period, and assessment of progress towards completion of the research and development activities. These procedures also included, among others, (i) testing management's process for estimating accrued research and development costs; (ii) evaluating the appropriateness of the method used by management to develop the estimates; (iii) evaluating the reasonableness of the factors used in determining the estimates related to progress towards completion of specific research and development activities and the associated cost incurred for services the Company has not yet been invoiced or otherwise notified of the actual cost at period end; and (iv) testing the completeness and accuracy of the underlying data including total costs included within executed contracts and actual billed expenses under these contracts.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
February 11, 2025

We have served as the Company's auditor since 2013.

Sage Therapeutics, Inc. and Subsidiaries
Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 81,021	$ 70,992
Marketable securities	423,397	682,192
Prepaid expenses and other current assets	17,749	31,825
Collaboration receivable - related party	9,134	83,009
Restricted cash	—	1,332
Total current assets	531,301	869,350
Property and equipment, net	890	1,921
Restricted cash	1,450	—
Right-of-use operating asset	10,753	4,458
Other long-term assets	2,828	6,548
Total assets	$ 547,222	$ 882,277
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 12,699	$ 10,318
Accrued expenses	57,598	67,264
Operating lease liability, current portion	1,318	5,165
Total current liabilities	71,615	82,747
Operating lease liability, net of current portion	10,518	—
Total liabilities	82,133	82,747
Commitments and contingencies (Note 6)		
Stockholders' equity:		
Preferred stock, $0.0001 par value per share; 5,000,000 shares authorized at December 31, 2024 and 2023; no shares issued or outstanding at December 31, 2024 and 2023	—	—
Common stock, $0.0001 par value per share; 120,000,000 shares authorized at December 31, 2024 and 2023; 61,359,242 and 60,046,676 shares issued at December 31, 2024 and 2023, respectively; 61,356,209 and 60,043,643 shares outstanding at December 31, 2024 and 2023, respectively	6	6
Treasury stock, at cost, 3,033 shares at December 31, 2024 and 2023	(400)	(400)
Additional paid-in capital	3,435,564	3,370,397
Accumulated deficit	(2,970,325)	(2,569,659)
Accumulated other comprehensive income (loss)	244	(814)
Total stockholders' equity	465,089	799,530
Total liabilities and stockholders' equity	$ 547,222	$ 882,277

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

Sage Therapeutics, Inc. and Subsidiaries
Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Year Ended December 31,		
	2024	2023	2022
Product revenue, net	$ 3,574	$ 10,454	$ 7,686
License and milestone revenue - related party	—	75,000	—
Collaboration revenue - related party	36,087	824	—
Other collaboration revenue[1]	1,582	177	—
Total revenues	41,243	86,455	7,686
Operating costs and expenses:			
Cost of revenues	9,444	2,159	813
Research and development	225,895	356,235	326,163
Selling, general and administrative	216,420	274,524	227,699
Restructuring	21,854	33,386	—
Total operating costs and expenses	473,613	666,304	554,675
Loss from operations	(432,370)	(579,849)	(546,989)
Interest income, net	31,675	38,743	14,190
Other income (expense), net	29	(383)	15
Net loss	$ (400,666)	$ (541,489)	$ (532,784)
Net loss per share—basic and diluted	$ (6.59)	$ (9.05)	$ (8.98)
Weighted average number of common shares outstanding—basic and diluted	60,765,913	59,836,441	59,306,094
Comprehensive loss:			
Net loss	$ (400,666)	$ (541,489)	$ (532,784)
Other comprehensive items:			
Unrealized gain (loss) on marketable securities	1,058	9,392	(7,546)
Total comprehensive loss	$ (399,608)	$ (532,097)	$ (540,330)

(1) Includes related-party amounts of $947 for the year ended December 31, 2024, and no related-party amounts for the years ended December 31, 2023 and 2022 (see Note 7).

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

Sage Therapeutics, Inc. and Subsidiaries
Consolidated Statements of Changes in Stockholders' Equity
(in thousands, except share data)

	Common Stock		Treasury Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount				
Balances at December 31, 2021	58,937,050	$ 6	3,033	$ (400)	$ 3,227,471	$ (2,660)	$ (1,495,386)	$ 1,729,031
Issuance of common stock from exercises of stock options	150,045	—	—	—	1,037	—	—	1,037
Issuance of common stock under the employee stock purchase plan	57,239	—	—	—	2,346	—	—	2,346
Vesting of restricted stock units, net of employee tax obligations	364,791	—	—	—	(43)	—	—	(43)
Stock-based compensation expense	—	—	—	—	60,558	—	—	60,558
Change in unrealized loss on available-for-sale securities	—	—	—	—	—	(7,546)	—	(7,546)
Net loss	—	—	—	—	—	—	(532,784)	(532,784)
Balances at December 31, 2022	59,509,125	6	3,033	(400)	3,291,369	(10,206)	(2,028,170)	1,252,599
Issuance of common stock from exercises of stock options	72,090	—	—	—	1,293	—	—	1,293
Issuance of common stock under the employee stock purchase plan	164,043	—	—	—	6,519	—	—	6,519
Vesting of restricted stock units, net of employee tax obligations	298,385	—	—	—	(903)	—	—	(903)
Stock-based compensation expense	—	—	—	—	72,119	—	—	72,119
Change in unrealized loss on available-for-sale securities	—	—	—	—	—	9,392	—	9,392
Net loss	—	—	—	—	—	—	(541,489)	(541,489)
Balances at December 31, 2023	60,043,643	6	3,033	(400)	3,370,397	(814)	(2,569,659)	799,530
Issuance of common stock from exercises of stock options	10,062	—	—	—	78	—	—	78
Issuance of common stock under the employee stock purchase plan	216,886	—	—	—	2,941	—	—	2,941
Vesting of restricted stock units, net of employee tax obligations	385,618	—	—	—	(403)	—	—	(403)
Stock-based compensation expense	—	—	—	—	54,504	—	—	54,504
Issuance of common stock upon public offering, net of issuance costs	700,000	—	—	—	8,047	—	—	8,047
Change in unrealized gain on available-for-sale securities	—	—	—	—	—	1,058	—	1,058
Net loss	—	—	—	—	—	—	(400,666)	(400,666)
Balances at December 31, 2024	61,356,209	$ 6	3,033	$ (400)	$ 3,435,564	$ 244	$ (2,970,325)	$ 465,089

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

Sage Therapeutics, Inc. and Subsidiaries
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2024	2023	2022
Cash flows from operating activities			
Net loss	$ (400,666)	$ (541,489)	$ (532,784)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	54,504	73,367	61,602
Premium on marketable securities	(344)	(132)	(1,500)
Amortization of (discount) premium on marketable securities	(6,481)	(6,340)	5,853
Depreciation expense	1,031	1,393	1,122
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	14,076	19,001	(10,985)
Collaboration receivable - related party	73,875	(69,349)	4,846
Other long-term assets	3,720	(1,778)	(519)
Right-of-use operating asset	5,302	6,074	5,577
Operating lease liabilities, current	(3,847)	(2,478)	175
Operating lease liabilities, non-current	(1,079)	(4,491)	(6,473)
Accounts payable	2,381	(8,495)	8,433
Accrued expenses and other liabilities	(9,666)	(5,868)	4,617
Net cash used in operating activities	(267,194)	(540,585)	(460,036)
Cash flows from investing activities			
Proceeds from sales and maturities of marketable securities	717,635	1,038,136	1,207,407
Purchases of marketable securities	(450,957)	(594,670)	(881,037)
Purchases of property and equipment	—	(553)	(937)
Net cash provided by investing activities	266,678	442,913	325,433
Cash flows from financing activities			
Proceeds from stock option exercises and employee stock purchase plan issuances	3,019	6,930	3,113
Payments of offering costs	(117)	—	—
Proceeds from public offerings of common stock, net of commissions and underwriting discounts	8,164	—	—
Payment of employee tax obligations related to vesting of restricted stock units	(403)	(903)	(43)
Net cash provided by financing activities	10,663	6,027	3,070
Net increase (decrease) in cash, cash equivalents and restricted cash	10,147	(91,645)	(131,533)
Cash, cash equivalents, and restricted cash at beginning of period	72,324	163,969	295,502
Cash, cash equivalents, and restricted cash at end of period	$ 82,471	$ 72,324	$ 163,969
Supplemental disclosure of non-cash operating activities			
Right-of-use assets obtained in exchange for new operating lease liabilities	$ 11,597	$ —	$ —
Purchases of property and equipment included in accounts payable	$ —	$ —	$ 137
Reconciliation of cash, cash equivalents, and restricted cash reported in the consolidated balance sheets			
Cash and cash equivalents	81,021	70,992	162,700
Restricted cash	1,450	1,332	1,269
Total cash, cash equivalents, and restricted cash shown in the statement of cash flows	$ 82,471	$ 72,324	$ 163,969

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

1. Nature of the Business

Sage Therapeutics, Inc. ("Sage" or the "Company") is a biopharmaceutical company with a mission to pioneer solutions to deliver life-changing brain health medicines, so every person can thrive.

The Company's product ZURZUVAE® (zuranolone) was approved by the U.S. Food and Drug Administration (the "FDA") on August 4, 2023 for the treatment of postpartum depression ("PPD") in adults. ZURZUVAE is a neuroactive steroid that is a positive allosteric modulator of $GABA_A$ receptors, targeting both synaptic and extrasynaptic $GABA_A$ receptors, and is the first oral, once-daily, 14-day treatment specifically indicated for adults with PPD. ZURZUVAE became commercially available for women with PPD in December 2023.

The Company's product ZULRESSO® (brexanolone) CIV injection is currently approved in the U.S. for the treatment of PPD in individuals 15 years old and older and was launched commercially in the U.S. in June 2019. ZULRESSO may only be administered in qualified, medically-supervised healthcare settings. The Company discontinued commercial availability of ZULRESSO in the U.S. as of December 31, 2024. The Company supported scheduled ZULRESSO infusions through the end of 2024. As a result of the decision to discontinue ZULRESSO commercial availability, during the year ended December 31, 2024, the Company incurred $5.4 million of incremental cost related to impairment of intangible assets, excess inventory write-off, prepaid and other current assets accelerated amortization, and accrued termination costs.

The Company has a portfolio of product candidates with a current focus on modulating two critical central nervous system ("CNS") receptor systems, GABA and NMDA. The GABA receptor family, which is recognized as the major inhibitory neurotransmitter in the CNS, mediates downstream neurologic and bodily function via activation of $GABA_A$ receptors. The NMDA-type receptors of the glutamate receptor system are a major excitatory receptor system in the CNS. Dysfunction in these systems is implicated in a broad range of CNS disorders. The Company is targeting diseases and disorders of the brain across its pipeline.

In October 2024, the Company executed a plan to reorganize its business operations, including a reduction of approximately 33% of the Company's total workforce and approximately 55% of the Company's research and development workforce. See Note 14, *Restructuring*, for further details.

The Company was incorporated under the laws of the State of Delaware on April 16, 2010, and commenced operations on January 19, 2011 as Sterogen Biopharma, Inc. On September 13, 2011, the Company changed its name to Sage Therapeutics, Inc.

Risks and Uncertainties

The Company is subject to risks and uncertainties common to companies in the biopharmaceutical industry, including, but not limited to, the risks associated with developing product candidates at each stage of non-clinical and clinical development; the challenges associated with gaining regulatory approval of such product candidates; the risks associated with the marketing and sale of pharmaceutical products; the potential for development by third parties of new technological innovations that may compete with the Company's products and product candidates; the dependence on key personnel; the challenges of protecting proprietary technology; the need to comply with government regulations; the high costs of drug development; the uncertainty of being able to secure additional capital when needed to fund operations; and the direct or indirect impacts of the macroeconomic environment and geopolitical events on its development activities, operations and financial condition.

The product candidates developed by the Company require approvals from the FDA or foreign regulatory authorities prior to commercial sales. There can be no assurance that the current and future product candidates of the Company will receive, or that ZURZUVAE will maintain, the necessary approvals. If the Company fails to successfully complete clinical development and generate results sufficient to file for regulatory approval or is denied approval or approval is

delayed for any of its product candidates, such occurrences may have a material adverse impact on the Company's business and its financial condition.

The Company is also subject to additional risks and uncertainties arising from changes to the macroeconomic environment and geopolitical events. U.S. and global financial markets have experienced volatility and disruption due to macroeconomic and geopolitical events such as rising inflation, the risk of a recession and ongoing conflicts in other countries. In addition, if equity and credit markets deteriorate, it may make any future debt or equity financing more difficult to obtain on favorable terms, and potentially more dilutive to its existing stockholders. The Company cannot predict at this time to what extent it and its collaborators, employees, suppliers, contract manufacturers and/or vendors could potentially be negatively impacted by these events.

Going Concern

Under Accounting Standards Update ("ASU") No. 2014-15, *Presentation of Financial Statements—Going Concern* (Subtopic 205-40), the Company has the responsibility to evaluate whether conditions and/or events raise substantial doubt about its ability to meet its future financial obligations as they become due within one year after the date that the financial statements are issued. The Company has incurred losses and negative cash flows from operations in each year since its inception, except for net income of $606.1 million for the year ended December 31, 2020, reflecting revenue recognized under a collaboration and license agreement with Biogen Inc. ("Biogen") (the "Biogen Collaboration Agreement"). As of December 31, 2024, the Company had an accumulated deficit of $3.0 billion. Until such time, if ever, as the Company can generate substantial product revenue and/or collaboration revenue and achieve sustained profitability, the Company expects to finance its cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other sources of funding. If the Company is unable to raise additional funds through equity or debt financings or other sources of funding when needed, the Company may be required to delay, limit, reduce or terminate product development or future commercialization efforts or grant rights to develop and market products or product candidates that the Company would otherwise prefer to develop and market itself.

The Company expects that, based on its current operating plans, the Company's existing cash, cash equivalents and marketable securities will be sufficient to fund its currently planned operations for at least the next 12 months from the filing date of these consolidated financial statements. At some point after that time, the Company anticipates it will require additional financing to fund its future operations. Even if the Company believes it has sufficient funds for its current or future operating plans, the Company may seek to raise additional capital if market conditions are favorable or in light of other strategic considerations.

2. Summary of Significant Accounting Policies

The following is a summary of significant accounting policies followed in the preparation of these consolidated financial statements.

