Risk Factors Comparison 2025-02-27 to 2024-02-28 Form: 10-K

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You should consider carefully the following information about the risks described below, together with the other information contained in this Annual Report and in our other public filings, in evaluating our business. If any of the following risks actually occurs, our business, financial condition, results of operations, and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock would likely decline. Risks Related to Our ~~Business~~ **Products and Product Candidates** Our prospects are highly dependent on the ~~continued~~ successful commercialization of **our products** ~~NUPLAZID and DAYBUE~~. To the extent we cannot maintain or increase sales of ~~NUPLAZID or~~ **our** ~~DAYBUE~~ **products**, our business, financial condition and results of operations may be materially adversely affected and the price of our common stock may decline. **We have two products that are** ~~In March 2023, we announced FDA approval~~ **approved** ~~of~~ **for commercialization in the U. S.: NUPLAZID and** DAYBUE ~~for the treatment of Rett syndrome in adult and pediatric patients two years of age and older, and DAYBUE became available for prescription in the United States in April 2023. NUPLAZID has been approved in the U. S. since April 2016 for the treatment of hallucinations and delusions associated with PDP~~. The ~~continued~~ successful commercialization of **such products** ~~NUPLAZID and DAYBUE~~ is subject to many risks, and there is no guarantee that we will be able to maintain or increase sales of **such products** ~~NUPLAZID and DAYBUE~~. **Our business** ~~There are numerous examples of failures to meet high expectations of market potential~~, **financial condition** ~~including by pharmaceutical companies with more experience~~ and **results** ~~resources than us. While we have established our commercial teams and have hired our U. S. sales forces for each~~ of **operations** ~~NUPLAZID and DAYBUE, we~~ may ~~need to further expand~~ **be materially adversely affected** and ~~develop sales forces as we pursue NUPLAZID and DAYBUE in other~~ -- **the price of** ~~indications and pursue DAYBUE in other jurisdictions. Even if we are successful in developing~~ our ~~commercial teams, there are~~ **common stock may decline because of** many factors ~~that could negatively impact the sales of our products or cause the continued commercialization of our products to be unsuccessful~~, **some** ~~including a number~~ of **which** ~~factors that~~ are outside our control ~~. The continued commercial success of NUPLAZID and DAYBUE currently depends on~~ **, including, but not limited to, the following: •** the extent to which patients, caregivers and physicians recognize and diagnose the indications for which **our products** ~~NUPLAZID and DAYBUE~~ are approved and accept and adopt **our products** ~~NUPLAZID and DAYBUE~~ as a treatment for such indications ~~,~~ **; • the scope** and **terms of the FDA** ~~we do not know whether our or others~~ ' **s approval** ~~estimates in this regard will be accurate. In addition, we have changed the price~~ of **our products, including the inclusion of a boxed warning for** NUPLAZID ~~in~~ **or** ~~the~~ **other warnings** ~~past,~~ and **precautions for our products; •** ~~in the future we may change the price of NUPLAZID and DAYBUE from time to time. Physicians~~ **physicians** may not prescribe ~~NUPLAZID or~~ **our** ~~DAYBUE~~ **products** and patients may be unwilling to use ~~NUPLAZID or~~ **our** ~~DAYBUE~~ **products**, due to a number of factors, including if coverage is not provided, coverage changes in the future, reimbursement is inadequate to cover a significant portion of the cost **, negative or changing perceptions of each product' s clinical profile and clinical benefits** or due to the prevalence and severity of any adverse side effects **; •** ~~. Further, with respect to DAYBUE, especially because Rett syndrome is a rare disease with a small physician, patient, caregiver and medical community,~~ the experiences of those adopting ~~DAYBUE~~ **our products** earlier could have significant impact on future adoption of ~~DAYBUE~~ **our products** by other physicians, patients and caregivers, either favorably or unfavorably, based on clinical benefits and side effects experienced **; • any new clinical data, post- approval studies or real world results, including in jurisdictions other than the U** . ~~While we have established~~ **S., could result in the FDA making changes to the product label or withdrawal from the market, and could impact regulatory approvals for other indications in the U. S. or other jurisdictions, if any, any of which could result in significant expense and delay or limit our ability to generate sales revenues; • our products are becoming available to a larger number of patients and patients' experiences and results with our products may not be consistent with, or may be more negative when compared to, the experiences and results of those treated in our clinical trials; • successful expansion and development of** our commercial team and ~~have hired our U. S.~~ sales ~~force~~ **forces ;** ~~for DAYBUE, we may need to further expand~~ and **•** ~~develop the team in order to successfully commercialize DAYBUE. Thus, significant uncertainty remains regarding the commercial potential of DAYBUE. Additionally,~~ any negative publicity related to ~~NUPLAZID or~~ **our** ~~DAYBUE~~ **products. Additionally** , ~~or~~ **our** ~~negative development in~~ **success is dependent on** our ~~post-~~ **ability to obtain regulatory approval for, and successfully commercialize, trofinetide in jurisdictions outside the U. S., including the EU. We will face in jurisdictions outside the U. S., such as the EU, if approved for** marketing ~~commitments~~, **risks** ~~in clinical development in additional indications, or in regulatory processes in other jurisdictions, may adversely impact our commercial results~~ and ~~potential of NUPLAZID or DAYBUE. Thus, significant uncertainty~~ **uncertainties** ~~remains regarding~~ **similar to** the **risks** ~~commercial potential of NUPLAZID~~ and ~~DAYBUE~~ **uncertainties faced in the U. S. with