Risk Factors Comparison 2025-02-11 to 2024-02-14 Form: 10-K

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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 ~~from healthcare professionals treating women with PPD~~ . 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** ~~PPD. For example, in its Practice Advisory related~~ **relative** to ~~use of~~ **other patients suffering from this disease.** ZURZUVAE ~~for the treatment of PPD, the American College of Obstetricians and Gynecologists (ACOG) characterizes ZURZUVAE as a treatment option for severe PPD that had onset within the third trimester of pregnancy or within 4 weeks postpartum. ZURZUVAE~~ may ~~also~~ 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 ~~providers~~ **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 ~~may~~ also **may** not achieve **or, even if achieved, maintain** broad market acceptance for the treatment of women with PPD if ~~payers~~ **payors** are not willing to provide reimbursement for the treatment or impose significant restrictions on reimbursement. ~~Payers~~ **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, ~~limiting reimbursement to women with severe PPD~~ **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 ~~women~~ **woman** with PPD, the prescription may not result in product being shipped to ~~a~~ **the** patient and ~~a~~ **/ 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 ~~, including as a result of the price we charge,~~ 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 ~~of our~~ 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 ~~involves~~ **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. ~~Success in non- clinical studies or in earlier clinical trials or interim results of clinical trials may not be repeated or observed in ongoing, future or completed studies or trials involving the same compound or other product candidates.~~ 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 ~~find that~~ **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~~ **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 ~~our ongoing dose- ranging study of SAGE- 324,~~ the KINETIC 2 Study, we **evaluated** ~~are evaluating~~ 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. ~~The results of clinical trials or non- clinical studies of our product candidates at any stage may not support further development or may not be sufficient to file for and obtain regulatory approval on the timelines we expect or at all. The FDA or other regulatory agencies may not agree with our interpretation of the results of clinical trials or non- clinical studies. Other decisions or actions of the FDA or other regulatory agencies may affect our plans, progress, results, timing or next steps. For example, we received a complete response letter, or CRL, related to the new drug application, or NDA, for zuranolone for the treatment of MDD. The FDA has taken the position that one or more additional clinical trials of zuranolone are required to support approval in MDD. We may never conduct additional trials or obtain regulatory approval of zuranolone for the treatment of MDD. Even if we conduct additional trials in MDD, there is no guarantee that the design and results of any additional clinical trials we conduct will be sufficient to obtain such regulatory approval. Even if we receive regulatory approval of zuranolone for the treatment of MDD, our commercialization efforts with respect to zuranolone for the treatment of MDD may not be successful.~~ Changes in formulation or the need to refine or scale- up the manufacturing process ~~as we do for any of our product candidates~~ 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 ~~than achieved with the earlier formulation or processes~~ . 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 ~~outside the U. S.~~ . 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 ~~any of~~ our product candidates in the indications we study, or do not support the safety ~~or ,~~ efficacy or ~~our~~ intended profile for ~~the~~ **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 ~~collaborator~~ **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** ~~We may never be able~~

~~to generate meaningful revenues from sales~~ 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 ~~at levels or on timing necessary to support our investment and goals. Our product ZULRESSO is approved~~ in the U. S. as **of December 31, 2024** ~~a treatment for PPD in individuals 15 years old and older~~ . ZULRESSO was first made commercially available in the U. S. in June 2019. ~~Our~~ **Since launch, our** revenues from sales of ZULRESSO **were** ~~have been~~ negatively impacted by significant barriers arising from the complex requirements for treatment and, ~~historically~~ **more recently** , by the ~~impacts~~ **introduction** of **ZURZUVAE** ~~the COVID- 19 pandemic. Some or all of these factors are expected to continue to impact revenues negatively in the future. ZULRESSO is administered~~ as a **treatment** ~~continuous infusion given over two and a half days. Because of the risk of serious harm resulting from excessive sedation or~~ **for** ~~sudden loss of consciousness during the ZULRESSO infusion, ZULRESSO is approved for administration