Basis of Presentation

The accompanying consolidated financial statements include those of the Company and its subsidiaries after elimination of all intercompany accounts and transactions. The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the U.S. ("GAAP").

Principles of Consolidation

The consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries. Intercompany accounts and transactions have been eliminated.

Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets

and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period.

Cash Equivalents

The Company considers all highly liquid investments with an original maturity of 90 days or less to be cash equivalents. As of December 31, 2024, cash equivalents were comprised of money market funds, U.S. government securities, and U.S. commercial paper. As of December 31, 2023, cash equivalents were comprised of money market funds and U.S. government securities.

Marketable Securities

Marketable securities consist of investments with original maturities greater than 90 days. The Company has classified its investments with maturities beyond one year as short-term, based on their highly liquid nature and because such marketable securities represent the investment of cash that is available for current operations. The Company considers its investment portfolio of marketable securities to be available-for-sale. Accordingly, these investments are recorded at fair value, which is based on quoted market prices. Unrealized gains and losses are reported as the accumulated other comprehensive items in stockholders' equity. When the fair value is below the amortized cost of the asset, an estimate of expected credit losses is made. The credit-related impairment amount is recognized in net income (loss); the remaining impairment amount and unrealized gains are reported as a component of accumulated other comprehensive items in stockholders' equity. Credit losses are recognized through the use of an allowance for credit losses account and subsequent improvements in expected credit losses are recognized as a reversal of an amount in the allowance for credit losses account. If the Company has the intent to sell the security or it is more likely than not that the Company will be required to sell the security prior to recovery of its amortized cost basis, then the allowance for the credit loss is written-off and the excess of the amortized cost basis of the asset over its fair value is recorded in the consolidated statements of operations and comprehensive loss. Regardless of the Company's intent to sell a security, it performs additional analysis on all securities with unrealized losses to evaluate losses associated with the creditworthiness of the security. Credit losses are identified where the Company does not expect to receive cash flows sufficient to recover the amortized cost basis of a security. The Company adjusts the cost of available-for-sale debt securities for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion are included in interest income. The cost of securities sold is based on the specific identification method. The Company includes interest and dividends on securities classified as available-for-sale in interest income.

Accounts Receivable

The Company's trade accounts receivable consist of amounts due from specialty distributors and specialty pharmacies that have been certified under a Risk Evaluation and Mitigation Strategy program in the U.S. related to sales of ZULRESSO and have standard payment terms that generally require payment within 30 to 90 days from the invoice date. The Company monitors the financial performance and creditworthiness of customers so that it can properly assess and respond to changes in their credit profiles. The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for bad debts against the trade account receivables, when appropriate. As of December 31, 2024 and 2023, trade accounts receivable were $0.4 million and $1.4 million, respectively, and are included in prepaid expenses and other current assets on the consolidated balance sheets. As of December 31, 2024, the Company has not provided any allowance for bad debts against the trade accounts receivable.

Inventory

Prior to the initial date that regulatory approval is received for a product candidate of the Company, costs related to the production of inventory are recorded as research and development expense on the Company's consolidated statements of operations and comprehensive loss in the period incurred.

Inventory is stated at the lower of cost or estimated net realizable value with cost determined on a first-in, first-out basis. Inventory costs may include purchases of raw materials, third-party contract manufacturing services, third-party packaging services, salary related expenses, overhead costs, and freight. Raw and intermediate materials that may be utilized for either research and development or commercial purposes, after approval of the product by the FDA, are classified as inventory. Amounts in inventory that are used for research and development purposes are charged to research

and development expense when the product enters the research and development process and can no longer be used for commercial purposes and, therefore, does not have an "alternative future use" as defined in authoritative guidance. The Company performs an assessment of the recoverability of capitalized inventory during each reporting period and, if needed, writes down any excess and obsolete inventory to its estimated net realizable value in the period it is identified. If they occur, such impairment charges are recorded as a component of cost of revenues in the consolidated statements of operations and comprehensive loss. As of December 31, 2024, the Company did not have any capitalized inventory on hand. As of December 31, 2023, inventory was $1.5 million, and is included in prepaid expenses and other current assets on the consolidated balance sheets.

Property and Equipment

Property and equipment are recorded at cost and depreciated over their estimated useful lives using the straight-line method. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is credited or charged to the Company's consolidated statements of operations and comprehensive loss. Repairs and maintenance costs are expensed as incurred.

Leases

The Company determines if an arrangement is a lease at contract inception. Operating lease assets represent the Company's right to use an underlying asset for the lease term and operating lease liabilities represent the Company's obligation to make payments arising from the lease. Operating lease assets and liabilities are recognized at the commencement date of the lease based upon the present value of lease payments over the lease term. When determining the lease term, the Company includes options to extend or terminate the lease when it is reasonably certain that the Company will exercise those options. The Company uses the Company's incremental borrowing rate when the implicit interest rate is not readily determinable based upon the information available at the commencement date of the lease in determining the present value of the lease payments and the implicit interest rate when readily determinable.

The lease payments used to determine the Company's operating lease assets may include lease incentives, stated rent increases and escalation clauses linked to rates of inflation, when determinable, and are recognized in the Company's operating lease assets in the Company's consolidated balance sheets. In addition, the Company's contracts may contain lease and non-lease components. The Company combines lease and non-lease components, which are accounted for together as lease components.

The Company's operating leases are reflected in the right-of-use operating asset; operating lease liability, current portion; and operating lease liability, net of current portion in the Company's consolidated balance sheets. Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term. Short-term leases, defined as leases that have a lease term of 12 months or less at the commencement date, are not recorded on the Company's consolidated balance sheets and are recognized in the consolidated statements of operations and comprehensive loss on a straight-line basis over the term of the lease.

Variable lease payments are the amounts owed by the Company to a lessor that are not fixed, such as reimbursement for common area maintenance and utilities costs for facility leases. Variable lease payments are expensed when incurred.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment and lease right-of-use assets. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends, and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset group for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset group to its carrying value. The impairment loss would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows. During the year ended December 31, 2024, the Company recorded $2.2 million of impairment losses on long-lived assets as a result of discontinuing the commercial availability of ZULRESSO. During the year ended December 31, 2023, the Company did not record any impairment losses on long-lived assets.

Cost of Revenues

Cost of revenues includes direct and indirect costs related to the manufacturing and distribution of ZULRESSO, including third-party contract manufacturing costs, packaging services, freight, third-party royalties payable on the Company's net product revenue of ZULRESSO and amortization of intangible assets associated with ZULRESSO. Cost of revenues also includes our proportionate share of ZURZUVAE manufacturing costs under the Biogen Collaboration Agreement, (for additional information, refer to Note 7, *Collaboration Agreements*). Cost of revenues may also include period costs related to certain inventory manufacturing services and inventory adjustment charges. Prior to receiving FDA approval of ZULRESSO in March 2019 and ZURZUVAE in August 2023, the Company manufactured inventory in preparation for launch. As a result, certain manufacturing costs associated with revenues were expensed prior to FDA approval and, therefore, a portion of such costs are not included in cost of revenues during the years ended December 31, 2024, 2023, and 2022.

Research and Development Costs and Accruals

Research and development expenses are comprised of costs incurred in performing research and development activities, including salaries and benefits, overhead costs, depreciation, contract services and other related costs. Research and development costs are expensed to operations as the related obligation is incurred.

The Company has entered into various research and development contracts with research institutions and other companies both inside and outside of the U.S. These agreements are generally cancelable, and related costs are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research and development costs. When billing terms under these contracts do not coincide with the timing of when the work is performed, the Company is required to make estimates of outstanding obligations to those third parties as of the end of the reporting period. Any accrual estimates are based on a number of factors, including the Company's knowledge of the progress towards completion of the research and development activities, invoicing to date under the contracts, communication from the research institution or other companies of any actual costs incurred during the period that have not yet been invoiced, and the costs included in the contracts. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the estimates made by the Company. The historical accrual estimates made by the Company have not been materially different from the actual costs.

Stock-Based Compensation

The Company recognizes stock-based compensation expense for grants under our equity incentive plans and employee stock purchase plan. The Company accounts for all stock-based awards granted to employees at their fair value and recognize compensation expense over the vesting period of the award. Determining the amount of stock-based compensation to be recorded requires the Company to develop estimates of fair values of stock options as of the grant date. The Company calculates the grant date fair values of stock options using the Black-Scholes valuation model, which requires the input of subjective assumptions, including but not limited to expected stock price volatility over the term of the awards, the expected term of stock options and the expected forfeiture rate. The fair value of restricted stock awards granted to employees is based upon the quoted closing market price per share on the date of grant.

The Company has performance conditions included in certain of its performance restricted stock units that are based upon the achievement of pre-specified clinical development, regulatory, commercial and/or financial performance events. As the outcome of each event has inherent risk and uncertainties, and a positive outcome may not be known until the event is achieved, the Company begins to recognize the value of the performance-based restricted stock awards when the Company determines the achievement of each performance condition is deemed probable, a determination which requires significant judgment by management. At the probable date, the Company records estimated cumulative expense to date, with remaining expense amortized over the remaining service period until achievement has occurred.

Treasury Stock

The Company records treasury stock at cost. Treasury stock consists of shares of the Company's common stock received from a then-employee as consideration for exercises of stock options.

Basic and Diluted Net Loss Per Share

Basic net loss per share is computed by dividing the net loss by the weighted average number of common shares outstanding for the period. For periods in which the Company has reported net losses, diluted net loss per share is the same as basic net loss per share, because dilutive common shares are not assumed to have been issued if their effect is antidilutive.

The Company reported a net loss for the years ended December 31, 2024, 2023 and 2022.

Concentration of Credit Risk and of Significant Suppliers

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents and marketable securities. The Company maintains accounts for all cash and cash equivalents at accredited financial institutions, and consequently, the Company believes that such funds are subject to minimal credit risk. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships. The Company's marketable securities, which primarily consist of U.S. government agency securities and treasuries, corporate bonds and commercial paper, potentially subject the Company to concentrations of credit risk. The Company has adopted an investment policy that limits the amounts the Company may invest in any one type of investment, defines allowable investments, and requires all investments held by the Company to minimum credit rating standards, thereby reducing credit risk exposure. The Company has no significant off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts, or other hedging arrangements.

The Company is dependent on third-party manufacturers to supply products for research and development activities for its programs. The Company also relies on and expects to continue to rely on third-party manufacturers to supply it with active pharmaceutical ingredients ("API") and formulated drugs; and to provide other services related to manufacturing activities for these programs. These programs could be adversely affected by a significant interruption in the supply of API and formulated drugs, or the interruption of manufacturing related services.

Income Taxes

The Company accounts for income taxes under the asset and liability method. Under this method, deferred tax assets and liabilities are recognized for the estimated future tax consequences attributable to differences between financial statement carrying amounts of existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using enacted rates in effect for the year in which these temporary differences are expected to be recovered or settled. Valuation allowances are provided if, based on the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of Accounting Standards Codification ("ASC") Topic 740, "*Income Taxes*". When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. The Company accrues for potential interest and penalties related to unrecognized tax benefits in income tax expense.

Fair Value Measurements

Fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. Financial assets and liabilities carried at fair value are classified and disclosed in one of the following three categories:

Level 1 — Quoted market prices in active markets for identical assets or liabilities.

Level 2 — Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 — Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The Company's cash equivalents and marketable securities at December 31, 2024 and 2023 were carried at fair value, determined according to the fair value hierarchy; see Note 3, *Fair Value Measurements*.

The carrying amounts reflected in the consolidated balance sheets for the collaboration receivable – related party, accounts payable, and accrued expenses approximate their fair values due to their short-term maturities at December 31, 2024 and 2023, respectively.

Comprehensive Income (Loss)

Comprehensive loss includes net loss and other changes in stockholders' equity that result from transactions and economic events other than those with stockholders. The Company's only element of other comprehensive income (loss) is unrealized gains and losses on marketable securities that are considered to be available-for-sale.

Revenue Recognition

Under ASC Topic 606, *Revenue from Contracts with Customers* ("Topic 606"), an entity recognizes revenue when or as performance obligations are satisfied by transferring control of promised goods or services to a customer, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. The Company assesses if these options provide a material right to the customer and if so, they are considered performance obligations. The exercise of a material right may be accounted for as a contract modification or as a continuation of the contract for accounting purposes.

Topic 606 applies to all contracts with customers, except for contracts that are within the scope of other standards, such as collaboration arrangements.

For contracts determined to be within the scope of Topic 606, the Company assesses whether the goods or services promised within each contract are distinct to identify those that are performance obligations. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract.

The Company allocates the transaction price (the amount of consideration it expects to be entitled to from a customer in exchange for the promised goods or services) to each performance obligation and recognizes the associated revenue when (or as) each performance obligation is satisfied. The Company's estimate of the transaction price for each contract includes all variable consideration to which the Company expects to be entitled.

Product Revenue, Net

Until the discontinuation of commercial availability of ZULRESSO as of December 31, 2024, the Company generated product revenue from the sale of ZULRESSO to a limited number of specialty distributors and specialty pharmacy providers in the U.S. The Company recognized product revenue, net of variable consideration related to certain allowances and accruals that are determined using the expected value method, in its consolidated financial statements at the point in time when control transfers to the customer, which was typically when the product has been delivered to the customer's location. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. The Company's only performance obligation identified for ZULRESSO was to deliver the product to the location specified by the customer's order.

The Company records shipping and handling costs associated with delivery of product to its customers within selling, general and administrative expenses on its consolidated statements of operations and comprehensive loss. The Company expenses incremental costs of obtaining a contract as incurred if the expected amortization period of the asset would be less than one year. If the Company were to incur incremental costs with an amortization period greater than a year, such costs would be capitalized as contract assets, as they are expected to be recovered, and would be expensed by amortizing on a systematic basis that is consistent with the transfer to the customer of the goods or services to which the asset relates. The Company did not have any contract assets (unbilled receivables) at December 31, 2024, as customer invoicing generally occurs before or at the time of revenue recognition. The Company did not have any contract liabilities at December 31, 2024, as the Company did not receive any payments in advance of satisfying its performance obligations to its customers. Amounts billed or invoiced that are considered trade accounts receivable are included in prepaid expenses and other current assets on the consolidated balance sheets.

As of December 31, 2024 and 2023, the Company had not provided any allowance for bad debts against the trade accounts receivable, and the amount of trade accounts receivable was not significant.