respect to commercialization outside of the U. S., including, but not limited to, government reimbursement of the cost of trofinetide**. If the commercialization of our products and future sales ~~are~~ **is** less successful than expected or perceived as disappointing, our stock price could decline significantly and the long- term success of our products and our company could be harmed. **Our** The terms of the FDA' s..... to permit the import or export of products ~~. If any of these actions were to occur, we may have to discontinue the commercialization of NUPLAZID, limit our sales and marketing efforts, conduct further post-approval studies, and / or discontinue or change any other ongoing or planned clinical studies, which in turn could result in significant expense and delay or limit our ability to generate sales revenues. As we continue to commercialize NUPLAZID and DAYBUE, each product is becoming available to a larger number of patients, and we do not know whether the results of~~

NUPLAZID and DAYBUE use in such larger number of patients will be consistent with the results from our clinical studies. As we continue to commercialize NUPLAZID and DAYBUE, each product is becoming available to a larger number of patients. We do not know whether the results, when a larger number of patients are exposed to NUPLAZID and DAYBUE, including results related to safety and efficacy, will be consistent with the results from the clinical studies of NUPLAZID and DAYBUE that served as the basis for their approval. New data relating to NUPLAZID and DAYBUE, including from adverse event reports and applicable post- marketing studies in the U. S., and from other ongoing clinical studies, may result in changes to the product label and may adversely affect sales, or result in withdrawal of NUPLAZID or DAYBUE from the market. The FDA and regulatory authorities in other jurisdictions may also consider the new data in reviewing NUPLAZID or DAYBUE marketing applications for indications other than in PDP or Rett syndrome, respectively, and / or in other jurisdictions, or impose additional post - approval requirements. If any of these actions were to occur, it could result in significant expense and delay or limit our ability to generate sales revenues. We rely on a limited internal commercial team and a limited network of third- party distributors and pharmacies to market and sell NUPLAZID and DAYBUE. If this approach ceases to be effective, our commercialization of NUPLAZID and DAYBUE may be adversely affected, and NUPLAZID and DAYBUE may not be profitable. We employ our own internal specialty sales forces to commercialize NUPLAZID and DAYBUE as part of our commercialization strategy in the U. S. If we receive marketing approval for pimavanserin or trofinetide in any other indication, we may need to increase our U. S. sales forces significantly, and also potentially expand our commercial, medical affairs and general and administrative support functions to support commercialization for that indication. In addition, in July 2023, we entered into an expanded license agreement with Neuren under which we have the exclusive worldwide rights to develop and commercialize trofinetide for Rett syndrome. If we obtain marketing approval outside the U. S. using those worldwide rights, we will need to establish one or more sales forces in the additional countries and expand operations to support any new market. Further, we will be competing with other pharmaceutical and biotechnology companies to recruit, hire, train and retain such personnel. These efforts will be expensive and time consuming, and we cannot be certain that we will be able to successfully expand, refine and further develop our sales forces and related functional teams. Additionally, our strategy in the U. S. includes distributing NUPLAZID and DAYBUE solely through a limited network of third- party specialty distributors and specialty pharmacies. While we have entered into agreements with each of these distributors and pharmacies to distribute NUPLAZID and DAYBUE in the U. S., they may not perform as agreed or they may terminate their agreements with us. Also, we may need to enter into agreements with additional distributors or pharmacies, and there is no guarantee that we will be able to do so on commercially reasonable terms or at all. In the event we are unable to maintain, or expand, if needed, our commercial teams, including our U. S. sales forces or any future sales forces in jurisdictions outside the U. S., or maintain and, if needed, expand, our network of third- party specialty distributors and specialty pharmacies, our ability to continue commercializing NUPLAZID and DAYBUE would be limited, and NUPLAZID and DAYBUE may not be profitable. If we do not obtain regulatory approval of pimavanserin for other indications in addition to treatment of hallucinations and delusions associated with PDP in the U. S., we will not be able to market pimavanserin for other indications in the U. S., which will limit our commercial revenues. Similarly, if we do not obtain regulatory approval of trofinetide outside the U. S. or for indications in addition to Rett syndrome, we will not be able to market trofinetide outside the U. S. or for other indications in the U. S., which will limit our commercial revenues. While pimavanserin has been approved in the U. S. by the FDA for the treatment of hallucinations and delusions associated with PDP, it has not been approved by the FDA for any other indications. Similarly trofinetide has been approved in the U. S. by the FDA for the treatment of Rett syndrome in adult and pediatric patients two years of age and older, it has not been approved by the FDA for any other indications, and it has not been approved in any other jurisdiction for this indication or for any other indication. In order to market pimavanserin or trofinetide for other indications or in other jurisdictions, we must obtain regulatory approval for each of those indications and in each of the applicable jurisdictions, and we may never be able to obtain such approval. Approval of NUPLAZID by the FDA for the treatment of hallucinations and delusions associated with PDP does not ensure that NUPLAZID will be approved by the FDA for any other indication. Similarly, approval