only in a medically- supervised healthcare setting that has been certified under a Risk Evaluation and Mitigation Strategy, or REMS, program and meets the other requirements of the REMS program, including requirements related to monitoring of the patient during the infusion. The actions required for a healthcare setting to be ready and willing to treat~~ women with PPD ~~are complex and time- consuming. These actions include becoming REMS- certified; achieving formulary approvals; establishing protocols for administering ZULRESSO; and securing satisfactory reimbursement. Sites must often negotiate reimbursement on a payor- by- payor basis under commercial coverage~~ . These requirements ~~have~~ created significant barriers to treatment **with ZULRESSO** for women with PPD. We ~~expect these barriers will continue to negatively impact ZULRESSO revenue growth. Our current commercial operations for ZULRESSO are limited to account management focused on geographies that have existing, active ZULRESSO treatment sites. We expect that the commercial availability of ZURZUVAE for women with PPD, our limited commercial efforts for ZULRESSO, and barriers to treatment with ZULRESSO will continue to substantially limit the revenue opportunity for ZULRESSO and the number of healthcare settings that are or become treatment sites for ZULRESSO. We may~~ also ~~find that certain healthcare settings that have in the past been active treatment sites may not be willing to remain infusion- ready as a result of the complex requirements related to administration of ZULRESSO and compliance with the REMS, related limitations and restrictions, or because of actual or perceived difficulties obtaining satisfactory reimbursement or limitations on coverage and reimbursement or for other reasons, including staffing shortages, or as a result of the commercial availability of ZURZUVAE as an oral 14- day treatment option for women with PPD. We continue to encounter~~ **encountered** other issues and challenges in commercializing ZULRESSO and generating revenues, including: • Some women with PPD who ~~need~~ **needed** treatment ~~find~~ **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 ~~may be~~ **have been** concerned about the risk of excessive sedation and sudden loss of consciousness. • More healthcare ~~providers~~ **professionals** than we expected **were** ~~have been~~ unwilling to accept ZULRESSO as a treatment ~~paradigm~~ for women with PPD **. •** ~~and this may continue; we believe this unwillingness is due primarily to the product profile and reimbursement challenges associated with~~ ZULRESSO ~~. • We compete~~ **competed** with lower cost antidepressants. • **Given** ~~In light of~~ the **complex requirements for** ~~commercial availability of ZURZUVAE as an oral~~ treatment ~~option for women with PPD~~ , **use** ~~healthcare settings may be less likely to complete the complex and time- consuming actions required to become infusion- ready, and those healthcare settings that have in the past been active treatment sites may not be willing to remain infusion- ready. • Given the mode of administration, the nature of the REMS and the current limitation on the administration~~ of ZULRESSO ~~to a medically- supervised healthcare setting certified under the REMS, use of ZULRESSO~~ in the U. S. **was** ~~has been~~ focused primarily on women with more severe symptoms of PPD ~~, and we expect that to continue~~ . • We ~~may be unable to fully comply with our obligations under the ZULRESSO REMS, which include auditing of healthcare settings, collection and analysis of required data, and other requirements, to the satisfaction of the FDA, or the FDA may require modifications to or additional restrictions under the ZULRESSO REMS. We also expect to continue to encounter~~ **encountered coverage and reimbursement** challenges **,** ~~related to coverage and reimbursement of ZULRESSO. These include~~ **including** restrictions related to the severity of PPD cases for which ZULRESSO ~~will~~ **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. ~~• For example, the availability, terms and timing of coverage for ZULRESSO by state Medicaid systems is expected to continue to vary significantly by state, and we encounter states that impose significant coverage restrictions or lengthy delays on reimbursement of ZULRESSO. Similarly, certain healthcare settings or patients may determine that the financial burdens of treatment are not acceptable.~~ A number of healthcare settings that ~~are~~ **were** willing to administer ZULRESSO to women with PPD who ~~have~~ **had** commercial insurance ~~do~~ **were** not ~~currently~~ **willing to** treat Medicaid patients, which adversely ~~affects~~ **affected** our ability to generate revenue from ZULRESSO. ~~Any~~ **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 ~~continue to~~ impair our ability to generate revenues or ~~could impair our ability to~~ 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. ~~There is no guarantee~~ **Any product or product candidate** that we ~~will be successful in our commercialization efforts with respect to ZULRESSO, or that we will be able to generate meaningful revenues or revenues at the levels or on the timing necessary to support our investment~~