The Company records reserves, based on contractual terms, for the following components of variable consideration related to ZULRESSO sold by the Company during the reporting period, as well as its estimate of product that remains in the distribution channel inventory of its customers at the end of the reporting period. On a quarterly basis, the Company updates its estimates, if necessary, and records any material adjustments in the period they are identified.

Chargebacks: The Company estimates chargebacks from its customers who directly purchase the product from the Company for discounts resulting from contractual commitments to sell products to eligible healthcare settings at prices lower than the list prices charged to its customers. Customers charge the Company for the difference between what they pay to the Company for the product and the selling price to the eligible healthcare settings. Reserves for chargebacks consist of credits that the Company expects to issue for units that remain in the distribution channel inventories at the end of each reporting period that the Company expects will be sold to eligible healthcare settings, and chargebacks that customers have claimed, but for which the Company has not yet issued a credit.

Government Rebates: The Company is subject to discount obligations under government programs, including Medicaid. The Company records reserves for rebates in the same period the related product revenue is recognized, resulting in a reduction of ZULRESSO product revenue and a current liability that is included in accrued expenses on its consolidated balance sheets. The Company's liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimates of future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel at the end of each reporting period.

Trade Discounts and Allowances: The Company generally provides customary invoice discounts on ZULRESSO sales to its customers for prompt payment and the Company pays fees for sales order management, data, and distribution services. The Company estimates its customers will earn these discounts and fees and deducts these discounts and fees in full from gross ZULRESSO revenue and accounts receivable at the time the Company recognizes the related revenue.

Financial Assistance: The Company provides voluntary financial assistance programs for ZULRESSO to patients with commercial insurance that have coverage and reside in states that allow financial assistance. The Company estimates the financial assistance amounts for ZULRESSO and records any such amounts within accrued expenses on its consolidated balance sheets. The calculation of the accrual for financial assistance is based on an estimate of claims and the cost per claim that the Company expects to receive using demographics for patients who have registered and been approved for assistance. Any adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability, which is included as a component of accrued expenses on the consolidated balance sheets.

Product Returns: Consistent with industry practice, the Company offers product return rights with respect to ZULRESSO to customers for damaged, defective or expiring product, provided it is within a specified period around the product expiration date as set forth in the Company's return goods policy. The Company estimates the amount of its product sales that may be returned by its customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized, as well as a reserve within accrued expenses on the consolidated balance sheets. Product returns have not been significant to date and are not expected to be significant in the future.

License, Milestone, and Collaboration Revenue

In assessing whether a promised good or service is distinct in the evaluation of a collaboration or license arrangement subject to Topic 606, the Company considers factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. The Company also considers the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, the Company is required to combine that good or service with other promised goods or services until it identifies a bundle of goods or services that is distinct.

The transaction price is then determined and allocated to the identified performance obligations in proportion to their standalone selling prices ("SSP") on a relative SSP basis. SSP is determined at contract inception and is not updated to reflect changes between contract inception and when the performance obligations are satisfied. Determining the SSP for performance obligations requires significant judgment. In developing the SSP for a performance obligation, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. In certain circumstances, the Company may apply the residual method to determine the SSP of a good or service if the SSP is considered highly variable or uncertain. The Company validates the SSP for performance obligations by evaluating whether changes in the key assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, the Company estimates the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services to a customer. The Company determines the amount of variable consideration by using the expected value method or the most likely amount method. The Company includes the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

If an arrangement includes development and regulatory milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control or the licensee's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received.

In determining the transaction price, the Company adjusts consideration for the effects of the time value of money if the timing of payments provides the Company with a significant benefit of financing. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. The Company assessed its arrangements with Shionogi & Co., Ltd. ("Shionogi") and Biogen and concluded that a significant financing component does not exist for either arrangement. For arrangements with licenses of intellectual property that include sales-based royalties or milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties or milestone payments relate, the Company recognizes royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty or milestone payment has been allocated has been satisfied.

The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time this is based on the use of an output or input method. Revenue from the Company's collaboration agreement with Shionogi has come from initial, upfront consideration upon execution of the agreement and for the supply of drug product for Shionogi's clinical trials. Revenue from the Company's collaboration agreement with Biogen has come from initial, upfront consideration related to the execution of the Biogen Collaboration Agreement, milestone payments and the Company's share of ZURZUVAE revenues under the elements of the arrangement accounted for under ASC Topic 808, *Collaborative Arrangements* ("Topic 808"). For additional information, see the Collaborative Arrangements section below and refer to Note 7, *Collaboration Agreements*.

Collaborative Arrangements

The Company analyzes its collaboration arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities and therefore within the scope of Topic 808. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of Topic 808 that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of Topic 808 and which elements of the collaboration are more reflective of a vendor-customer relationship and therefore within the scope of Topic 606. For elements of collaboration arrangements that are accounted for pursuant to Topic 808, an appropriate recognition method is determined and applied consistently, either by analogy to authoritative accounting literature or by applying a reasonable and rational policy election. For those elements of the arrangement that are accounted for pursuant to Topic 606, the Company applies the five-step model described above and presents the arrangement as license and milestone revenue or other collaboration revenue in the consolidated statements of operations and comprehensive loss.

For collaboration arrangements that are within the scope of Topic 808, the Company evaluates the income statement classification for presentation of amounts due from or owed to other participants associated with multiple activities in a collaboration arrangement based on the nature of each separate activity. Payments or reimbursements that are the result of a collaborative relationship instead of a vendor-customer relationship are recorded as an increase to collaboration revenue, an increase to or reduction of cost of revenues, research and development expense or selling, general and administrative expense, depending on the nature of the activity. For additional information relating to the accounting for the co-commercialization of ZURZUVAE in the U.S. with Biogen under Topic 808, refer to Note 7, *Collaboration Agreements.*

Recently Adopted Accounting Pronouncements

In November 2023, the Financial Accounting Standards Board ("FASB") issued ASU 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures* ("ASU 2023-07"). ASU 2023-07 requires disclosure of incremental segment information on an annual and interim basis. The amendments also require companies with a single reportable segment to provide all disclosures required by this amendment and all existing segment disclosures in ASC 280, Segment Reporting. The amendments are effective for fiscal years beginning after December 15, 2023, and interim periods beginning after December 15, 2024. The Company adopted ASU 2023-07, effective December 31, 2024, in these consolidated financial statements. ASU 2023-07 only impacted the disclosures and did not impact the consolidated financial statements. See Note 15, *Segment Information*, for disclosures related to the adoption of ASU 2023-07.

Recently Issued Accounting Pronouncements

In December 2023, FASB issued ASU 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures* ("ASU 2023-09"). ASU 2023-09 modifies the rules on income tax disclosures to enhance the transparency and decision-usefulness of income tax disclosures, particularly in the rate reconciliation table and disclosures about income taxes paid. The amendments are intended to address investors' requests for income tax disclosures that provide more information to help them better understand an entity's exposure to potential changes in tax laws and the ensuing risks and opportunities and to assess income tax information that affects cash flow forecasts and capital allocation decisions. The guidance also eliminates certain existing disclosure requirements related to uncertain tax positions and unrecognized deferred tax liabilities. The guidance is effective for all entities for annual periods beginning after December 15, 2025. All entities should apply the guidance prospectively but have the option to apply it retrospectively. Early adoption is permitted. The Company is continuing to assess the timing of adoption and the potential impacts of ASU 2023-09 on the consolidated financial statements and related disclosures.

In November 2024, the FASB issued ASU 2024-03, *Income Statement - Reporting Comprehensive Income - Expense Disaggregation Disclosures (Subtopic 220-40)* ("ASU 2024-03"). ASU 2024-03 modifies the rules on income statement disclosures to enhance the transparency of and include more detailed information about the types of expenses, including purchases of inventory, employee compensation, depreciation, amortization, and depletion, in commonly presented expense captions such as cost of sales, research and development, and selling, general and administrative expenses. The amendments are intended to address investors' requests for income statement expense disclosures that provide more information to help them better understand the components of an entity's expenses, make their own judgments about the entity's performance, and more accurately forecast expenses, and enable investors to better assess an entity's prospects for future cash flows. It will also provide contextual information for an entity's presentation and consideration of management's discussion and analysis of financial position and results of operations. The guidance is effective for all entities for annual periods beginning after December 15, 2026. All entities should apply the guidance prospectively but have the option to apply it retrospectively. Early adoption is permitted. The Company is continuing to assess the timing of adoption and the potential impacts of ASU 2024-03 on the consolidated financial statements and related disclosures.

3. Fair Value Measurements

The Company's cash equivalents are classified within Level 1 and Level 2 of the fair value hierarchy. The Company's investments in marketable securities are classified within Level 2 of the fair value hierarchy.

The fair values of the Company's marketable securities are based on prices obtained from independent pricing sources. Consistent with the fair value hierarchy described in Note 2, *Summary of Significant Accounting Policies*, marketable securities with validated quotes from pricing services are reflected within Level 2, as they are primarily based on observable pricing for similar assets or other market observable inputs. Typical inputs used by these pricing services include, but are not limited to, reported trades, benchmark yields, issuer spreads, bids, offers or estimates of cash flow, prepayment spreads and default rates. The Company performs validation procedures to ensure the reasonableness of this data. The Company performs its own review of prices received from the independent pricing services by comparing these prices to other sources. After completing the validation procedures, the Company did not adjust or override any fair value measurements provided by the pricing services as of December 31, 2024 and 2023.

The following tables summarize the Company's cash equivalents and marketable securities as of December 31, 2024 and 2023:

	December 31, 2024			
	Total	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
	(in thousands)			
Cash equivalents:				
Money market funds	$ 73,845	$ 73,845	$ —	$ —
U.S. government securities	5,397	—	5,397	—
U.S. commercial paper	997	—	997	—
Total cash equivalents	80,239	73,845	6,394	—
Marketable securities:				
U.S. government securities	36,457	—	36,457	—
U.S. corporate bonds	269,013	—	269,013	—
International corporate bonds	52,461	—	52,461	—
U.S. commercial paper	30,373	—	30,373	—
International commercial paper	24,144	—	24,144	—
U.S. certificates of deposit	900	—	900	—
U.S. municipal securities	10,049	—	10,049	—
Total marketable securities	423,397	—	423,397	—
	$ 503,636	$ 73,845	$ 429,791	$ —

	December 31, 2023			
	Total	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
	(in thousands)			
Cash equivalents:				
Money market funds	$ 59,852	$ 59,852	$ —	$ —
U.S. government securities	8,695	—	8,695	—
Total cash equivalents	68,547	59,852	8,695	—
Marketable securities:				
U.S. government securities	166,925	—	166,925	—
U.S. corporate bonds	210,198	—	210,198	—
International corporate bonds	97,675	—	97,675	—
U.S. commercial paper	23,370	—	23,370	—
International commercial paper	46,900	—	46,900	—
U.S. certificates of deposit	8,830	—	8,830	—
U.S. municipal securities	128,294	—	128,294	—
Total marketable securities	682,192	—	682,192	—
	$ 750,739	$ 59,852	$ 690,887	$ —

During the years ended December 31, 2024 and 2023, there were no transfers among the Level 1, Level 2 and Level 3 categories.

4. Investments

The following tables summarize the fair value and amortized cost of the Company's available-for-sale securities by major security type, including gross unrealized gains and losses and credit losses, as of December 31, 2024 and 2023:

	December 31, 2024				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Credit Losses	Fair Value
			(in thousands)		
Assets:					
U.S. government securities	$ 36,444	$ 18	$ (5)	$ —	$ 36,457
U.S. corporate bonds	268,841	305	(133)	—	269,013
International corporate bonds	52,411	65	(15)	—	52,461
U.S. commercial paper	30,373	—	—	—	30,373
International commercial paper	24,144	—	—	—	24,144
U.S. certificates of deposit	900	—	—	—	900
U.S. municipal securities	10,040	9	—	—	10,049
	$ 423,153	$ 397	$ (153)	$ —	$ 423,397

	December 31, 2023				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Credit Losses	Fair Value
			(in thousands)		
Assets:					
U.S. government securities	$ 167,165	$ 107	$ (347)	$ —	$ 166,925
U.S. corporate bonds	210,491	191	(484)	—	210,198
International corporate bonds	97,698	99	(122)	—	97,675
U.S. commercial paper	23,360	11	(1)	—	23,370
International commercial paper	46,935	3	(38)	—	46,900
U.S. certificates of deposit	8,830	—	—	—	8,830
U.S. municipal securities	128,527	26	(259)	—	128,294
	$ 683,006	$ 437	$ (1,251)	$ —	$ 682,192

As of December 31, 2024 and 2023, the Company had $3.4 million and $4.2 million, respectively, of accrued interest receivable relating to the Company's available-for-sale securities which is included within prepaid expenses and other current assets in the accompanying consolidated balance sheets. No accrued interest receivable was written off during years ended December 31, 2024, 2023, and 2022. Realized gains or losses were immaterial for the years ended December 31, 2024, 2023, and 2022.

The following tables summarize the fair value and the unrealized losses of the Company's marketable securities that have been in a loss position for either less than twelve months or greater than twelve months as of December 31, 2024 and 2023:

	December 31, 2024					
	Less than 12 months		Greater than 12 months		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
			(in thousands)			
U.S. government securities	$ 11,032	$ (5)	$ —	$ —	$ 11,032	$ (5)
U.S. corporate bonds	83,946	(129)	10,197	(4)	94,143	(133)
International corporate bonds	7,312	(15)	—	—	7,312	(15)
	$ 102,290	$ (149)	$ 10,197	$ (4)	$ 112,487	$ (153)

	December 31, 2023					
	Less than 12 months		Greater than 12 months		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
	(in thousands)					
U.S. government securities	$ 52,521	$ (96)	$ 41,911	$ (251)	$ 94,432	$ (347)
U.S. corporate bonds	111,901	(246)	43,851	(238)	155,752	(484)
International corporate bonds	43,708	(87)	6,014	(35)	49,722	(122)
U.S. commercial paper	7,848	(1)	—	—	7,848	(1)
International commercial paper	37,300	(38)	—	—	37,300	(38)
U.S. municipal securities	90,095	(143)	31,345	(116)	121,440	(259)
	$ 343,373	$ (611)	$ 123,121	$ (640)	$ 466,494	$ (1,251)

As of December 31, 2024 and 2023, the unrealized losses on the Company's investments in U.S. government securities, U.S. corporate bonds, international corporate bonds, and U.S. municipal securities were caused by interest rate increases. The Company purchased those investments at a premium relative to their face amount. The current credit ratings are all within the guidelines of the investment policy of the Company and the Company does not expect the issuers to settle any security at a price less than the amortized cost basis of the investment. The Company does not intend to sell the investments and it is not probable that the Company will be required to sell the investments before recovery of their amortized cost basis.