of DAYBUE by the FDA for the treatment of Rett syndrome does not ensure that DAYBUE will be approved by the FDA for any other indication. For example, following the successful completion of our Phase 3 HARMONY study, we submitted an sNDA to the FDA for the treatment of DRP on June 3, 2020. On April 2, 2021, we received a complete response letter (CRL) from the FDA, indicating that the FDA had completed its review of the application and determined that it could not be approved in its present form. In February 2022, we resubmitted the aforementioned sNDA refining the proposed indication to treatment of hallucinations and delusions associated with ADP. On August 4, 2022 we received a CRL from the FDA regarding our ADP sNDA resubmission. At this time, we are not planning to conduct any additional studies for pimavanserin in ADP. We initiated the Phase 3 ADVANCE- 2 study of pimavanserin for the treatment of the negative symptoms of schizophrenia in August 2020. We completed the enrollment with top- line results expected in the first quarter of 2024. There is no guarantee that our ongoing study will be successful, or that the FDA will approve pimavanserin for that indication. The research, testing, manufacturing, packaging, labeling, approval, sale, import, export, marketing, and distribution of pharmaceutical product candidates are subject to extensive regulation by the FDA and other regulatory authorities in the U. S. and other countries, whose regulations differ from country to country. We will be required to comply with different regulations and policies of the jurisdictions where we seek approval for our product candidates, and we have not yet identified all of the requirements that we will need to satisfy to submit NUPLAZID or DAYBUE for approval for other indications or in other jurisdictions. This will require additional time, expertise and expense, including the potential need to conduct additional studies or development work for other jurisdictions beyond the work that we have conducted to support our existing approvals for NUPLAZID or DAYBUE. If we do not receive marketing approval for NUPLAZID or DAYBUE for any other indication, we will never be able to commercialize NUPLAZID or DAYBUE for any other indication in the U. S. If we do not receive marketing approval for DAYBUE in other jurisdictions, we will never be able to commercialize DAYBUE in other jurisdictions. Even if we do receive additional regulatory approvals,

~~we may not be successful in commercializing those opportunities. If the results or timing of regulatory filings, the regulatory process, regulatory developments, clinical trials or preclinical studies, or other activities, actions or decisions related to NUPLAZID or DAYBUE do not meet our or others' expectations, the market price of our common stock could decline significantly and the long- term success of the product and our company could be harmed. If we are unable to effectively train and equip our sales forces, our ability to successfully commercialize NUPLAZID and DAYBUE will be harmed. NUPLAZID is the first drug approved by the FDA for the treatment of hallucinations and delusions associated with PDP, and DAYBUE is the first drug approved by the FDA for the treatment of Rett syndrome. As a result, we are and will continue to be required to expend significant time and resources to train our sales forces to be credible, persuasive, and compliant with applicable laws in marketing NUPLAZID and DAYBUE to physicians and healthcare providers, and for NUPLAZID, long- term care facilities and other healthcare providers, as appropriate. In addition, we must ensure that consistent and appropriate messages about NUPLAZID and DAYBUE are being delivered to our potential customers by our sales forces. If we are unable to effectively train our sales forces and equip them with current, effective materials, including medical and sales literature to help them inform and educate potential customers about the benefits of NUPLAZID and DAYBUE, and their proper administration, our efforts to successfully commercialize NUPLAZID and DAYBUE, could be put in jeopardy, which would negatively impact our ability to generate product revenues. NUPLAZID and DAYBUE~~ may not gain maximal acceptance among physicians, patients, caregivers and the medical community, thereby limiting our potential to generate revenues. The degree of market acceptance by physicians, healthcare professionals, patients, caregivers and third- party payors of **our** ~~NUPLAZID, DAYBUE and any other product~~ **products** ~~for which we obtain regulatory approval~~ , and our profitability and growth, will depend on a number of factors, including: • the ability to provide acceptable evidence of safety and efficacy; • the scope of the approved indication (s) for the product; • the inclusion of any warnings or contraindications in the product label; • the relative convenience and ease of administration; • the **relative timing, or perceived timing, in which patients experience outcomes; • the** prevalence and severity of any actual or expected adverse side effects; • the availability of alternative treatments; • the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies ~~, and~~ **; •** our ability to increase awareness of our approved products through marketing efforts; • pricing and cost effectiveness, which may be subject to regulatory control; • effectiveness of our or our collaborators' sales and marketing strategy; • publicity concerning us, our products or competing products and treatments; and • our ability to obtain and maintain sufficient third- party insurance coverage or adequate reimbursement levels. If a product does not provide a treatment regimen that is at least as beneficial as the current standard of care or otherwise does not provide patient benefit, that product will not achieve market acceptance and will not generate sufficient revenues to achieve or maintain profitability. With respect to **our products** ~~NUPLAZID and DAYBUE~~ specifically, successful commercialization will depend on whether and to what extent physicians, patients, caregivers, long- term care facilities and pharmacies, over whom we have no control, determine to utilize **our products** ~~NUPLAZID and DAYBUE~~ . NUPLAZID is available **in the U. S.