~~and goals. ZURZUVAE, ZULRESSO, our current products if approved in additional indications, our current or future product candidates, and any future products, if successfully developed~~ -- **develop** ~~and approved,~~ 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 ~~warnings~~ -- **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 ~~of our product candidates~~ , as part of an expanded access program, ~~if initiated for any of our products or product candidates,~~ in commercial use or in post- approval studies ~~of any approved product~~ . 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 ~~current or future~~ product **or product** ~~candidates~~ - **candidate that we may** ~~, or any future products, if successfully developed~~ -- **develop** ~~and approved~~ , 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** ~~know~~ **known** side effects ~~, caused by ZURZUVAE, ZULRESSO, any current product if approved in additional indication (s), any other existing or future product candidate, or any future approved product~~ . • 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 ~~prior to the initiation of development or during development of our product candidates~~ which could cause us or our collaborators to have to stop, delay or restrict further development; ~~or~~ **•** 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 ~~the FDA or other~~ regulatory authorities, that our product candidates are safe and that the benefits outweigh the safety risks, and the ~~FDA or~~ applicable ~~foreign~~ 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 ~~sued and~~ 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 ~~the FDA and~~ regulatory authorities ~~outside of the U. S.~~ 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 ~~will~~ **would** be needed. ~~The FDA and regulatory~~ **Regulatory** authorities ~~outside the U. S.~~ 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 ~~the FDA or other~~ 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 ~~, as has been the case to date with respect to the NDA for zuranolone for the treatment of MDD~~ ; • 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 ~~the FDA or~~ regulatory authorities ~~outside the U. S.~~ for marketing approval; • ~~the FDA or~~ regulatory authorities ~~outside the U. S.~~ 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; • ~~the FDA or~~ regulatory authorities ~~outside the U. S.~~ 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 ~~may~~ **could** cause the study or trial to fail; • ~~the FDA or~~ regulatory authorities ~~outside the U. S.~~ may determine that the number, design, size, conduct, implementation or ~~result~~ **results** of our non- clinical studies or clinical trials ~~is~~ **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** ; • ~~the~~

~~FDA or~~ regulatory or other ~~government~~ **governmental** authorities ~~outside the U. S.~~ may require that we or our collaborators conduct additional non- clinical studies and clinical trials prior to approval or post- approval; • ~~the FDA or applicable foreign~~ regulatory authorities may not approve the formulation, labeling or specifications of any of our product candidates; • ~~the FDA or applicable foreign~~ 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 ~~, the FDA may require a REMS as a condition of approval or post- approval for our product candidates~~ , or may modify an existing REMS or may impose other limitations or restrictions, like a boxed warning, as ~~was~~ **is** the case with ZURZUVAE; • ~~the FDA or applicable foreign~~ 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 • ~~the FDA or applicable foreign~~ regulatory ~~agencies~~ **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 ~~has~~ imposed post- approval obligations in connection with approval of ~~ZULRESSO and~~ 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. ~~We~~ **Although we expect to complete these studies, we** may not be able to fulfill these obligations in accordance with the FDA' s ~~timelines~~ **requirements** , or at all. The FDA recommended **controlled substance** scheduling with respect to ~~both~~ ZURZUVAE **under the CSA** ~~(zuranolone) and ZULRESSO (brexanolone)~~ , ~~and both~~ **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 ~~agencies~~ **authorities** may slow the time necessary for new drugs to be reviewed and / or approved by necessary government ~~agencies~~ **authorities** , which would adversely affect our business. ~~For example, the U. S. government has shut down several times in recent history and certain regulatory agencies, including the FDA, had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs in the future, 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.~~ Fast Track and Breakthrough Therapy designations from the FDA, PRIority Medicines, or PRIME, designation from the ~~European Medicines Agency, or~~ EMA, ~~ILAP~~ **Innovative Licensing and Access Pathway** designation from the ~~MHRA~~ **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 ~~and ZULRESSO~~ 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. ~~We or our collaborators may find that our ongoing or future clinical trials of~~