As of December 31, 2024, all marketable securities held by the Company had remaining contractual maturities of one year or less, except for U.S. corporate bonds and international corporate bonds with a fair value of $30.7 million that had maturities of one to two years.

As of December 31, 2023, all marketable securities held by the Company had remaining contractual maturities of one year or less, except for U.S. government securities, U.S. corporate bonds, international corporate bonds and municipal securities with a fair value of $110.3 million that had maturities of one to two years.

All marketable securities, including those with remaining contractual maturities of more than one year, are classified as current assets on the balance sheet because they are considered to be "available-for-sale" and the Company can convert them into cash to fund current operations.

There have been no impairments of the Company's assets measured and carried at fair value during the years ended December 31, 2024 and 2023.

5. Balance Sheet Components

Property and Equipment, net

The following table summarizes property and equipment, net, as of December 31, 2024 and 2023:

	December 31,	
	2024	2023
	(in thousands)	
Computer hardware and software	$ 852	$ 2,114
Furniture and equipment	822	1,786
Leasehold improvements	—	5,509
	1,674	9,409
Less: Accumulated depreciation	(784)	(7,488)
	$ 890	$ 1,921

Depreciation expense for the years ended December 31, 2024, 2023, and 2022 was $1.0 million, $1.4 million, and $1.1 million, respectively.

The useful life for computer hardware and software is three years, furniture and equipment is five years, and leasehold improvements is the lesser of the useful life or the term of the respective lease.

Accrued Expenses

The following table summarizes accrued expenses as of December 31, 2024 and 2023:

	December 31, 2024	December 31, 2023
	(in thousands)	
Accrued research and development costs	$ 19,758	$ 26,040
Restructuring	15,307	10,589
Employee-related	14,840	21,339
Professional services	7,114	8,589
Other	579	707
	$ 57,598	$ 67,264

As of December 31, 2024 and 2023, accrued research and development costs includes $0.4 and $4.3 million, respectively, of accrued expenses related to canceling excess purchase commitments for manufacturing as a result of the complete response letter ("CRL") received in August 2023 from the FDA related to the New Drug Application ("NDA") for zuranolone for the treatment of major depressive disorder ("MDD"). During the year ended December 31, 2023, $28.9 million of expenses related to the cancelation of excess purchase commitments were recorded as research and development expense in the consolidated statements of operations and comprehensive loss, net of amounts subject to reimbursement under the Biogen Collaboration Agreement of $14.5 million.

6. Leases, Commitments and Contingencies

Operating Leases

The Company leases office space and certain equipment. All of the leases recorded on the consolidated balance sheets are operating leases. The Company's leases have remaining lease terms ranging from less than one year to approximately five years. Some of the leases include options to extend the leases for up to five years. These options were not included for the purpose of determining the right-of-use assets and associated lease liabilities as the Company determined that the renewal of these leases is not reasonably certain so only the original lease term was taken into consideration. The leases do not include any restrictions or covenants that had to be accounted for under the lease guidance.

During the fiscal years ended December 31, 2024, 2023, and 2022, the Company leased office space in three multi-tenant buildings in Cambridge, Massachusetts, consisting of 63,017 square feet in the first building, under an operating lease that expired on August 31, 2024; 40,419 square feet in the second building, under an operating lease that expired on August 31, 2024; and 30,567 square feet in the third building, under an operating lease that commenced in August 2024 that will expire on February 28, 2030; and in a multi-tenant building in Raleigh, North Carolina, consisting of 15,525 square feet under an operating lease that expired on November 30, 2024.

In January 2024, the Company entered into the lease agreement (the "New Lease") for office space in a multi-tenant building in Cambridge, Massachusetts (the "New Premises"). The accounting lease commencement in accordance with ASC 842, *Leases*, occurred on August 2, 2024, and the Company recorded a total associated right-of-use asset of $11.6 million and the corresponding lease liability of $10.0 million. This includes a reclassification of $1.5 million from prepaid expenses and other current assets to right-of-use asset related to build out costs which were determined to be owned by the lessor. The contractual term of the New Lease commenced on September 1, 2024 (the "Term Commencement Date"), which is the date the Company relocated its headquarters to the New Premises. The Company's

obligation for the payment of rent for the New Premises begins six months after the Term Commencement Date (the "Rent Commencement Date"). The New Lease has an initial term of approximately sixty-six months, measured from the Term Commencement Date (the "New Lease Term"). The Company has the option to extend the New Lease one time for an additional five-year period, subject to the terms therein; however, the exercise of the option to extend the lease term was not determined to be reasonably certain, and the Company will therefore recognize lease expense through the expiration of the New Lease Term in February 2030.

In connection with its entry into the New Lease, and as a security deposit, the Company has provided the Landlord a letter of credit in the amount of approximately $1.4 million, classified within long-term restricted cash on the consolidated balance sheets, which the Company and the Landlord have agreed may be reduced to approximately $1.2 million following the third anniversary of the Rent Commencement Date, provided that no event of default by the Company has occurred. The Landlord has the right to terminate the New Lease upon customary events of default.

During the year ended December 31, 2021, the Company entered into a sublease for a portion of the leased office space in the second multi-tenant building in Cambridge, Massachusetts, which was terminated effective April 5, 2024.

The following table shows the amounts of operating leases in the balance sheets as of December 31, 2024 and 2023:

Balance sheet location	Balance sheet caption	December 31, 2024	December 31, 2023
		(in thousands)	
Assets			
Right-of-use operating asset	Right-of-use operating asset	$ 10,753	$ 4,458
Liabilities			
Current operating lease liabilities	Operating lease liability, current portion	1,318	5,165
Long-term operating lease liabilities	Operating lease liability, net of current portion	10,518	—
		$ 11,836	$ 5,165

The following table shows the amounts of lease expense by lease type that was recognized during the years ended December 31, 2024, 2023, and 2022:

	Year Ended December 31, 2024	2023	2022
		(in thousands)	
Operating lease cost	$ 5,972	$ 6,748	$ 6,748
Variable lease cost	1,454	1,957	1,846
Short-term lease cost	20	20	206
Sublease income	—	(434)	(421)
	$ 7,446	$ 8,291	$ 8,379

The Company made an accounting policy election not to apply the recognition requirements to short-term leases. The Company recognizes the lease payments for short-term leases as expense on a straight-line basis over the lease term, and variable lease payments in the period in which the obligation for those payments is incurred.

The minimum lease payments are expected to be as follows:

Years Ending December 31,	(In thousands)
2025	$ 2,461
2026	2,976
2027	3,059
2028	3,144
2029	3,232
Thereafter	542
Total lease payments	15,414
Less imputed interest	(3,578)
Present value of operating lease liabilities	$ 11,836

The following table shows the weighted average remaining lease term and weighted average discount rate of the operating leases:

	Year ended December 31,	
	2024	2023
Weighted average remaining lease term in years	5.17	0.69
Weighted average discount rate	10.0%	7.5%

The interest rate implicit in lease contracts is typically not readily determinable and as such, the Company uses its incremental borrowing rate based on the information available at the lease commencement date, which represents an internally developed rate that would be incurred to borrow, on a collateralized basis, over a similar term, an amount equal to the lease payments in a similar economic environment.

The following table shows the supplemental disclosure of cash flow information related to the operating leases included in cash flows used by operating activities in the consolidated statements of cash flows:

	Year Ended December 31,		
	2024	2023	2022
	(in thousands)		
Cash paid for amounts included in the measurement of lease liabilities	$ 3,958	$ 7,643	$ 7,468
Right-of-use assets obtained in exchange for operating lease obligations:	$ 11,597	$ —	$ —

Legal Proceedings

On August 28, 2024, named plaintiff Darren Korver filed a purported federal securities class action lawsuit in the Southern District of New York against the Company and individuals, Barry E. Greene and Kimi Iguchi (the "Securities Class Action"). The complaint in the Securities Class Action alleges violations of U.S. securities laws under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder and seeks an as-yet unspecified amount of damages allegedly sustained by parties who purchased Sage stock between April 12, 2021 and July 23, 2024, as well as applicable attorneys' fees and costs. The Company denies any allegations of wrongdoing and intends to vigorously defend against the Securities Class Action.

On October 16, 2024, the Company received a subpoena from the Enforcement Division of the SEC requesting documents and information related to the Company's NDA for zuranolone for the treatment of MDD, including communications with the FDA and any communications containing material nonpublic information. The Company is cooperating with the SEC and intends to continue to provide information responsive to the SEC's requests.

At this time, the Company is unable to predict the outcome of the Securities Class Action or the SEC investigation or reasonably estimate a range of possible losses.

On January 16, 2025, the Company commenced litigation against Biogen in the Delaware Court of Chancery seeking declaratory, injunctive and other relief. In its complaint, the Company alleges that Biogen breached the standstill provision in the stock purchase agreement it entered into with Biogen on November 27, 2020 (the "Biogen Stock Purchase Agreement"), by making an unsolicited acquisition proposal and related public disclosures. On this basis, the Company also sought a temporary restraining order enjoining Biogen from future breaches of the standstill provision. At a hearing held on January 28, 2025, the Court granted the Company's motion for a temporary restraining order against Biogen MA Inc., and entered an implementing order on January 30, 2025 (the "TRO Order"). Pursuant to the TRO Order, unless consented to by the Company in writing or otherwise ordered by the court, Biogen MA Inc. and its directors, officers, agents, employees, attorneys, representatives, persons in active concert or participation with it, and anyone acting under its direction or control are enjoined from taking any action inconsistent with the Biogen Stock Purchase Agreement's contractual prohibitions against (i) making a public acquisition proposal, (ii) making a private acquisition proposal that is reasonably expected to require public disclosure, or (iii) publicly encouraging any acquisition proposal. Various motions and related items (whether procedural, discovery-related and/or substantive in nature) occur from time to time with respect to this matter. The Company intends to continue to vigorously pursue its claims against Biogen, but the Company is unable to predict the outcome of the litigation at this time.

7. Collaboration Agreements

Shionogi

In June 2018, the Company entered into a strategic collaboration with Shionogi for the clinical development and commercialization of zuranolone for the treatment of MDD and other potential indications in Japan, Taiwan and South Korea (the "Shionogi Territory"). In October 2018, the Company entered into a supply agreement with Shionogi for the Company to supply zuranolone clinical material to Shionogi.

Under the terms of the collaboration and license agreement, Shionogi is responsible for all clinical development and regulatory filings for zuranolone in MDD and other indications in the Shionogi Territory and would be responsible for commercialization of zuranolone in the Shionogi Territory, if zuranolone is successfully developed and obtains marketing approval in any of the countries within the Shionogi Territory. Shionogi was required to make an upfront payment to the Company of $90.0 million, and the Company was originally eligible to receive additional payments of up to $485.0 million if certain regulatory and commercial milestones are achieved by Shionogi. The potential future milestone payments originally included up to $70.0 million for the achievement of specified regulatory milestones, up to $30.0 million for the achievement of specified commercialization milestones, and up to $385.0 million for the achievement of specified net sales milestones. The potential future milestone payments for achievement of specified regulatory milestones was reduced to $55.0 million upon failure to received FDA approval of zuranolone for the treatment of MDD in the U.S. prior to December 31, 2023. The Company is eligible to receive tiered royalties on sales of zuranolone in the Shionogi Territory, if development efforts are successful, with tiers averaging in the low to mid-twenty percent range, subject to other terms of the agreement. As between the Company and Shionogi, the Company maintains exclusive rights to develop and commercialize zuranolone outside of the Shionogi Territory. The upfront cash payment and any payments for milestones and royalties are non-refundable and non-creditable. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any milestone payments or any royalty payments from Shionogi.

The Company concluded that Shionogi meets the definition of a customer because the Company is delivering intellectual property and know-how rights for the zuranolone program in support of territories in which the parties are not jointly sharing the risks and rewards. In addition, the Company determined that the Shionogi collaboration met the requirements to be accounted for as a contract, including that it is probable that the Company will collect the consideration to which the Company is entitled in exchange for the goods or services that will be delivered to Shionogi.

The Company determined that the performance obligations in the Shionogi collaboration agreement included the license to zuranolone and the supply of certain materials during the clinical development phase, which includes the supply

of API. The performance obligation related to the license to zuranolone was determined to be distinct from other performance obligations and therefore was a separate performance obligation for which control was transferred upon signing. The obligation to provide certain clinical materials, including API for use during the development period, was determined to be a separate performance obligation. Given that Shionogi is not obligated to purchase any minimum amount or quantities of commercial API, the supply of API to Shionogi for commercial use was determined to be an option for Shionogi, rather than a performance obligation of the Company at contract inception and will be accounted for if and when exercised. The Company also determined that there was no separate material right in connection with the supply of API for commercial use as the expected pricing was not at a discount. Given this fact pattern, the Company has concluded the agreement has two performance obligations.

Under the clinical supply agreement, the Company is obligated to manufacture and supply to Shionogi (i) clinical quantities of API reasonably required by Shionogi for the development of licensed products in the Shionogi Territory under the collaboration and license agreement and (ii) quantities of drug product reasonably required for use by Shionogi in Phase 1 clinical trials of zuranolone in the Shionogi Territory under the collaboration and license agreement, in the quantities agreed to by the parties. Collaboration revenue from the clinical supply agreement, which excludes the $90.0 million upfront payment, pertains to the clinical material sold under the terms of the clinical supply agreement. The Company records the costs related to the clinical supply agreement in research and development expense on its consolidated statements of operations and comprehensive loss. During the years ended December 31, 2024 and 2023, $0.6 million and $0.2 million, respectively, of collaboration revenue was recognized from the Company's agreement with Shionogi. During the year ended December 31, 2022, no collaboration revenue was recognized from the Company's agreement with Shionogi.