** to treat hallucinations and delusions associated with PDP, and DAYBUE is available **in the U. S.** to treat Rett syndrome, both indications for which no other FDA- approved pharmaceutical treatments currently exist. ~~Because~~ **DAYBUE is also the first and only product approved in Canada for the treatment** of ~~this~~ **Rett syndrome. As there are no approved competitors for our products** , it is particularly difficult to estimate **the** ~~NUPLAZID' s and DAYBUE' s~~ market potential **for our products** and how physicians, patients, caregivers, long- term care facilities and payors will respond to changes in the price of **our products** ~~NUPLAZID and DAYBUE~~ . Industry sources and analysts have a divergence of estimates for the near- and long- term market potential of **our products** ~~NUPLAZID and DAYBUE~~ , and a variety of assumptions directly impact the estimates for ~~NUPLAZID~~ **our products** ~~' s and DAYBUE' s~~ market potential, including assumptions regarding the prevalence of PDP and Rett syndrome, the rate of diagnosis of PDP and Rett syndrome, the prevalence and rate of hallucinations and delusions in patients diagnosed with PDP with respect to NUPLAZID, the rate of physician adoption ~~of NUPLAZID and DAYBUE~~ , the potential impact of payor restrictions ~~regarding NUPLAZID and DAYBUE~~ , and patient adherence and compliance rates. Small differences in these assumptions can lead to widely divergent estimates of the market potential of **our products** ~~NUPLAZID and DAYBUE~~ . For example, with respect to NUPLAZID, certain research suggests that patients with Parkinson' s disease may be hesitant to report symptoms of PDP to their treating physicians for a variety of reasons, including apprehension about societal stigmas relating to mental illness. Research also suggests that physicians who typically treat patients with Parkinson' s disease may not ask about or identify symptoms of PDP. For these reasons, even if PDP occurs in high rates among patients with Parkinson' s disease, it may be underdiagnosed. Even if PDP is diagnosed, physicians may not prescribe treatment for hallucinations and delusions associated with PDP, and if they do prescribe treatment, they may prescribe drugs other than NUPLAZID, even though they are not approved in PDP. Further, NUPLAZID may take several weeks to show efficacy. Even if NUPLAZID is prescribed for the treatment of hallucinations and delusions associated with PDP, patients may stop taking NUPLAZID because they may not see results in the timeframe they desire **or expect** . Similarly, even if DAYBUE is prescribed for the treatment of Rett syndrome, issues may arise with respect to patient acceptance, adherence **, persistence** and compliance rates for a variety of reasons, including due to the expected **clinical benefits** or **expected and** actual side effects a patient might incur. If patients do not adhere to the recommended dosing of DAYBUE, **or do not maintain the recommended dosing of DAYBUE for sufficient periods of time,** patients and physicians may believe that DAYBUE is less effective, and as a result they may ~~stop~~ **discontinue** taking it and prescribing it **. Additionally, if physicians or patients titrate DAYBUE below the recommended doses, patients may not experience the desired outcomes, and physicians or patients may develop negative beliefs about the effectiveness of DAYBUE and / or discontinue its use** . The label for NUPLAZID also contains a " boxed " warning ~~that elderly patients with DRP treated~~ **related** ~~with antipsychotic drugs are at~~ **to particularly important prescribing information,** ~~an~~ **and** ~~increased~~ **the FDA reminded healthcare providers to be aware of the** ~~risk~~ **risks described in the** ~~of death, and that~~ NUPLAZID **prescribing information following** ~~is~~ **its observation** ~~not approved for the treatment~~ of **potentially concerning prescribing** ~~patients~~

patterns ~~with dementia who experience psychosis unless their hallucinations and delusions are related to Parkinson' s Disease~~ . There has also been attention to publicly reported deaths of patients that were prescribed NUPLAZID, and the FDA conducted an evaluation of available information about NUPLAZID. ~~In the past, the FDA has observed potentially concerning prescribing patterns with NUPLAZID, such as the concomitant use of other antipsychotic drugs or drugs that can cause QT prolongation, a potential cause of heart rhythm disorder. The FDA reminded healthcare providers to be aware of the risks described in the NUPLAZID prescribing information and that none of the other antipsychotic medications are approved for the treatment of PDP. Regardless, perceptions~~ **Perceptions** that NUPLAZID is unsafe, even if unfounded, may discourage physicians from prescribing or patients from taking NUPLAZID. The commercial success of **our products** ~~NUPLAZID and DAYBUE~~ depends on acceptance by patients, caregivers and physicians, and there are a number of factors that could skew our or others' estimates about prescribing behaviors and market adoption. If we fail to gain the acceptance of patients, caregivers and physicians, or if our estimates are inaccurate, these events could negatively impact our business, results of operations, financial condition and prospects **. If we do not obtain regulatory approval of trofinetide outside North America, we will not be able to market trofinetide outside North America, which will limit our commercial revenues. DAYBUE was approved in 2023 in the U. S. by the FDA, and in October 2024 in Canada by Health Canada, for the treatment of Rett syndrome in adult and pediatric patients two years of age and older. In January 2025, we submitted a marketing authorization application for the approval of trofinetide for the treatment of Rett syndrome in the EU. If we do not receive marketing approval for trofinetide in the EU or other jurisdictions outside of North America, including Japan, we will never be able to commercialize trofinetide in such jurisdictions. Even if we do receive additional regulatory approvals, we may not be successful in commercializing those opportunities. If the results or timing of regulatory filings, the regulatory