~~dalzanemdor (SAGE- 718), SAGE- 324 or any of our other current or future product candidates may fail to meet their primary endpoints.~~ 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 ~~our ongoing~~ **the KINETIC 2 Study, for which we reported negative results in July 2024, we observed a** dose- ~~ranging~~ **relationship in the incidence of CNS depressant TEAEs and in the frequency of TEAEs leading to** study **drug discontinuation** ~~of SAGE- 324, we are evaluating multiple doses, including the same maximum dose of SAGE- 324 that we evaluated~~ in ~~prior studies~~ **the study** . Any of ~~these~~ **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 ~~will be completed, and results announced~~ , or whether future trials will begin, as planned or expected, if at all, as the commencement, enrollment ~~and~~ **,** completion **and announcement of results** of clinical trials ~~and announcement of results~~ 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 ~~European Union, or~~ 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; • ~~the FDA or applicable~~ regulatory authorities ~~outside the U. S.~~ 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 ~~FDA or~~ 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, ~~the FDA or other~~ regulatory authorities, the IRB or ethics ~~committees~~ **committee, or EC,** at the sites where the IRBs or **ECs** ~~ethics committees~~ 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 **,** ~~or of ZULRESSO~~ for commercial use ~~, including if we eventually obtain regulatory approvals in additional indications,~~ 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 ~~rely~~ **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 ~~must typically~~ **may be required to** complete a pre- approval inspection by the FDA and other comparable foreign regulatory ~~agencies~~ **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 ~~applicable~~ **other** foreign regulatory ~~agencies~~ **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** ~~In addition, we~~ have no direct control over our contract manufacturers' ability to maintain adequate quality control, quality assurance and qualified personnel. **All** ~~Furthermore, 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 ~~, and we intend to enter into a long- term supply agreement at the appropriate time with at least one of our contract manufacturing organizations, or CMOs, for ZURZUVAE drug substance. We have long- term supply agreements with our contract manufacturers with respect to ZULRESSO drug substance and drug product~~ . We have an inventory of ZURZUVAE ~~and ZULRESSO~~ 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 ~~SAGE- 324 or~~ **our product candidates** ~~dalzanemdor (SAGE- 718)~~ . 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 ~~not willing~~ **unwilling** to enter into long- term supply agreements, or are ~~not willing~~ **unwilling** or ~~are~~ unable to supply drug substance or drug product to us, we could be required to engage new **CMOs** ~~contract manufacturers~~ 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** ~~contract manufacturer~~ will need to complete validation batches ~~, pass an inspection by the FDA and other applicable foreign regulatory agencies,~~ 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** ~~contract manufacturers~~ to manufacture commercial quantities of ZURZUVAE ~~and ZULRESSO~~ 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** ~~contract manufacturers~~ , we may not be able to

successfully commercialize any approved product, including ZURZUVAE ~~and ZULRESSO~~ , or successfully complete development of our current or future product candidates. ~~ZURZUVAE~~ **Any of** ~~or~~ **our** ~~any of our other~~ current or future products or product candidates, **including ZURZUVAE** ~~if our ongoing development efforts are successful~~ , 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 ~~product~~ **products** , or requiring other onerous and time- consuming forms of utilization management, such as prior authorization procedures **.** ~~, or they~~ **They** may limit the amount of reimbursement **or restrict access altogether** . These restrictions or limitations might impede appropriate use of our ~~product~~ **products** for ~~the~~ **any** approved ~~indication~~ **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 ~~significant~~ uncertainty related to **maintaining** third- party payor coverage and reimbursement of ZURZUVAE ~~, given the early phase of its commercialization,~~ 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 ~~ZURZUVAE, ZULRESSO or~~ any **of our products and** product ~~candidate~~ **candidates** ~~that we or our collaborators may successfully develop and commercialize or that coverage will be available~~ on reasonable terms **or at all** . Market acceptance for any of our ~~marketed~~ **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 ~~and ZULRESSO~~ 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 ~~providers~~ **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 ~~ZURZUVAE, or~~ any of our ~~other~~ current or future products ~~or product candidates~~ , **including ZURZUVAE** ~~if successfully developed and approved by the FDA or other applicable regulatory