The Company completed the evaluation of the SSP of each of the performance obligations and determined that the SSP of the license performance obligation was $90.0 million. The Company recognized the transaction price allocated to the license performance obligation of $90.0 million as revenue during the quarter upon delivery of the license to Shionogi and resulting ability of Shionogi to use and benefit from the license, which was in the three months ended June 30, 2018. The remaining transaction price related to the performance obligation for the supply of certain clinical material is not significant. The potential milestone payments that the Company is eligible to receive were excluded from the transaction price, as all milestone amounts were fully constrained based on the probability of achievement. The Company will re-evaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjust its estimate of the transaction price.

Biogen

In November 2020, the Company entered into the Biogen Collaboration Agreement to jointly develop and commercialize SAGE-217 products and SAGE-324 products. Concurrently, the Company also entered into the Biogen Stock Purchase Agreement, under which BIMA purchased shares of the Company's common stock. The Biogen Collaboration Agreement became effective on December 28, 2020 (the "Effective Date").

Under the terms of the Biogen Collaboration Agreement, the Company granted Biogen co-exclusive licenses to develop and commercialize SAGE-217 products and SAGE-324 products (each, a "Product Class" and together, the "Licensed Products") in the U.S., an exclusive license to develop and commercialize SAGE-217 products in all countries of the world other than the U.S. and the Shionogi Territory, and an exclusive license to develop and commercialize SAGE-324 products in all countries of the world other than the U.S. The Company refers to the territories outside the U.S. to which Biogen has rights under the Biogen Collaboration Agreement with respect to the applicable Licensed Product as the "Biogen Territory".

In September 2024, Biogen notified the Company of its termination of the Biogen Collaboration Agreement solely with respect to products containing the Company's SAGE-324 products on a worldwide basis, effective February 17, 2025 (the "SAGE-324 Termination"), in accordance with the required notice period. As a result of the SAGE-324 Termination, as of February 17, 2025 (the "SAGE-324 Termination effective date"), all licenses granted by the Company to Biogen or by Biogen to the Company regarding the SAGE-324 products shall expire with respect to the SAGE-324 products on a worldwide basis. Biogen shall grant to the Company an irrevocable, perpetual license for any Biogen background technology, Biogen collaboration technology or joint collaboration technology that exists as of February 17,

2025 with respect to the SAGE-324 products, in each case in accordance with the terms of the Biogen Collaboration Agreement.

In connection with the effectiveness of the Biogen Collaboration Agreement and the closing of the sale of shares to BIMA in December 2020, the Company received $1.5 billion in consideration, comprised of an upfront payment of $875.0 million and the $650.0 million purchase price for 6,241,473 newly issued shares of the Company's common stock (the "Biogen Shares"). As a result of the purchase of the Biogen Shares, Biogen is a related party of the Company.

The Company was initially eligible to receive additional payments of up to $1.6 billion from Biogen if certain regulatory and commercial milestones were achieved. The potential future milestone payments for SAGE-217 products included up to $475.0 million for the achievement of specified regulatory and commercial milestones, including a milestone payment of $75.0 million for the first commercial sale of ZURZUVAE for the treatment of women with PPD in the U.S. and, if approved, a milestone payment of $150.0 million for the first commercial sale of ZURZUVAE for the treatment of MDD in the U.S., and up to $300.0 million for the achievement of specified net sales milestones. In the fourth quarter of 2023, the Company achieved the $75.0 million milestone for the first commercial sale of ZURZUVAE for the treatment of women with PPD in the U.S. Because the Company and Biogen have agreed not to pursue further development of zuranolone for the treatment of MDD in the U.S., the Company will not receive the $150.0 million milestone payment for the first commercial sale of ZURZUVAE for the treatment of MDD in the U.S.

The potential future milestone payments for SAGE-324 products initially included up to $520.0 million for the achievement of specified regulatory and commercial milestones and up to $300.0 million for the achievement of specified net sales milestones. As a result of the SAGE-324 Termination, the Company will not receive any milestone payments for SAGE-324 products under the Biogen Collaboration Agreement.

The Company is also eligible to receive tiered royalties on net sales of SAGE-217 products in the Biogen Territory at percentage rates ranging from the high teens to low twenties.

Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, and the challenges of launching and commercializing a product, if approved, the Company may never receive any additional milestone payments or any royalty payments under the Biogen Collaboration Agreement.

Development and commercialization activities in the U.S. under the Biogen Collaboration Agreement are conducted pursuant to plans agreed to by the Company and Biogen and overseen by a joint steering committee that consists of an equal number of representatives of each party. The Company and Biogen share equally in the costs for development and commercialization, as well as the profits and losses upon FDA approval and commencement of product sales, in the U.S., subject to the Company's opt-out right described below. Biogen is solely responsible for all development activities and costs related to any development and commercialization of SAGE-217 products and, prior to the SAGE-324 Termination, SAGE-324 products, for the Biogen Territory, and the Company will receive royalties on any sales in the Biogen Territory, as mentioned above. Biogen is the principal and records sales of SAGE-217 products globally.

The Company is obligated to supply API and bulk drug product for the Biogen Territory and API, bulk drug product and final drug product for the U.S. to support development and commercialization activities. Biogen has the right to assume manufacturing responsibilities for API for the Biogen Territory at any time during the term of the agreement, and the agreement further provides that Biogen will, within a reasonable period of time after the Effective Date, assume manufacturing responsibility for bulk drug product for the Biogen Territory.

Unless terminated earlier, the Biogen Collaboration Agreement will continue on a Licensed Product-by-Licensed Product and country-by-country basis until the date on which (a) in any country in the Biogen Territory, the royalty term has expired for all Licensed Products in a Product Class in such country, and (b) for the U.S., the parties agree to permanently cease to commercialize all Licensed Products in a Product Class. Biogen also has the right to terminate the Biogen Collaboration Agreement for convenience in its entirety, on a Product Class-by-Product Class basis (such as the SAGE-324 Termination) or as to a particular region, upon advance written notice. The Company has an opt-out right to convert the co-exclusive licenses in the U.S. to an exclusive license to Biogen on a Product Class-by-Product Class basis. Following the exercise of the opt-out right, the Company would no longer share equally in the profits and losses in the

U.S. and would be entitled to receive certain royalty payments at percentage rates ranging from the high teens to low twenties and additional sales milestones.

The Company concluded that the Biogen Collaboration Agreement and the Biogen Stock Purchase Agreement should be combined and treated as a single arrangement for accounting purposes as the agreements were entered into contemporaneously and in contemplation of one another. The Company determined that the combined agreements had elements that were within the scope of Topic 606 and Topic 808.

As of the Effective Date, the Company identified the following promises in the Biogen Collaboration Agreement that were evaluated under the scope of Topic 606: delivery of (i) a co-exclusive license for SAGE-217 products in the U.S.; (ii) an exclusive license for SAGE-217 products in the Biogen Territory; (iii) a co-exclusive license for SAGE-324 products in the U.S.; (iv) an exclusive license for SAGE-324 products in the Biogen Territory; (v) the clinical manufacturing supply of API and bulk drug product for SAGE-217 products in the Biogen Territory; and (vi) the clinical manufacturing supply of API and bulk drug product for SAGE-324 products in the Biogen Territory.

The Company also evaluated whether certain options outlined within the Biogen Collaboration Agreement represented material rights that would give rise to a performance obligation and concluded that none of the options convey a material right to Biogen and therefore are not considered separate performance obligations within the Biogen Collaboration Agreement.

The Company assessed the above promises at contract inception and determined that the co-exclusive licenses for SAGE-217 products and SAGE-324 products in the U.S. are reflective of a vendor-customer relationship and therefore represent performance obligations within the scope of Topic 606. The co-exclusive license for SAGE-217 products and SAGE-324 products in the U.S. are considered functional intellectual property and distinct from other promises under the contract. The exclusive licenses for SAGE-217 products and SAGE-324 products in the Biogen Territory are considered functional licenses that are distinct in the context of the Biogen Collaboration Agreement as Biogen can benefit from the licenses on its own or together with other readily available resources. As the co-exclusive licenses in the U.S. and the exclusive licenses in the Biogen Territory are delivered at the same time, they are considered one performance obligation at contract inception. The clinical manufacturing supply of API and bulk drug product for SAGE-217 products and SAGE-324 products for the Biogen Territory are considered distinct in the context of the Biogen Collaboration Agreement as Biogen can benefit from the manufacturing services together with the licenses transferred by the Company at the inception of the agreement. Therefore, each represents a separate performance obligation within a contract with a customer under the scope of Topic 606 at contract inception.

The Company determined the transaction price under Topic 606 at the inception of the Biogen Collaboration Agreement to be $1.1 billion, consisting of the upfront payment of $875.0 million plus $232.5 million in excess proceeds from the equity investment under the Biogen Stock Purchase Agreement, when measured at fair value, plus future variable consideration for manufacturing supply of clinical API and bulk drug product for the Biogen Territory. The amount of variable consideration related to the future manufacturing services was not material. At inception, the Company determined that any variable consideration related to clinical development and regulatory or commercial milestones is deemed to be fully constrained and therefore excluded from the transaction price due to the high degree of uncertainty and risk associated with these potential payments, as the Company determined that it could not assert that it was probable that a significant reversal in the amount of cumulative revenue recognized will not occur. The Company also determined that royalties and sales milestones relate solely to the licenses of intellectual property and are therefore excluded from the transaction price under the sales- or usage-based royalty exception of Topic 606. Revenue related to these royalties and sales milestones will only be recognized when the associated sales occur, and relevant thresholds are met. As such, the entirety of the $1.1 billion transaction price was allocated to the transfer of the co-exclusive licenses for SAGE-217 products and SAGE-324 products in the U.S. and the exclusive licenses for SAGE-217 products and SAGE-324 products in the Biogen Territory and was recognized as license revenue during the year ended December 31, 2020.

In the fourth quarter of 2023, the Company achieved a milestone for the first commercial sale of ZURZUVAE for the treatment of women with PPD in the U.S. and recognized license and milestone revenue – related party of $75.0 million during the fourth quarter of the year ended December 31, 2023. Payment of the $75.0 million milestone was

received in January 2024. During the years ended December 31, 2024 and 2022, no license and milestone revenue – related party was recognized related to the Biogen Collaboration Agreement.

The Company considers the collaborative activities associated with the co-development, co-commercialization, and co-manufacturing of SAGE-217 products and, through the SAGE-324 Termination effective date, SAGE-324 products in the U.S. to be separate units of account within the scope of Topic 808 as the Company and Biogen are both active participants in the development and commercialization activities and are exposed to significant risks and rewards that are dependent on the development and commercial success of the activities in the arrangement.

While Biogen is considered the principal in transactions with customers for the sale of ZURZUVAE globally, the Company is also engaged in significant commercialization activities, including maintaining its own U.S. direct sales force. The Company presents its proportionate share of Biogen's ZURZUVAE sales to customers in the U.S. as collaboration revenue - related party. Payments to or reimbursements from Biogen related to the agreement of the parties to share equally in all revenue and costs are accounted for as an increase to collaboration revenue, an increase to or reduction of cost of revenues, research and development expenses, or selling, general and administrative expenses, in the consolidated statements of operations and comprehensive loss, depending on the nature of the activity.

To record its proportionate share of collaboration revenue from Biogen's sales of ZURZUVAE to customers in the U.S., the Company utilizes certain information from Biogen, including revenue from the sale of the product and associated reserves on revenue.

The following table summarizes the Company's proportionate share of the activity under the Biogen Collaboration Agreement accounted for under Topic 808, including activities associated with the sale of ZURZUVAE in the U.S., as well as costs during the periods related to the development of SAGE-217 products and SAGE-324 products, as reflected in our consolidated statements of operations and comprehensive loss:

	Year Ended December 31,		
	2024	2023	2022
		(in thousands)	
Collaboration revenue - related party	$ 36,087	$ 824	$ —
Cost of revenues	5,428	504	—
Research and development expenses	20,617	94,325	86,028
Selling, general and administrative expenses	58,950	89,599	51,870

The revenue, cost and expense categories in the table above reflects the following reimbursement amounts to (from) Biogen to account for the sharing of economics under the Biogen Collaboration Agreement:

	Year Ended December 31,		
	2024	2023	2022
		(in thousands)	
Collaboration revenue - related party	$ (36,087)	$ (824)	$ —
Cost of revenues	(2,723)	504	—
Research and development expenses	(15,680)	(76,208)	(73,227)
Selling, general and administrative expenses	10,881	16,496	(2,230)

As of December 31, 2024, the Company recorded a collaboration receivable – related party of $9.1 million, representing net reimbursement for amounts due for the three months ended December 31, 2024. As of December 31, 2023, the Company recorded a collaboration receivable – related party of $83.0 million, consisting of $8.0 million of net reimbursement for amounts due for the three months ended December 31, 2023 and the $75.0 million milestone achieved.

During the year ended December 31, 2024, no payments were made to Biogen and the Company received $118.1 million from Biogen for the amounts due for the three months ended December 31, 2023 and the nine months ended September 30, 2024. During the year ended December 31, 2023, no payments were made to Biogen and the Company received $65.7 million from Biogen for the amounts due for the three months ended December 31, 2022 and the nine months ended September 30, 2023. During the year ended December 31, 2022, no payments were made to Biogen and the

Company received $80.3 million from Biogen for the amounts due for the three months ended December 31, 2021 and the nine months ended September 30, 2022.

During the year ended December 31, 2024, the Company recorded $0.9 million of other collaboration revenue related to providing development and regulatory support to Biogen in the Biogen Territory under the Biogen Collaboration Agreement. During the years ended December 31, 2023 and 2022, no other collaboration revenue was recognized related to the Biogen Collaboration Agreement.

Accounting for the Biogen Stock Purchase Agreement

In connection with the execution of the Biogen Collaboration Agreement, the Company and BIMA entered into the Biogen Stock Purchase Agreement. Pursuant to the Biogen Stock Purchase Agreement, the Company sold the Biogen Shares to BIMA at a price of approximately $104.14 per share for aggregate consideration of $650.0 million. The sale of the shares to BIMA closed on December 31, 2020.

The Biogen Stock Purchase Agreement includes certain standstill provisions that terminate on the earliest of (i) a specified regulatory milestone under the Biogen Collaboration Agreement, (ii) the date one year following the termination of the Biogen Collaboration Agreement and (iii) the seventh anniversary of the Effective Date.

The Company determined the fair value of the common shares was determined to be $417.5 million, which was $232.5 million less than the proceeds received from BIMA for the issuance of the Company's common stock under the Biogen Stock Purchase Agreement. As such, the $232.5 million in excess proceeds has been included in the $1.1 billion transaction price of the Biogen Collaboration Agreement determined above.