process, regulatory developments, clinical trials or preclinical studies, or other activities, actions or decisions related to DAYBUE or trofinetide do not meet our or others' expectations, the market price of our common stock could decline significantly and the long- term success of the product and our company could be harmed** . Our ability to generate product revenues will be diminished if coverage for our products from **commercial or government** payors is decreased or if patients have unacceptably high ~~co~~ **out** - ~~pay amounts~~ **of- pocket requirements** . Patients who are prescribed medicine for the treatment of their conditions generally rely on third- party payors, including governmental healthcare programs, such as Medicare and Medicaid, managed care organizations and commercial payors, among others, to reimburse all or part of the costs associated with their prescription drugs. Coverage and adequate reimbursement from third- party payors ~~is~~ **are** critical to product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor drug products when lower cost therapeutic alternatives are already available or subsequently become available. Even with coverage for ~~NUPLAZID, DAYBUE or~~ **our** ~~other~~ products ~~we may market~~ , the resulting reimbursement payment rates might not be adequate or may require **out- of- pocket obligations, such as deductibles and** co- **pay or coinsurance** payments **,** that patients find unacceptably high. Patients may not use **our products** ~~NUPLAZID and DAYBUE~~ if coverage is not provided or reimbursement is inadequate to cover a significant portion of its cost. In addition, the market for **our products** ~~NUPLAZID and DAYBUE~~ depends significantly on access to third- party payors' drug formularies, or lists of medications for which third- party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, 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 alternative is available, even if not approved for the indication for which **our products** ~~NUPLAZID and DAYBUE~~ are approved **. Legislators, policymakers and healthcare insurance funds in the EU and the United Kingdom may continue to propose and implement cost- containing measures to keep healthcare costs down, particularly due to the financial strain that the COVID- 19 pandemic placed on national healthcare systems of European countries. These measures could include limitations on the prices we would be able to charge for product candidates that we may successfully develop and for which we may obtain regulatory approval or the level of reimbursement available for these products from governmental authorities or third- party payors. Consequently, a downward trend in prices of medicinal products in some countries could contribute to similar downward trends elsewhere** . Third- party payors, whether governmental or commercial **, whether in the U. S. or globally** , are developing increasingly sophisticated methods of controlling healthcare costs. The current environment is putting pressure on companies to price products below what they may feel is appropriate. Selling ~~NUPLAZID or~~ **our** ~~DAYBUE~~ **products** at less than an optimized price would impact our revenues and could impact our overall success as a company. We have changed, and may continue to change, the price of ~~NUPLAZID or~~ **our** ~~DAYBUE~~ **products** from time to time, however, we do not know if the price we have selected, or may select in the future, for ~~NUPLAZID or~~ **our** ~~DAYBUE~~ **products** is or will be the optimized price. Additionally, we do not know whether and to what extent third- party payors will react to any possible future changes in the price of ~~NUPLAZID or~~ **our** ~~DAYBUE~~ **products** . In the U. S., no uniform policy of coverage and reimbursement for drug products exists among third- party payors **. Outside the U. S., reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies** . Further, one payor' s determination to provide coverage and reimbursement for a product does not ensure that other payors will also provide coverage and reimbursement for the product. Therefore, coverage and reimbursement for ~~NUPLAZID~~ **our products both in the U. S.** and ~~DAYBUE~~ **outside** may differ significantly from payor to payor. As a result, the coverage determination process is often a time- consuming and costly process that will require us to provide scientific and clinical support for the use of **our products** ~~NUPLAZID and DAYBUE~~ to each payor separately, with no assurance that coverage will be obtained. Coverage policies and third- party payor reimbursement rates may change at any time. Therefore, even if favorable coverage and reimbursement status is attained, less favorable coverage policies and reimbursement rates may be implemented in the future. ~~If~~ **In most international markets, where the government is the primary payor, manufacturers must operate in an environment of government- directed cost- containment programs – designs such as price controls, international**

reference pricing, mandatory discounts and rebates, regulatory hurdles and restrictions on physician- level prescribing. In these markets, healthcare services and determination of a product' s pricing and reimbursement are impacted by government control. For example, the EU provides options for EU Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. An EU Member State may approve a specific price for the medicinal product, it may refuse to reimburse a product at the price set by the manufacturer or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Many EU Member States also periodically review their reimbursement procedures for medicinal products, which could have an adverse impact on reimbursement status. Moreover, in order to obtain reimbursement for our products in some European countries, including some EU Member States, we may be required to compile additional data comparing the cost- effectiveness of our products to other available therapies in a Health Technology Assessment (HTA). An HTA of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including those representing the larger markets. The HTA process is the procedure to assess therapeutic, economic and societal impact of a given medicinal product