authorities~~ , does not achieve an adequate level of acceptance by patients, healthcare ~~providers~~ **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 ZULRESSO are~~ , 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 ~~has~~ 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 ~~the ZULRESSO REMS or~~ any REMS imposed ~~for a future~~ **on any of our** ~~product~~ **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 ~~emerge~~ **be approved** that adversely affect the amount of revenue we are able to generate from the sale of ZURZUVAE ~~, ZULRESSO,~~ 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** ~~and ZULRESSO both compete~~ **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. ~~We expect that the commercial availability of ZURZUVAE will further limit our commercial opportunity for ZULRESSO. In addition, ZULRESSO and~~ 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. ~~If approved in the future for the treatment of MDD, zuranolone may also face competition as patients with MDD are typically treated with a variety of low- cost antidepressant medications, including SSRIs, SNRIs and atypical antipsychotics. Zuranolone, if approved in the future for the treatment of MDD, may also face competition from AXS- 05, a combination formulation of an NMDA receptor antagonist, dextromethorphan, with bupropion approved for the treatment of MDD in adults and esketamine, which is approved for the treatment of treatment- resistant depression and depressive symptoms in adults with MDD with acute suicidal ideation or behavior, and from cariprazine, which has been approved for the adjunctive treatment of MDD in patients who are receiving ongoing antidepressant therapy. A number of other companies are developing product candidates intended for the treatment of MDD.~~ In the field of neuroactive steroids focused specifically on modulation of GABAA 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 GABAA positive allosteric modulator neuroactive steroid, to treat seizures associated with CDKL5 deficiency disorder, a rare, genetic epilepsy. Other GABAA competitors include darigabat, which is being developed by Cerevel Therapeutics, Inc. **(acquired by AbbVie Inc.)** for the treatment of epilepsy and panic disorder ~~. SAGE- 324, a novel GABAA receptor positive allosteric modulator, is in Phase 2 development for essential tremor. If successfully developed and approved as a treatment for essential tremor, SAGE- 324 will face competition from current first-~~

~~line treatments which include β- adrenergic blocker propranolol and anticonvulsant primidone. Other companies are also developing potential treatments for essential tremor, including a Phase 3 T- type calcium channel modulator being developed by Praxis Precision Medicines, Inc. and a T- type calcium channel modulator that Jazz Pharmaceuticals, Inc. is currently evaluating in Phase 2b development. Dalzanemdor (SAGE- 718) is an oxysterol- based positive allosteric modulator of the NMDA receptor, which we are exploring in certain cognition- related disorders associated with NMDA receptor dysfunction, including cognitive impairment associated with diseases such as Huntington' s disease, Parkinson' s disease and Alzheimer' s disease. A number of other companies are working to develop products to treat Huntington' s disease. In addition, several companies have developed or are developing products for the treatment of Parkinson' s disease and Alzheimer' s disease~~ . 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 ~~in whole or in part~~ , 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 ~~have~~ 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. ~~Although~~ **Because** we ~~may become eligible~~ **and Biogen have agreed not** to ~~earn certain~~ **pursue further development for zuranolone for the treatment of MDD in the U. S., we will not receive the $ 150. 0 million** milestone ~~payments~~ **payment for the first commercial sale of ZURZUVAE for the treatment of MDD** in ~~connection~~ **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 ~~collaborations~~ **collaboration agreement solely with respect to SAGE- 324 on a worldwide basis** , ~~we may never meet such milestones~~ **effective February 17, 2025. We are evaluating next steps, if any,** ~~or~~ **for** ~~actually receive such milestone payments~~ **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 ~~investigational new drug, or~~ 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 ~~collaboration~~ **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 ~~or~~ **our** ~~commercialize our products~~ **product candidates** ~~, if approved~~ , 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** ~~contract manufacturers~~ 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 ~~ZULRESSO and~~ ZURZUVAE ~~, if successfully commercialized,~~ 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 ~~, ZULRESSO,~~ and any future approved products **,** and the use of our product candidates in clinical trials ~~will~~ 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 ~~providers~~ **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. ~~We~~ **Although we** maintain product liability insurance coverage ~~with a $ 20. 