8. Preferred Stock

The Board of Directors of the Company (the "Board") is authorized, without action by the stockholders, to designate and issue up to an aggregate of 5,000,000 shares of preferred stock in one or more series. The Board can designate the rights, preferences and privileges of the shares of each series and any of its qualifications, limitations or restrictions. The Board may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of common stock. As of December 31, 2024 and 2023, the Company had no shares of preferred stock issued or outstanding and preferred stock is classified within stockholders' equity.

9. Common Stock

As of December 31, 2024 and 2023, the Company authorized 120,000,000 shares of common stock with a par value of $0.0001 per share.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to receive dividends, as may be declared by the Board, if any. As of December 31, 2024 and 2023, no dividends have been declared.

As of December 31, 2024, the Company had received 3,033 shares of the Company's common stock from a then-employee as consideration for exercises of stock options. The total cost of shares held in treasury at December 31, 2024 was $0.4 million.

Sales Agreement

On September 16, 2024, the Company entered into a Sales Agreement (the "ATM Sales Agreement") with TD Securities (USA) LLC, as sales agent ("TD Cowen"), with respect to an "at the market offering" program pursuant to which the Company may offer and sell shares of its common stock having an aggregate offering price of up to $250.0 million (the "Shares"), from time to time through TD Cowen (the "ATM Offering"). Upon the Company's entry into the ATM Sales Agreement, the prior sales agreement with Cowen and Company, LLC, an affiliate of TD Cowen, dated November 7, 2023 (the "Original Sales Agreement") was terminated. At the time of such termination, $241.7 million out of an aggregate of $250.0 million of shares remained unsold under the Original Sales Agreement.

Upon delivery of a placement notice, and subject to the terms and conditions of the ATM Sales Agreement, TD Cowen may sell the Shares by methods deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended. The Company may sell the Shares in amounts and at times to be determined by the Company from time to time subject to the terms and conditions of the ATM Sales Agreement, but the Company has no obligation to sell any of the Shares in the ATM Offering.

The Company or TD Cowen may suspend or terminate the ATM Offering upon notice to the other parties and subject to other conditions. TD Cowen will act as sales agent on a commercially reasonable efforts basis consistent with its normal trading and sales practices, applicable state and federal laws, rules and regulations, and the rules of the Nasdaq Global Market.

The Company has agreed to pay TD Cowen commission for its service in acting as agent in the sale of the Shares in the amount of up to 3.0% of the gross proceeds from the sale of the Shares pursuant to the ATM Sales Agreement.

During the year ended December 31, 2024 the Company sold an aggregate of 700,000 shares under the Original Sales Agreement at an average price per share of $11.90 and received gross proceeds of approximately $8.3 million, before deducting commissions, underwriting discounts, and offering costs of $0.3 million. During the year ended December 31, 2023, the Company did not sell any shares under the Original Sales Agreement.

During the year ended December 31, 2024, the Company did not sell any shares under the ATM Sales Agreement. As of December 31, 2024, $250.0 million of shares remain available for issuance and sale under the ATM Sales Agreement.

10. Stock-Based Compensation

Equity Plans

On July 2, 2014, the stockholders of the Company approved the 2014 Stock Option and Incentive Plan (the "2014 Plan"), which became effective immediately prior to the completion of the Company's initial public offering. The 2014 Plan provided for the grant of restricted stock awards, restricted stock units, incentive stock options and non-statutory stock options. The 2014 Plan replaced the Company's 2011 Stock Option and Grant Plan (the "2011 Plan").

On June 10, 2024, the stockholders of the Company approved the 2024 Equity Incentive Plan (the "2024 Plan"), which had been previously approved by the Board. Upon stockholder approval, the 2024 Plan became effective immediately and replaced the 2014 Plan. The 2024 Plan provides for the grant of incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock, restricted stock units, other stock-based awards, and cash awards. The total number of shares initially reserved for issuance under the 2024 Plan is equal to the sum of (i) 5,500,000 shares of the Company's common stock and (ii) such additional number of shares of the Company's common stock (up to 11,002,166 shares) as is equal to the number of shares of common stock subject to awards granted under the 2014 Plan that were outstanding as of June 10, 2024, and which awards expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right (subject, however, in the case of incentive stock options, to any limitations under the Internal Revenue Code of 1986, as amended, and any regulations thereunder).

The Company no longer grants stock options or other awards under either its 2014 Plan or its 2011 Plan, and there are no stock options or other awards outstanding under the 2011 Plan. Any stock options and other awards outstanding under the 2014 Plan remain outstanding and effective in accordance with their terms.

On December 15, 2016, the Board approved the 2016 Inducement Equity Plan (as amended and restated, the "2016 Plan"). The 2016 Plan provides for the grant of equity awards to individuals who have not previously been an employee or a non-employee director of the Company to induce them to accept employment and to provide them with a proprietary interest in the Company. On September 20, 2018, the Board amended the 2016 Plan to increase the total number of shares reserved for issuance by 1,200,000 shares. On April 16, 2024, the Board amended the 2016 Plan to reduce the number of shares reserved for issuance thereunder to 428,074 shares and to provide that no further grants may be made under the 2016 Plan after April 16, 2024.

Terms of equity grants, including vesting requirements, are determined by the Board or the Compensation Committee of the Board, subject to the provisions of the applicable plan. Stock options granted by the Company that are not performance-based are considered time-based because they vest based on the continued service of the grantee with the Company during a specified period following grant. These awards, when granted to employees, generally vest ratably over four years, with 25% vesting at the one-year anniversary, and generally expire 10 years after the date of grant.

As of December 31, 2024, the total number of shares underlying outstanding awards under the 2024 Plan, the 2014 Plan and the 2016 Plan was 8,758,214 and the total number of shares available for future issuance under the 2024 Plan was 7,490,967 shares.

On July 2, 2014, the Company's stockholders approved the 2014 Employee Stock Purchase Plan (the "ESPP"), which had been previously approved by the Board. The ESPP became effective upon the completion of the IPO. A total of 282,000 shares of common stock were authorized for issuance under the ESPP. On June 16, 2022, the Company's stockholders approved an amendment to the ESPP to add 300,000 shares of common stock to the ESPP. On June 16, 2023, the Company's stockholders approved an amendment to the ESPP to add 500,000 shares of common stock to the ESPP. As amended, a total of 1,082,000 shares of common stock have been authorized for issuance under the ESPP. As of December 31, 2024, 662,806 shares have been issued and 419,194 shares are available for future issuance under the ESPP.

Option Exchange Program

On January 23, 2024, the Company initiated a tender offer related to a one-time stock option exchange program pursuant to which eligible non-executive officer employees were given the opportunity to exchange certain outstanding stock options (the "Eligible Options") to purchase shares of the Company's common stock for replacement options to purchase a lesser number of shares of common stock (the "Option Exchange") upon the terms and subject to the conditions set forth in the Offer to Exchange Eligible Options for Replacement Options dated January 23, 2024 (the "Offer to Exchange"). Stock options eligible for exchange had an exercise price per share of $35.00 or greater, in addition to certain other requirements, and were exchanged for replacement options with an exercise price per share equal to the fair market value of the Company's common stock on the date of grant of the replacement options, which was February 21, 2024. The consummation of the Option Exchange was subject to approval by the Company's stockholders, which approval was received at the special meeting of stockholders held on January 31, 2024. The Company accepted for exchange Eligible Options to purchase a total of 3,079,608 shares of the Company's common stock. All tendered Eligible Options were cancelled effective as of February 21, 2024, and promptly thereafter, in exchange thereof, the Company granted replacement options for a total of 1,483,113 shares of the Company's common stock, pursuant to the terms of the Offer to Exchange and the 2014 Plan. The exercise price per share of the replacement options was $22.20 per share, which was the closing price per share of the Company's common stock on the Nasdaq Global Market on February 21, 2024. The replacement options vest over 18 months from the date of grant and have a term of seven years.

The Company expects to incur a total of $1.7 million of additional stock-based compensation expense as a result of the Option Exchange, to be recognized over the 18-month vesting period of the replacement options.

Restricted Stock Units

The following table summarizes activity relating to time-based restricted stock units and performance restricted stock units:

	Shares	Weighted Average Grant Date Fair Value
Outstanding as of December 31, 2023	3,088,394	$ 34.27
Granted	1,338,925	$ 22.76
Vested	(430,704)	$ 26.32
Forfeited	(996,225)	$ 34.99
Outstanding as of December 31, 2024	3,000,390	$ 30.04

Time-based restricted stock units

During the years ended December 31, 2024 and 2023, the Company granted 938,470 and 1,734,717 time-based restricted stock units, respectively, to its employees and consultants. During the year ended December 31, 2022, the Company did not grant any time-based restricted stock units.

During the years ended December 31, 2024, 2023 and 2022 there were 272,844, 51,851, and 366,014 time-based restricted stock units that vested, respectively. The fair value on the date of vesting for the years ended December 31, 2024, 2023 and 2022 was $2.8 million, $1.8 million, and $12.4 million, respectively.

At December 31, 2024, 1,788,137 time-based restricted stock units were both outstanding and unvested, and the total unrecognized stock-based compensation expense related to these awards was $13.8 million, which is expected to be recognized over the remaining weighted average vesting period of 1.43 years.

Performance restricted stock units

During the year ended December 31, 2022, the Company granted 705,380 performance restricted stock units to its employees and consultants. The majority of these performance restricted stock units vest upon the achievement of certain clinical and regulatory development milestones related to product candidates and commercial milestones.

During the year ended December 31, 2023, the Company granted 905,012 performance restricted stock units to its employees and consultants. The majority of these performance restricted stock units vest upon the achievement of certain clinical and regulatory development milestones related to product candidates and commercial milestones. Certain performance restricted stock units vest upon the Company reaching specified measures of total stockholder return.

During the year ended December 31, 2024, the Company granted 400,455 performance restricted stock units to its employees. The majority of these performance restricted stock units vest upon the achievement of certain commercial milestones. Certain performance restricted stock units vest upon the Company reaching specified measures of total stockholder return.

Recognition of stock-based compensation expense associated with performance restricted stock units, except for those with milestones that are measures of total stockholder return, commences when the performance condition is considered probable of achievement, using management's best estimates, which consider the inherent risk and uncertainty regarding the future outcomes of the milestones. Recognition of stock-based compensation associated with performance restricted stock units with milestones that are measures of total stockholder return commences on the grant date and is recorded independently of the vesting outcomes of the grants.

During the year ended December 31, 2024, the criteria for one vesting milestone for outstanding performance restricted stock units was considered probable. The Company recognized stock-based compensation expense related to the probable vesting of this performance restricted stock unit of $4.0 million. There remains an estimated $0.4 million of expense to be recognized as of December 31, 2024.

As of December 31, 2023 and 2022, for performance restricted stock units that were outstanding, and other than performance restricted stock units for which vesting is tied to total stockholder return, the achievement of the milestones that had not been met was considered not probable, and therefore no expense has been recognized related to these awards in the years ended December 31, 2023 and 2022, respectively.

During the years ended December 31, 2024 and 2023, the Company recorded $0.8 million and $0.7 million, respectively, of stock-based compensation expense related to performance restricted stock units for which vesting is tied to total stockholder return.

No performance restricted stock units vested during the year ended December 31, 2022.

During the year ended December 31, 2023, the criteria for three vesting milestones for outstanding performance restricted stock units were achieved. The total fair value of the performance restricted stock units that vested upon achievement of these milestones was $9.6 million at vesting date, and the Company recognized stock-based compensation expense related to the vesting of these performance restricted stock units of $14.3 million.

During the year ended December 31, 2024, the criteria for one vesting milestone for outstanding performance restricted stock units were achieved. The total fair value of the performance restricted stock units that vested upon achievement of this milestone was $1.4 million at vesting date, and the Company recognized stock-based compensation expense related to the vesting of these performance restricted stock units of $3.6 million.

At December 31, 2024, 1,212,253 performance restricted stock units were both outstanding and unvested, and the total unrecognized stock-based compensation expense related to these awards was $42.9 million.

Stock Option Rollforward

The following table summarizes activity related to time-based and performance-based stock options:

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2023	8,118,041	$ 76.02	5.66	$ 475
Granted	2,275,745	$ 21.08		
Exercised	(10,062)	$ 7.69		
Forfeited	(4,563,788)	$ 79.14		
Expired	(62,112)	$ 24.09		
Outstanding as of December 31, 2024	5,757,824	$ 52.52	5.34	$ —
Vested and expected to vest as of December 31, 2024	5,129,145	$ 50.56	5.17	$ —
Exercisable as of December 31, 2024	4,014,487	$ 58.04	4.42	$ —

As of December 31, 2024, the Company had unrecognized stock-based compensation expense related to its outstanding and unvested time-based stock option awards of $24.1 million, which is expected to be recognized over the remaining weighted average vesting period of 3.18 years.

The intrinsic value of stock options exercised during the years ended December 31, 2024, 2023, and 2022 was $0.1 million, $1.9 million and $4.4 million, respectively.

Performance-Based Stock Options

Recognition of stock-based compensation expense associated with performance-based stock options commences when the performance condition is considered probable of achievement, using management's best estimates, which consider the inherent risk and uncertainty regarding the future outcomes of the milestones.

As of December 31, 2024, 2023 and 2022, for performance-based stock option grants that were outstanding, the achievement of the milestones that had not been met was considered not probable, and therefore no expense has been recognized related to these awards in the years ended December 31, 2024, 2023 and 2022, respectively.

During the years ended December 31, 2024, 2023 and 2022, the Company granted no stock options to purchase shares of common stock that contain performance-based vesting criteria.

During the years ended December 31, 2024 and 2022, no milestones were achieved under performance-based stock options.

During the year ended December 31, 2023, the criteria for one regulatory development milestone was achieved under performance-based stock options granted in connection with the hiring of its chief executive officer. During the year ended December 31, 2023, the Company recognized stock-based compensation expense related to this milestone of $10.7 million.

As of December 31, 2024, 455,000 performance-based stock options were both outstanding and unvested, the total unrecognized stock-based compensation expense related to these awards was $24.9 million before the application of the forfeiture rate and the timing of recognition of this stock-based compensation expense is subject to judgment of the Company as to when the performance conditions are considered probable of being achieved.