in the national healthcare systems of the individual country. The outcome of an HTA will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product currently varies between EU Member States. In December 2021, Regulation No 2021 / 2282 on HTA, was adopted in the EU. This regulation, which entered into application on January 12, 2025 and has a phased implementation, is intended to boost cooperation among EU Member States in assessing health technologies, including new medicinal products, and providing the basis for cooperation at EU level for joint clinical assessments in these areas. This regulation permits EU Member States to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU Member States continue to be responsible for assessing non- clinical (e. g., economic, social, ethical) aspects of health technologies, and making decisions on pricing and reimbursement. So, for present and future considerations, if we are unable to obtain coverage of, and adequate payment levels for, ~~NUPLAZID, DAYBUE or~~ **our** ~~any other~~ products we may market to third- party payors, physicians may limit how much or under what circumstances they will prescribe or administer them and patients may decline to purchase them. This in turn could affect our ability to successfully commercialize **our products** ~~NUPLAZID, DAYBUE~~ or any other products we may market, and thereby adversely impact our profitability, results of operations, financial condition, and future success. ~~We~~ **Our products** are **subject** ~~solely responsible for the development and commercialization of pimavanserin and trofinetide. We have full responsibility for the pimavanserin and trofinetide programs throughout the world. We expect our research and development costs for continued development of pimavanserin and trofinetide~~ to ~~be substantial. We are currently undertaking~~ ongoing ~~development work~~ **regulatory requirements that could cause us significant expense and delay** ~~for~~ -- **or limit our ability to generate sales revenues** ~~pimavanserin and trofinetide, including clinical trials of pimavanserin for indications other than in PDP~~ . In **connection with** the **FDA** ~~event of~~ approval ~~for additional indications or in jurisdictions outside the U. S., we would need to add significant resources, in order to further commercialize pimavanserin and trofinetide, and to conduct the necessary sales and marketing activities, and to conduct further development activities. With respect to NUPLAZID, our current strategy is to continue to commercialize NUPLAZID for the treatment~~ of ~~hallucinations and delusions associated with PDP in the U. S. using our specialty sales force that are focused on promoting NUPLAZID to physicians who treat PDP patients, including neurologists, psychiatrists and long- term care physicians. With respect to~~ DAYBUE, **we agreed** ~~our current strategy is~~ to ~~continue to commercialize DAYBUE for the treatment of Rett syndrome in the U. S. and other~~ -- **the following** ~~foreign jurisdictions in which DAYBUE may be approved, if any, using our specialty sales force focused on promoting DAYBUE to physicians who treat Rett syndrome patients, including those at Centers of Excellence, high volume institutions and in the community setting. In selected markets outside of the U. S. in which DAYBUE may be approved, if any, we may choose to commercialize DAYBUE independently or by establishing one or more strategic alliances. Without future additional resources or collaboration partners in selected markets outside of the U. S. for DAYBUE, we might not be able to realize the full value of DAYBUE. Furthermore, even though NUPLAZID is approved for the treatment of hallucinations and delusions associated with PDP, a failure in a subsequent pimavanserin study for another indication, including our ongoing study in schizophrenia, or any additional studies, or a failure in our~~ post- marketing **requirements (PMRs): a clinical study of renal impairment in healthy volunteers, nonclinical carcinogenicity** studies ~~could harm our ability to successfully market NUPLAZID for the treatment of hallucinations~~ and ~~delusions associated with PDP or could lead to it being withdrawn~~ **nonclinical in vitro and clinical in vivo drug interaction studies. The FDA has released us** from **one of the five PMRs. In addition, we have fulfilled one of the five PMRs. Of the remaining** ~~the~~ **three PMRs** ~~market. Similarly~~ , **we have completed one** ~~even though DAYBUE is approved for the treatment of Rett syndrome in adult~~ and ~~pediatric patients two years of age~~ **are awaiting the FDA' s acknowledgement** and **acceptance. The results of** ~~older, a failure in a subsequent trofinetide study for another indication or~~ any ~~additional studies, or a failure in our~~ post- marketing **study may cause the FDA to update the label, request additional** studies ~~to NUPLAZID,has been completed and we are awaiting FDA' s acknowledgement and acceptance.In connection with the FDA approval of DAYBUE,we agreed to the following PMCs:a clinical study of renal impairment in healthy volunteers,nonclinical carcinogenicity studies and nonclinical in vitro drug interaction studies.The results of any post- marketing study may cause the FDA to update the label~~ and / ~~or cause the FDA to request additional studies~~ or require risk mitigation plans.The manufacturing processes,labeling,packaging,distribution,adverse event reporting,storage,advertising,promotion and