0 million annual aggregate coverage limit. Nevertheless~~ , 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 ~~, ZULRESSO,~~ 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 ~~, ZULRESSO,~~ 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 ~~agencies~~ **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 ~~providers~~ **professionals**, patients, healthcare settings, and others who play a role in the recommendation, prescription, reimbursement and administration of ZURZUVAE ~~and ZULRESSO~~, 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 ZULRESSO~~ 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~~ **Anti** - ~~kickback~~ **Kickback** ~~statute~~ **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 ~~health~~ **healthcare** ~~care~~ 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~~ **Anti** - ~~kickback~~ **Kickback** ~~statute~~ **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 ~~providers~~ **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 ~~our employees~~ **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** ~~plan to~~ enroll subjects in our ~~ongoing or~~ 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 ~~United Kingdom, or~~ 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. ~~The CCPA also has been amended through a recent referendum in California that creates additional obligations that went into effect on January 1, 2023. In November 2020, California voters approved the California Privacy Rights Act, or CPRA, ballot initiative which introduced significant amendments to the CCPA and established and funded a dedicated California privacy regulator, the California Privacy Protection Agency, or the CPPA. New implementing regulations will be issued under the CPRA that may lead to new or additional obligations for us.~~ 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 ~~residents~~ **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** ~~at least eleven~~ 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 ~~recently~~ 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** ~~consumer health data and other states likely will~~ **well** ~~consider similar legislation~~ **as the federal Video Privacy Protection Act. The rise** in ~~2024 and beyond~~ **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 ~~CCPA and other enacted or potential~~ laws ~~in other states and~~ at the **state and** federal ~~level~~ **levels** exemplify the vulnerability of our business to the evolving regulatory environment related to the privacy, security and confidentiality of personal data and ~~protected~~ **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 ~~the CCPA~~ **applicable laws** and continue to assess ~~the~~ **their** impact ~~of the CPRA, and other federal and state legislation,~~ 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. ~~Additionally, in October 2022, President Joe Biden signed an executive order to implement the EU- U. S. Data Privacy Framework, which would serve as a replacement to the EU- U. S. Privacy Shield. The European Union initiated the process to adopt an adequacy decision for the EU- U. S. Data Privacy Framework in December 2022 and the European Commission adopted the adequacy decision on July 10, 2023. The adequacy decision will permit U. S. companies who self- certify to the EU- U. S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the European Union to the United States. However, some privacy advocacy groups have already suggested that they will be challenging the EU- U. S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU- U. S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue may impact our activities with companies in the EU, and any potential future business operations in the EU.~~ 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 ~~agencies~~ **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 ~~agencies~~ **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 ~~, ZULRESSO,~~ 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** ~~United Kingdom~~ , including those related to the pricing of prescription pharmaceuticals, as the **UK** ~~United Kingdom~~ determines which EU laws to replicate or replace, which could impair our ability to transact business in the EU and the **UK** ~~United Kingdom~~ 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 GABAA 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 ~~European patent~~ **patents have, in the past,** ~~covering brexanolone i. v. has~~ been opposed by ~~a~~ third ~~party~~ **parties** , and ~~the opposition~~ **further such** proceedings ~~are ongoing~~ **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 ~~, ZULRESSO,~~ 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** ~~, ZULRESSO, and~~ 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 ~~, ZULRESSO,~~ 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 ~~product~~ **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 ~~materially~~ -- **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 ~~product~~ **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 ~~product~~ **products** or any of our product candidates, the defendant could counterclaim that the patent covering our ~~product~~ **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** ~~For example,~~ our granted ~~European patent~~ **patents have, in the past,** ~~covering brexanolone i. v. has~~ been opposed by ~~a~~ third ~~party~~ **parties** , and ~~the opposition~~ **further such** proceedings ~~are ongoing~~ **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 ~~would~~ **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 ~~2022~~ **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 ~~ZULRESSO and~~ 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 ~~fail to~~ **/ 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.