Stock-Based Compensation Expense

The following table summarizes stock-based compensation expense recognized during the years ended December 31, 2024, 2023, and 2022:

	Year Ended December 31,		
	2024	2023	2022
	(in thousands)		
Research and development	$ 18,885	$ 24,813	$ 25,888
Selling, general and administrative	35,587	47,716	35,714
Restructuring	32	838	—
	$ 54,504	$ 73,367	$ 61,602

The stock-based compensation expense of $32 thousand is related to the restructuring during the year ended December 31, 2024 and represents the incremental amount related to modifying the exercise period for outstanding, vested stock option grants that had been granted to employees whose employment was terminated in the restructuring. The expense was recorded within the restructuring expenses on the consolidated statements of operations and comprehensive loss.

The stock-based compensation expense of $0.8 million is related to the restructuring during the year ended December 31, 2023 and represents the incremental amount related to modifying the exercise period for outstanding, vested stock option grants that had been granted to employees whose employment was terminated in the restructuring. The expense was recorded within the restructuring expenses on the consolidated statements of operations and comprehensive loss.

The following table summarizes stock-based compensation expense by award type recognized during the years ended December 31, 2024, 2023, and 2022:

	Year Ended December 31,		
	2024	2023	2022
	(in thousands)		
Stock options	$ 26,609	$ 47,695	$ 54,971
Restricted stock units	27,058	24,424	5,587
Employee stock purchase plan	837	1,248	1,044
	$ 54,504	$ 73,367	$ 61,602

For stock option awards, the fair value is estimated at the grant date using the Black-Scholes option-pricing model, taking into account the terms and conditions upon which stock options are granted. For grants with service based vesting conditions, the fair value of the stock options is amortized on a straight-line basis for stock option awards to employees, non-employee directors and non-employee consultants over the requisite service period of the awards.

The weighted average grant date fair value per share of stock options granted under the Company's stock option plans during the years ended December 31, 2024, 2023, and 2022 was $14.23, $29.53 and $25.96, respectively.

The fair value of each stock option granted under the Company's equity plans has been calculated on the date of grant using the following weighted average assumptions:

	Year Ended December 31,		
	2024	2023	2022
Expected dividend yield	0%	0%	0%
Expected volatility	76%	72%	73%
Risk-free interest rate	4.24%	3.85%	2.49%
Expected term	6.01 years	6.01 years	6.03 years

Expected dividend yield: the Company has not paid, and does not anticipate paying, any dividends in the foreseeable future.

Risk-free interest rate: the Company determined the risk-free interest rate by using a weighted average equivalent to the expected term based on the U.S. Treasury yield curve in effect as of the date of grant.

Expected volatility: the Company uses the historical volatility of its publicly traded common stock, as there is adequate historical data for the duration of the expected term.

Expected term (in years): the expected term represents the period that the Company's stock option grants are expected to be outstanding. The expected term of the stock options granted to employees, non-employee directors and non-employee consultants by the Company has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" stock options. Under this approach, the weighted average expected life is presumed to be the average of the vesting term and the contractual term of the stock option. This approach is used because the Company does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term due to the limited period of time that its stock has been publicly traded.

Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from estimates. The Company estimates forfeitures based on historical terminations. For the years ended December 31, 2024, 2023, and 2022, the weighted-average forfeiture rates were 15.1%, 16.6% and 19.2%, respectively.

11. Net Loss Per Share

The following table shows the calculation of basic and diluted net loss per share for the years ended December 31, 2024, 2023, and 2022:

	Year Ended December 31,		
	2024	2023	2022
Basic net loss per share:			
Numerator:			
Net loss (in thousands)	$ (400,666)	$ (541,489)	$ (532,784)
Denominator:			
Weighted average common stock outstanding - basic and diluted	60,765,913	59,836,441	59,306,094
Net loss per share - basic and diluted	$ (6.59)	$ (9.05)	$ (8.98)

The following table summarizes potential dilutive securities outstanding at the end of each reporting period that were excluded from the calculation of diluted net loss per share because including them would have been anti-dilutive as of December 31, 2024, 2023, and 2022:

	Year Ended December 31,		
	2024	2023	2022
Stock options	5,302,824	7,663,041	7,138,350
Restricted stock units	1,788,137	1,662,363	160,403
Employee stock purchase plan	52,436	61,402	76,105
	7,143,397	9,386,806	7,374,858

Stock options and restricted stock units that are outstanding and contain performance-based vesting criteria for which the performance conditions have not been met are excluded from the calculation of potential dilutive securities above.

12. Income Taxes

Loss before income tax expense consists of the following:

	Year Ended December 31,		
	2024	2023	2022
	(in thousands)		
Domestic	$ (401,549)	$ (541,656)	$ (532,539)
Foreign	883	167	(245)
	$ (400,666)	$ (541,489)	$ (532,784)

There is no current or deferred provision for income taxes because the Company has historically incurred and utilized operating losses prior to the year ended December 31, 2024. As of December 31, 2024, the Company continues to maintain a full valuation allowance against its net deferred tax assets. The reported amount of income tax expense for the years differs from the amount that would result from applying domestic federal statutory tax rates to pretax losses primarily because of changes in the valuation allowance.

A reconciliation of the U.S. statutory rate to the Company's effective tax rate is as follows:

	Year Ended December 31,		
	2024	2023	2022
Tax due at statutory rate	21.0%	21.0%	21.0%
State taxes, net of federal	1.9	4.1	1.8
Stock-based compensation	(10.2)	(1.7)	(1.9)
Federal and state tax credits	2.9	2.4	2.1
Change in valuation allowance	(15.4)	(26.2)	(23.0)
Other	(0.2)	0.4	—
	0.0%	0.0%	0.0%

For the year ended December 31, 2024, the impact from stock-based compensation on the Company's effective tax rate was primarily caused by cancellations of vested non-qualified stock options.

Significant components of the Company's net deferred tax assets at December 31, 2024 and 2023 are as follows:

	December 31,	
	2024	2023
	(in thousands)	
Net operating losses	$ 490,891	$ 428,785
Tax credits	145,113	133,602
Capitalized research and development expenses	128,001	110,690
Stock-based compensation	23,967	53,860
Accrued expenses	5,491	7,018
Depreciation and amortization	1,914	1,456
Lease liability	2,748	1,207
Right of use asset	(2,497)	(1,042)
Other	1,090	(382)
Total net deferred tax asset before valuation allowance	796,718	735,194
Valuation allowance	(796,718)	(735,194)
	$ —	$ —

On August 16, 2022, the Inflation Reduction Act of 2022 (the "IRA") was signed into law. The IRA introduced new tax provisions, including a 15.0% corporate alternative minimum tax and a 1.0% excise tax on stock repurchases. The provisions of the IRA are effective for periods after December 31, 2022. The enactment of the IRA did not result in any material adjustments to the Company's income tax provision or net deferred tax assets as of December 31, 2024 and 2023.

As of December 31, 2024, the Company had federal net operating loss carryforwards of $2.0 billion, of which $30.4 million begin to expire in 2033 and the remainder do not expire but are subject to 80% limitation. As of December 31, 2024, the Company had state net operating loss carryforwards of $1.1 billion that begin to expire in 2033. As of December 31, 2024, the Company had federal and state research and development tax credits carryforwards of $90.5 million and $18.4 million, respectively, which begin to expire in 2031 and 2032, respectively. As of December 31, 2024, the Company had federal orphan drug tax credit carryforwards of $40.1 million, which begin to expire in 2034.

As of December 31, 2024, net deferred tax assets before the valuation allowance increased $61.5 million, primarily due to the capitalization of research and development expenses and the increase of federal and state net operating loss carryforwards due to the loss generated for the year ended December 31, 2024, offset by the cancelation of vested nonqualified stock options resulting from the workforce reductions during the years ended December 31, 2024 and 2023. This increase in net deferred tax assets was offset by a corresponding increase in the valuation allowance.

Management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are comprised principally of federal and state net operating loss, capitalized research and development expenses and tax credit carryforwards. Under the applicable accounting standards, management has considered the Company's history of losses and concluded that it is more likely than not that the Company will not recognize the benefits of its federal and state deferred tax assets. Accordingly, a full valuation allowance of $796.7 million and $735.2 million has been established at December 31, 2024 and 2023, respectively. The valuation allowance increased by $61.5 million for the year ended December 31, 2024, primarily due to the capitalization of research and development expenses and generation of net operating losses, offset by the cancelation of vested nonqualified stock options. The valuation allowance increased by $141.9 million and $122.7 million for the years ended December 31, 2023 and 2022, respectively, primarily due to the capitalization of research and development expenses and generation of net operating losses.

Pursuant to Section 382 of the Internal Revenue Code of 1986, as amended, (the "Code"), and similar state tax law, certain substantial changes in the Company's ownership may result in a limitation on the amount of net operating loss and tax credit carryforwards that may be used in future years. Utilization of the net operating loss and tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Code, due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of net

operating loss and tax credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. The Company completed a Section 382 study through December 31, 2020. Based on the study, the Company underwent two ownership changes for Section 382 purposes which occurred on March 11, 2014 and December 31, 2015. As a result of the ownership changes, the Company's net operating loss and tax credit carryforwards as of the ownership change dates are subject to limitation under Section 382; however, these limitations are not expected to cause any of the impacted net operating loss and tax credit carryforwards to expire unused. Subsequent ownership changes, as defined by Section 382, may potentially further limit the amount of net operating loss and tax credit carryforwards that could be utilized to offset future taxable income and tax.

The Company applies the authoritative guidance on accounting for and disclosure of uncertainty in tax positions, which requires the Company to determine whether a tax position of the Company is more likely than not to be sustained upon examination, including resolution of any related appeals of litigation processes, based on the technical merits of the position. For tax positions meeting the more likely than not threshold, the tax amount recognized in the financial statements is reduced by the largest benefit that has a greater than fifty percent likelihood of being realized upon the ultimate settlement with the relevant taxing authority.

The following table reconciles the beginning and ending amounts of gross unrecognized tax benefits, excluding interest and penalties, if any, for the years ended December 31, 2024, 2023, and 2022:

	2024	2023	2022
		(in thousands)	
Balance as of January 1	$ 7,743	$ 6,846	$ 6,084
Increases related to current year tax positions	520	655	697
Increases related to prior year tax positions	15	242	65
Balance as of December 31	$ 8,278	$ 7,743	$ 6,846

For the years ended December 31, 2024, 2023, and 2022, the increases in unrecognized tax benefits related to current year and prior year tax positions with respect to the Company's federal and state tax credits.

The Company's policy is to record interest and penalties related to income taxes as part of the tax provision. As of December 31, 2024 and 2023, the Company had no accrued interest or penalties related to income taxes and no amounts have been recognized in the Company's statements of operations and comprehensive loss for the years ended December 31, 2024, 2023, and 2022.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal, state and foreign jurisdictions, where applicable. There are currently no pending tax examinations, and the Company's tax returns are generally open under statute from 2021 to the present. Tax attributes such as net operating losses and tax credits generated prior to 2021 and utilized in open years may still be adjusted upon examination.

13. Employee Benefit Plan

The Company maintains a 401(k) profit sharing plan (the "401(k) Plan") for its employees. Each employee may elect to contribute a portion of his or her compensation to the 401(k) Plan, subject to annual limits established by the Internal Revenue Service. For the years ended December 31, 2024, 2023, and 2022, the Company matched 50% of eligible contributions to the 401(k) Plan up to 6% of employee contributions. For the years ended December 31, 2024, 2023, and 2022 the Company contributed $2.9 million, $3.9 million, and $3.0 million, respectively, to the 401(k) Plan.

14. Restructuring

In August 2023, the Company implemented a strategic corporate reorganization and reprioritization of its pipeline (the "2023 Restructuring"). The 2023 Restructuring included a reduction of the Company's workforce by approximately 40%, designed to right-size the organization as the Company worked to achieve sustained growth and support the commercialization of ZURZUVAE for the treatment of women with PPD. During the year ended December 31, 2023, the

Company recorded $33.4 million of expense related to the 2023 Restructuring, primarily for one-time termination benefits to the affected employees, primarily for cash payments of severance, healthcare benefits and outplacement assistance.

As of December 31, 2024, the Company has paid substantially all of the accrued 2023 Restructuring charges and during the year ended December 31, 2024, the Company recorded a $0.5 million reversal of related expense. Total restructuring charges incurred through December 31, 2024 are $32.9 million, which is the total expected amount to be incurred.

In October 2024, the Company implemented a plan to reorganize its business operations (the "2024 Restructuring"), including to focus investment on the ongoing launch of ZURZUVAE for the treatment of women with PPD and its prioritized pipeline development efforts. As part of the 2024 Restructuring, the Company implemented a reduction of approximately 33% of the Company's total workforce and approximately 55% of the Company's research and development workforce. During the year ended December 31, 2024, the Company recorded $22.3 million of expense for the 2024 Restructuring, primarily for one-time termination benefits to the affected employees, primarily consisting of cash payments of severance, healthcare benefits and outplacement assistance.

The Company expects that substantially all of the accrued 2024 Restructuring charges as of December 31, 2024 will be paid in cash by June 30, 2025. The Company expects to incur a total of $23.6 million of expense related to the 2024 Restructuring, including $1.3 million of expense which will be recorded in future periods, primarily consisting of one-time termination benefits.

The following table summarizes activity related to the restructuring accrual inclusive of both the 2023 and 2024 Restructuring:

	Year Ended December 31,	
	2024	2023
	(in thousands)	
Balance as of January 1	$ 10,589	$ —
Restructuring expenses incurred, net	21,854	33,386
Cash paid	(16,939)	(19,163)
Non-cash activity	(197)	(3,634)
Balance as of December 31	$ 15,307	$ 10,589

15. Segment Information

Operating segments are defined as components of an entity for which separate financial information is available and that is regularly reviewed by the Chief Operating Decision Maker ("CODM") in deciding how to allocate resources to an individual segment and in assessing performance. The Company operates as a single reporting segment, focused on discovering, developing and delivering brain health medicines. The Company's measure of segment profit or loss is net loss. The CODM is the chief executive officer ("CEO"). The CODM manages and allocates resources to the operations of the Company on a total company basis. Managing and allocating resources on a consolidated basis enables the CEO to assess the overall level of resources available and how to best deploy these resources across functions, therapeutic areas and research and development projects that are in line with the Company's long-term company-wide strategic goals. Consistent with this decision-making process, the CEO uses consolidated financial information for purposes of evaluating performance, forecasting future period financial results, allocating resources and setting incentive targets. Operating expenses are used to monitor budget versus actual results. The CODM also uses net loss in competitive analysis by benchmarking to the Company's peer group. The competitive analysis along with the monitoring of budgeted versus actual results are used in assessing performance of the segment. All the Company's long-lived assets are held in the United States and all the Company's revenues are derived from the United States.