recordkeeping for **our products** ~~NUPLAZID and DAYBUE~~ will also continue to be subject to extensive and ongoing regulatory requirements **in the U.S.,Canada and in other foreign countries in which we obtain marketing approvals** .These requirements include submissions of safety and other post- marketing information and reports,registration,as well as continued compliance with cGMPs,good clinical practices,international council for harmonization guidelines and good laboratory practices,each of which are regulations and guidelines enforced by ~~the FDA~~ **regulatory authorities** for all of our nonclinical and clinical development and for any clinical trials that we conduct post- approval.Discovery of any issues post-approval,including any safety concerns,such as **carcinogenicity,** unexpected side effects or drug- drug interaction problems,adverse events of unanticipated severity or frequency,or concerns over misuse or abuse of the product,problems with the facilities where the product is manufactured,tested,packaged or distributed,or failure to comply with regulatory requirements,may result in,among other things,restrictions on **our products** ~~NUPLAZID,DAYBUE~~ or on us,including:• withdrawal of approval,addition of warnings or narrowing of the approved indication in the product label;• requirement of a Risk Evaluation and Mitigation Strategy to mitigate the risk of off- label use in populations where the FDA may believe that the potential risks of use may outweigh its benefits;• voluntary or mandatory recalls;• warning letters;• suspension of any ongoing clinical studies;• refusal by the FDA or ~~other~~ **comparable foreign** regulatory authorities to approve pending applications or supplements to approved applications filed by us,or suspension or revocation of product approvals;• restrictions on operations,including restrictions on the marketing or manufacturing of the product or the imposition of costly new manufacturing requirements;or • seizure or detention,or refusal to permit the **import or export of products.If any of these actions were to occur,we may have to discontinue the commercialization of the applicable product,limit our sales and marketing efforts,conduct further post- approval studies,and / or discontinue or change any other ongoing or planned clinical studies,which in turn** could ~~harm~~ **result in significant expense and delay or limit** our ability to ~~successfully~~ **generate sales revenues. We rely on a limited network of third- party distributors and pharmacies to** market **and sell our products. If this approach ceases to be effective, commercialization of our products may be adversely affected, and our products may not be profitable. Our strategy includes distributing NUPLAZID in the U. S. and** DAYBUE ~~for~~ **or trofinetide, as applicable, in the U. S., Canada and other jurisdictions in which marketing is approved solely through a limited network of third- party specialty distributors, specialty pharmacies or other third- party partners. While we have entered into agreements with each of these distributors and pharmacies to distribute NUPLAZID in the U. S. and DAYBUE in the U. S. and Canada, we will need to enter into similar agreements in any jurisdictions in which trofinetide is approved, and such distributors and pharmacies may not perform as agreed or** ~~the~~ **they** ~~treatment of Rett syndrome in adult and pediatric patients~~ **may terminate their agreements with us. Also, we may need** ~~two~~ **to** ~~years of age and older~~ **enter into agreements with additional distributors, pharmacies** or ~~could lead to it being withdrawn from the~~ **other** ~~market~~ **entities, and there is no guarantee that we will be able to do so on commercially reasonable terms or at all** . ~~If~~ **In the event** we are unable to **maintain and** ~~develop pimavanserin for other indications~~ , **if needed, expand,** ~~or~~ **our** ~~trofinetide for other indications~~ **network of third- party specialty distributors and specialty pharmacies,** ~~or~~ **our** ~~in other jurisdictions~~ **ability to continue commercializing our products would be limited** , ~~we~~ **and our products** may not be **profitable** ~~able to maximize the potential of the compounds and that could have a material adverse effect on our future revenues and our success as a company~~ . Drug development is a long, expensive and unpredictable process with a high risk of failure **, and there is no guarantee that our products or product candidates will be successful in ongoing or future clinical trials or obtain regulatory approval** . Preclinical testing and clinical trials are long, expensive and unpredictable processes that can be subject to delays ~~. It may take several years to complete the preclinical testing and clinical development necessary to commercialize a drug, and delays or failure can occur at any stage~~ . Preliminary, initial, top- line or interim results of clinical trials do not necessarily predict final results and such results may change as more patient data becomes available and are subject to audit and verification procedures that could result in material changes in the final results. In addition, success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials even after promising results in earlier trials. **Even if we or our collaborators successfully complete the clinical trials of product candidates,the product candidates may fail for other reasons.** Of the large number of product candidates in development,only a small percentage result in the submission of an NDA to the FDA or comparable regulatory filing to regulatory authorities in other jurisdictions,and even fewer are approved for marketing. **We cannot assure you that,** ~~Even~~ **even** if clinical trials are completed, **either** we or our collaborators **will** ~~may not~~ submit applications for required authorizations to manufacture and / or market potential products or **that** any such application **will** ~~may not~~ be reviewed and approved by the appropriate regulatory authorities in a timely manner,if at all. **Even if we** ~~Our clinical trials face a number of risks,and our~~ **or** ~~product candidates may fail regardless of whether~~ our collaborators successfully complete the clinical trials **of product candidates** and apply for such required authorizations **,the product candidates,such as pimavanserin and trofinetide,may fail** for **other** ~~a number of~~ reasons,including **the possibility that the product candidates will** :• ~~a product candidate may~~ fail to receive the regulatory clearances required to market them as drugs;• ~~a product candidate may~~ be subject to proprietary rights held by others requiring the negotiation of a license agreement prior to marketing;• ~~a product candidate may~~ be difficult or expensive to manufacture on a commercial scale;• ~~a product candidate may~~ have adverse side effects that make their use less desirable; **or** • ~~a product candidate may~~ fail to compete with product candidates or other treatments commercialized by competitors **.** ~~;• a product candidate may not prove to be efficacious or safe;• patients may die or~~ Our drug development programs are at various stages of development and the historical rate of failures for product candidates **in our industry** is extremely high. **We** ~~For example, we had an unsuccessful Phase 3 trial with NUPLAZID in 2009 and we~~ have had several clinical studies evaluating pimavanserin ~~in other indications~~ that did not achieve statistical significance on certain endpoints ~~. In addition~~ , ~~following~~ **including** the ~~successful~~ **unsuccessful** ~~completion of our~~ Phase 3 ~~HARMONY~~ **ADVANCE- 2** study **of** ~~, we submitted a Supplemental New Drug Application (sNDA) to the FDA for~~ pimavanserin for the