** , ~~for example~~ new indications, dosages or strengths of an existing drug **)** . This three- year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs 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 ~~additional~~ litigation costs, damages and reputational harm, which could lead to lower revenues. Increased risk of generic competition with ZURZUVAE ~~, ZULRESSO,~~ 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 ~~, ZULRESSO,~~ 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 ~~, ZULRESSO,~~ 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 ~~is~~ **was** in the first quarter of 2023; the first Part D inflation rebate period ~~is~~ **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 ~~(beginning~~ **, 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 ~~. For example, even if we successfully find a path to regulatory approval of zuranolone for the treatment of MDD, the IRA may negatively impact our potential future revenues~~ . 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 ~~or for taking price increases that exceed inflation~~ . 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. ~~In addition, the IRA potentially raises risks related to individuals participating in a Medicare Part D prescription drug plan who may experience a gap in coverage if they required coverage above their initial annual coverage limit before they reached the higher threshold, or " catastrophic period " of the plan. Individuals requiring services exceeding the initial annual coverage limit and below the catastrophic period, must pay 100 % of the cost of their prescriptions until they reach the catastrophic period. Among other things, the IRA contains many provisions aimed at reducing this financial burden on individuals by eliminating the coverage gap starting in 2025, reducing the co- insurance and co- payment costs, expanding eligibility for lower income subsidy plans, and imposing price caps on annual out- of- pocket expenses, each of which could have potential pricing and reporting implications.~~ 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 ~~, ZULRESSO,~~ 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 ~~and ZULRESSO~~, 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 **.** ~~, and despite~~ **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 ~~be~~ 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 ~~two~~ **one** approved ~~products~~ **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, ~~2023~~ **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** ~~. In addition, we achieved the~~ 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 ~~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~~ . As of December 31, ~~2023~~ **2024** , our cash, cash equivalents and marketable securities were $ ~~753~~ **504** . ~~2~~ **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 $ ~~541~~ **400** . ~~5~~ **7** million for the year ended December 31, ~~2023~~ **2024** , and our accumulated deficit was $ ~~2~~ **3** . ~~6~~ **0** billion as of December 31, ~~2023~~ **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 ~~increasing levels of~~ 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** ~~In August 2023, we implemented a strategic corporate reorganization and reprioritization of our pipeline to support goals for long- term business growth. As a result,~~ we expect that our operating expenses will decrease in **2025 as compared to** 2024 as ~~compared to~~ **a result of our pipeline prioritization and anticipated cost savings from the October** ~~2023~~ **2024** ~~. We~~ **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~~ **these** costs **will** include the **costs and** expenses associated with **:** our sales and marketing activities; **conducting** ~~advancement of planned and ongoing~~ clinical trials **of current** ~~for dalzanemdor (SAGE- 718)~~ and ~~SAGE- 324~~ **future product candidates** ; **continuing certain research activities** ~~the cost of future clinical trials~~ ; outsourced manufacturing; **pursuing potential business development activities;** and the impact of future decisions and activities ~~, including decisions made with respect to development of zuranolone for the treatment of MDD~~ . 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. ~~We expect to continue to incur additional significant and operating losses for the foreseeable future.~~ 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 ~~expect that our revenue opportunity for ZULRESSO will continue~~ **discontinued** ~~to be limited, particularly in light of the~~ commercial availability of ~~ZURZUVAE~~ **ZULRESSO in the U** . ~~In~~ **S. as of December 31, 2024, and as a result will no longer generate** ~~addition~~ **additional** ~~, we~~ **revenue from ZULRESSO. We began to** generate revenue from sales of ZURZUVAE ~~, which became commercially available~~ in ~~late~~ **December** 2023 ~~. We also 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~~ . 