The following table is representative of the significant expense categories regularly provided to the CODM when managing the Company's single reporting segment. A reconciliation to the consolidated net loss for the years ended December 31, 2024, 2023 and 2022 is included at the bottom of the table below.

	Year Ended December 31,		
	2024	2023	2022
		(in thousands)	
Revenues	$ 41,243	$ 86,455	$ 7,686
Cost of revenues	9,444	2,159	813
Program expenses [1]			
ZULRESSO	5,101	4,395	17,083
zuranolone (ZURZUVAE)	30,482	94,174	68,155
SAGE-324	10,173	16,574	14,646
dalzanemdor (SAGE-718)	58,248	56,536	50,584
Other research and development programs	33,277	52,975	49,750
Non-program expenses [2]	85,405	113,388	96,825
People and staff augmentation	165,158	220,188	195,214
Restructuring	21,854	33,386	—
Other segment items [3]	22,767	34,169	47,400
Net loss	$ (400,666)	$ (541,489)	$ (532,784)

(1) Includes external research and development, and selling, general and administrative expenses.
(2) Includes information technology, infrastructure, facilities, legal, commercial data and systems, chemistry platform, intellectual property, and other general and administrative expense.
(3) Includes stock-based compensation expense, interest income, and other (income) expense.

16. Subsequent Events

On January 10, 2025, the Company received an unsolicited, non-binding acquisition proposal from Biogen to acquire all outstanding shares of the Company not already owned by Biogen for $7.22 per share. On January 27, 2025, the Board of Directors (the "Board") unanimously rejected the unsolicited, non-binding acquisition proposal received from Biogen. The Company further announced that the Board has initiated a process to explore strategic alternatives for the Company. On January 16, 2025, the Company commenced litigation against Biogen in the Delaware Court of Chancery seeking declaratory, injunctive and other relief. In its complaint, the Company alleges that Biogen breached the standstill provision in the Biogen Stock Purchase Agreement by making an unsolicited acquisition proposal and related public disclosures. See Note 6, *Commitments and Contingencies*, for further details.

Exhibit Index

Exhibit No.	Description
3.1	Fifth Amended and Restated Certificate of Incorporation of the Registrant, as currently in effect (incorporated by reference to Exhibit 3.1 of the Registrant's Current Report on Form 8-K (File No. 000-36544) filed on July 25, 2014)
3.2	Amended and Restated Bylaws of the Registrant, as currently in effect (incorporated by reference to Exhibit 3.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on June 16, 2023)
4.1	Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.1 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
4.2	Description of Securities (incorporated by reference to Exhibit 4.2 of the Registrant's Annual Report on Form 10-K (File No. 001-36544) filed on February 27, 2020)
10.1+	2014 Stock Option and Incentive Plan and forms of award agreements thereunder (incorporated by reference to Exhibit 10.2 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.2+	Offer letter by and between the Registrant and Kimi Iguchi, dated February 7, 2013 (incorporated by reference to Exhibit 10.10 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.3+	Non-Solicitation, Confidentiality and Assignment Agreement by and between the Registrant and Kimi Iguchi, dated March 8, 2013 (incorporated by reference to Exhibit 10.14 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.4	Form of Indemnification Agreement to be entered into between the Registrant and its directors (incorporated by reference to Exhibit 10.16 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.5	Form of Indemnification Agreement to be entered into between the Registrant and its officers (incorporated by reference to Exhibit 10.17 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.6+	Severance and Change In Control Agreement between the Registrant and Kimi Iguchi, dated September 30, 2014, as amended (incorporated by reference to Exhibit 10.15 of the Registrant's Register Statement on Form 10-K (File No. 001-36544) filed on February 16, 2023)
10.7+	2016 Annual Bonus Incentive Plan (incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K (File No. 001-36544) filed on May 3, 2016)
10.8+	Amended and Restated 2016 Inducement Equity Plan and forms of agreements thereunder, as amended and restated on September 20, 2018 (incorporated by reference to Exhibit 10.1 of the Registration's Quarterly Report on Form 10-Q (File No. 001-36544) filed on November 6, 2018)
10.9+	Form of Performance-Based Restricted Stock Unit Award Agreement Under the Sage Therapeutics, Inc. 2014 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.2 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on May 2, 2023)
10.10†	Biogen Collaboration and License Agreement by and among the Registrant, Biogen MA Inc. and Biogen International GmbH, dated November 27, 2020 (incorporated by reference to Exhibit 10.30 of the Registrant's Register Statement on Form 10-K (File No. 001-36544) filed on February 16, 2023)
10.11†	Stock Purchase Agreement by and between the Registrant and Biogen MA Inc., dated November 27, 2020 (incorporated by reference to Exhibit 10.39 of the Registrant's Annual Report on Form 10-K (File No. 001-36544) filed on February 24, 2021)

Exhibit No.	Description
10.12+	Offer Letter by and between the Registrant and Barry Greene, dated December 15, 2020 (incorporated by reference to Exhibit 10.40 of the Registrant's Annual Report on Form 10-K (File No. 001-36544) filed on February 24, 2021)
10.13+	Severance and Change In Control Agreement between the Registrant and Barry Greene, dated December 15, 2020 (incorporated by reference to Exhibit 10.41 of the Registrant's Annual Report on Form 10-K (File No. 001-36544) filed on February 24, 2021)
10.14+	Offer Letter by and between the Registrant and Christopher Benecchi, dated September 13, 2021 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on November 2, 2021)
10.15+	Severance and Change In Control Agreement between the Registrant and Christopher Benecchi, dated September 13, 2021, as amended (incorporated by reference to Exhibit 10.36 of the Registrant's Register Statement on Form 10-K (File No. 001-36544) filed on February 16, 2023)
10.16	Side Letter to Biogen Collaboration and License Agreement, by and among the Registrant, Biogen MA Inc. and Biogen International GmbH, dated October 21, 2021 (incorporated by reference to Exhibit 10.4 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on November 2, 2021)
10.17+	2014 Employee Stock Purchase Plan, as amended, dated June 15, 2023 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on August 7, 2023)
10.18+	Offer Letter by and between the Registrant and Laura Gault, dated October 18, 2022 (incorporated by reference to Exhibit 10.39 of the Registrant's Register Statement on Form 10-K (File No. 001-36544) filed on February 16, 2023)
10.19+	Severance and Change in Control Agreement between the Registrant and Laura Gault, dated October 18, 2022, as amended (incorporated by reference to Exhibit 10.40 of the Registrant's Annual Report on Form 10-K (File No. 001-36544) filed on February 16, 2023)
10.20+	Non-Employee Director Compensation Program, adopted June 10, 2024 (incorporated by reference to Exhibit 10.5 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on July 31, 2024)
10.21	Office Lease Agreement between the Registrant and 55 Cambridge Parkway, LLC, dated January 22, 2024 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on April 25, 2024)
10.22+	Offer letter by and between the Registrant and Anne Marie Cook, dated August 6, 2015 (incorporated by reference to Exhibit 10.2 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on April 25, 2024)
10.23+	Severance and Change in Control Agreement between the Registrant and Anne Marie Cook, dated September 15, 2015, as amended (incorporated by reference to Exhibit 10.3 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on April 25, 2024)
10.24+	2024 Equity Incentive Plan (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on July 31, 2024)
10.25+	Form of Option Agreement under the 2024 Equity Incentive Plan (incorporated by reference to Exhibit 10.2 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on July 31, 2024)
10.26+	Form of Restricted Stock Unit Agreement under the 2024 Equity Incentive Plan (incorporated by reference to Exhibit 10.3 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on July 31, 2024)
10.27+	Form of Non-Employee Director Option Agreement under the 2024 Equity Incentive Plan (incorporated by reference to Exhibit 10.4 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on July 31, 2024)
10.28+	Amendment to Amended and Restated 2016 Inducement Equity Plan (incorporated by reference to Exhibit 10.6 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on July 31, 2024)
10.29	ATM Sales Agreement, dated as of September 16, 2024, by and between the Company and TD Securities (USA) LLC (incorporated by reference to Exhibit 1.2 of the Registrant's Registration Statement on Form S-3 (File No. 333-282162) filed on September 17, 2024)
10.30+*	Separation Agreement between the Registrant and Kimi Iguchi, dated October 31, 2024

Exhibit No.	Description
10.31+*	Consulting Agreement between the Registrant and Kimi Iguchi dated October 31, 2024
10.32+*	Separation Agreement between the Registrant and Anne Marie Cook, dated October 31, 2024
10.33+*	Promotion Letter Agreement by and between the Registrant and Gregory Shiferman, effective November 1, 2024
10.34+*	Severance and Change in Control Agreement between the Registrant and Gregory Shiferman, effective November 1, 2024
10.35+*	Promotion Letter Agreement by and between the Registrant and Christopher Benecchi, effective November 1, 2024
19.1*	Amended and Restated Sage Therapeutics, Inc. Insider Trading Policy, dated June 15, 2023
21.1*	Subsidiaries of the Registrant
23.1*	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm
24.1*	Power of Attorney (see signature page of this Annual Report on Form 10-K)
31.1*	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1***	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
97*	Compensation Recovery Policy of the Registrant
101.INS*	Inline XBRL Instance Document (the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document)
101.SCH*	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents
104*	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101.*)

(+) Management contract or compensatory plan or arrangement.

(*) Filed herewith.

(**) Confidential treatment has been granted by the Securities and Exchange Commission as to certain portions.

(***) The certifications furnished in Exhibit 32.1 hereto are deemed to accompany this Annual Report on Form 10-K and will not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended. Such certifications will not be deemed to be incorporated by reference into any filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

(†) Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

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.

SAGE THERAPEUTICS, INC.

Date: February 11, 2025

By: /s/ Barry E. Greene

Barry E. Greene
Chief Executive Officer, President and Director
(Principal Executive Officer)

We, the undersigned directors and officers of Sage Therapeutics, Inc., hereby severally constitute and appoint Barry E. Greene and Christopher Benecchi, and each of them singly, our true and lawful attorneys-in-fact, with full power to them, and to each of them singly, to sign for us and in our names in the capacities indicated below, any and all amendments to this Annual Report on Form 10-K, and to file or cause to be filed the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as each of us might or could do in person, and hereby ratifying and confirming all that said attorneys-in-fact, and each of them, or their substitute or substitutes, shall do or cause to be done by virtue of this power of attorney.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons in the capacities indicated below and on the dates indicated.

Signature	Title	Date
/s/ Barry E. Greene Barry E. Greene	Chief Executive Officer, President and Director (Principal Executive Officer)	February 11, 2025
/s/ Christopher Benecchi Christopher Benecchi	Chief Operating Officer (Principal Financial and Accounting Officer)	February 11, 2025
/s/ Michael F. Cola Michael F. Cola	Director	February 11, 2025
/s/ James Frates James Frates	Director	February 11, 2025
/s/ Geno Germano Geno Germano	Director	February 11, 2025
/s/ Elizabeth Barrett Elizabeth Barrett	Director	February 11, 2025
/s/ George Golumbeski George Golumbeski, Ph.D.	Director	February 11, 2025
/s/ Jessica Federer Jessica Federer	Director	February 11, 2025

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Executive Leadership

Barry Greene
Chief Executive Officer

Chris Benecchi
Chief Operating Officer

Pamela Herbster
VP, Head of People

Michael Quirk, Ph.D.
Chief Scientific Officer
and Interim Head of R&D

Vanessa Proctor
SVP, Corporate Affairs

Gregory Shiferman
SVP, General Counsel
and Secretary

Board of Directors

Barry Greene
President and Chief Executive Officer, Sage Therapeutics, Inc.
Director, Karyopharm Therapeutics, Inc.

Liz Barrett
President, Chief Executive Officer and Director, UroGen Pharma Ltd.
Director, Allogene Therapeutics, Inc.

Michael F. Cola
Advisor, Mayo Ventures
Advisor, Yale Ventures,
Director at Phathom Pharmaceuticals, Inc.

Jessica Federer
Senior External Advisor, McKinsey & Company
Advisor, Yale Ventures, Blavatnik Fund
Board Member, Angelni Ventures

James M. Frates
Chief Financial Officer, Amylyx Pharmaceuticals, Inc.

Geno Germano
Director, Precision Biosciences, Inc.
Director, Orbital Therapeutics, Inc.

George Golumbeski, Ph.D.
Partner, DROIA Ventures
Chairperson and Director, Shattuck Labs, Inc.

ANNUAL MEETING
The annual meeting of stockholders will be held virtually on Wednesday, June 11, 2025, at 9:00 a.m. Eastern Time. Any stockholder as of the record date for the annual meeting may listen to the annual meeting and participate live via webcast at www.virtualsharehodermeeting.com/SAGE2025.

INDEPENDENT AUDITORS
PRICEWATERHOUSECOOPERS LLP
101 Seaport Boulevard, Suite 500
Boston, MA 02110
(617) 530–5000

INVESTOR INQUIRIES
ir@sagerx.com

STOCK LISTING
Nasdaq: SAGE

TRANSFER AGENT
The transfer agent is responsible, among other things, for handling stockholder questions regarding lost stock certificates, address changes, including duplicate mailings, and changes in ownership or name in which shares are held. These requests may be directed to the transfer agent at the following address:

COMPUTERSHARE TRUST COMPANY
Computershare Investor Services
P.O. Box 43078
Providence, RI 02940-3078
www.computershare.com/us/contact

SEC FORM 10-K
A copy of Sage's annual report on Form 10-K filed with the Securities and Exchange Commission is available free of charge from the company's Investor Relations Department by emailing ir@sagerx.com.

Please read the section titled "Risk Factors" in our annual report on Form 10-K for a description of risks and uncertainties that could impact the potential for our business and future results.

Sage Therapeutics®

CORPORATE HEADQUARTERS
55 Cambridge Parkway
Cambridge, MA 02142
(617) 299–8380

www.sagerx.com

Nasdaq: SAGE

company/sage-therapeutics

@sagebiotech

ThisIsSage

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Seeing the brain differently *makes a world of difference*