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** ~~and satisfactory reimbursement of such product in the medical community~~ , ~~with~~ patients and ~~with~~ 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 ~~or for approved products in additional indications~~ ; 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 ~~or for any existing product approved in additional indications~~ , 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** ~~in the medical community~~ , ~~with~~ patients and ~~with~~ 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 ~~may~~ **will** need to raise additional funding ~~at some point in the future~~ , 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 ~~and ZULRESSO~~ for the treatment of women with PPD in the U. S. **We** ~~, and~~ are **also** advancing our **prioritized pipeline of** product candidates ~~, including dalzanemdor (SAGE- 718) and SAGE- 324,~~ through non- clinical and clinical development. Commercializing products and developing additional small molecule products are expensive. In **October 2024 and** August 2023, we implemented ~~a~~ strategic corporate ~~reorganization~~ **reorganizations** ~~and reprioritization of our pipeline~~ to support **our** ~~goals~~ **goal** ~~for~~ **of** long- term business growth. **Although** ~~As a result,~~ we expect that our operating expenses will decrease in **2025 as compared to** 2024 as

~~compared to~~ **a result of our pipeline prioritization and anticipated cost savings from the October** ~~2023~~ **2024** ~~. We~~ **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; ~~the costs of planned and ongoing~~ clinical trials **of our current** ~~for dalzanemdor (SAGE- 718)~~ and ~~SAGE- 324~~ **future product candidates** ; ~~the cost~~ **pursuing potential business development activities; continuation** of ~~future clinical trials~~ **certain research activities** ; and the impact of future decisions and activities ~~, including decisions made with respect to development of zuranolone for the treatment of MDD~~ . We ~~may seek~~ **will need to raise** additional capital in the future to fund operating needs. ~~We may~~ **Our cash need needs will increase further** ~~to raise additional funds sooner than we currently expect~~ 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, ~~2023~~ **2024** , our cash, cash equivalents and marketable securities were $ ~~753~~ **504** . ~~2~~ **4** million. Based upon our current operating plan, we anticipate that our existing cash, cash equivalents and marketable securities as of December 31, ~~2023~~ **2024** , ~~along~~ **together** with ~~the milestone payment received in January 2024,~~ 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 ~~into~~ **to mid-** ~~2026~~ **2027** . We ~~do~~ **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 ~~anticipate receipt of any milestone payments from collaborations in~~ **realized, we may adjust our operating plan accordingly, including** the ~~remainder~~ **deferral or reduction** of ~~2024~~ **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 ~~August~~ **October** ~~2023~~ **2024 corporate** reorganization at the levels we expect. In addition, our operating plan may change. We may ~~need or~~ choose to seek additional funds ~~sooner than planned,~~ 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 ~~future development efforts for, obtain regulatory approval for, and to commercialize~~ our **operations** ~~product candidates, if approved~~ . 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 ~~. Failure to obtain capital if and 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 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 ~~after~~ **in** ~~the~~ **those instances** ~~issuance of the CRL for zuranolone for the treatment of MDD~~ , 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** ~~The incurrence of indebtedness would result in increased fixed payment obligations, and we may be required~~ to ~~agree~~ **obtain capital if and when needed may force us** to **delay** ~~certain restrictive covenants~~ , **limit** ~~such as limitations on our~~ **or terminate** ~~ability to incur additional debt, limitations on our ability to acquire, sell or~~ **our product development efforts or** ~~license intellectual property rights and~~ other ~~operating~~ **operations , including the commercialization of any approved product** ~~restrictions that could adversely impact our ability to conduct our business~~ . We could also be required to seek funds through arrangements with ~~collaborative~~ **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 ~~may~~ **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 ~~collaboration~~ **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 ~~, including positive or negative key data from such studies or clinical trials~~, 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 ~~other~~ 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.