treatment of ~~DRP on June 3,~~ **the negative symptoms of schizophrenia in March** ~~2020~~ **2024** ~~. On April~~ **and the unsuccessful Phase** 2 **study** ~~, 2021, we received a CRL indicating that the FDA had completed its review~~ of **pimavanserin** ~~the application and determined that it could not be approved in its present form. In February 2022, we resubmitted the aforementioned DRP sNDA with updated labeling~~ for the treatment of **irritability** ~~hallucinations and delusions~~ associated with **autism spectrum disorder in pediatric populations (Pediatric Phase 2 Trial) in October** ~~ADP to the FDA based on previously submitted studies and new analyses. On August 4, 2022~~ **2024** ~~, we received a CRL from the FDA regarding our submission of the sNDA~~ . At this time, we are not planning to conduct any additional **clinical** studies for pimavanserin **. With the completion of the Pediatric Phase 2 Trial, we believe we now have completed the FDA' s requirements to qualify** for **a pediatric exclusivity for pimavanserin. However,** ~~the~~ **there** ~~treatment of hallucinations~~ **is no assurance that FDA will confirm that such requirements have been met** and ~~delusions associated with ADP~~ **that the pediatric exclusivity will be granted** . An unfavorable outcome in any of our ongoing or future development efforts **for trofinetide** or in the post- marketing studies for ~~NUPLAZID or~~ DAYBUE could be a major set- back for the programs and for us, generally. In particular, an unfavorable outcome in our ~~NUPLAZID~~ **trofinetide** ~~program~~ **programs** or in the post- marketing studies for ~~NUPLAZID or~~ DAYBUE **,** may require us to delay, devote additional substantial resources to, reduce the scope of, or eliminate ~~this~~ **the affected** program and could have a material adverse effect on us and the value of our common stock. **Also, although we have submitted a marketing application for the approval of trofinetide in the EU, there is no guarantee we will receive regulatory approval.** We are currently conducting several studies **with our product candidates** , including our Phase 2 study evaluating the efficacy and safety of an internally- developed compound known as ACP- 204, ~~which is akin to pimavanserin,~~ as a potential treatment for the treatment of hallucinations and delusions associated with ADP and our Phase 3 COMPASS study evaluating the efficacy and safety of ACP- 101 (intranasal carbetocin) for the treatment of hyperphagia in PWS and may conduct additional studies ~~in the future. In connection~~ with **these and** ~~clinical trials, we face risks that: • a product candidate may not prove to be efficacious or safe; • patients may die or suffer~~ other ~~adverse effects for reasons that may or may not be related to the product candidate being tested; • the results may not be consistent with positive results of earlier trials; and • the results may not meet the level of statistical significance required by the FDA or other regulatory agencies. If we do not successfully complete preclinical and clinical development, we will be unable to market and sell products derived from our~~ product candidates **in the future. We plan to initiate** ~~and~~ **an additional Phase 2 study of ACP- 204 in LBDP in the third quarter of 2025 and** to ~~generate product revenues~~ **initiate a Phase 2 study of ACP- 711 in essential tremor in 2026. Drug development is a long, expensive and unpredictable process** . Even if we do successfully complete clinical trials, those results are not necessarily predictive of results of additional trials that may be needed before ~~an NDA~~ **a marketing application** may be submitted to ~~the FDA~~ **regulatory authorities** . **If we** ~~Of the large number of drugs in development, only a small percentage result in the submission of an NDA to the FDA and even fewer~~ are **unable to develop, or obtain marketing approval for, or, if** approved ~~for~~ **, successfully** ~~commercialization~~ **commercialize** ~~. Delays~~ **our product candidates** , ~~suspensions~~ **we may not be able to generate sufficient revenue** and ~~terminations in~~ **our business operations and financial performance may be materially and adversely affected. Expanded access** ~~our~~ **or compassionate use programs could subject us to additional risks. We currently provide and may provide in the future access to unapproved products or product candidates outside of** clinical trials **through expanded access or compassionate use programs (sometimes referred to as right to try programs). These patients generally have life- threatening illnesses for which there are no alternative therapies or they have exhausted all other available therapies. There are a number of risks that we may face as a result of our expanded access or compassionate use programs. For example, the risk for serious adverse events in certain of these patient populations is high, which, if those adverse events are determined (or perceived) to be drug- related, could have a negative impact on the safety profile of our products and product candidates and cause significant delays, result in an inability to successfully commercialize our products and materially harm our business. In certain jurisdictions, we may be required to provide our products for free if we participate in expanded access or compassionate use programs in certain jurisdictions. In other jurisdictions we may be required to return some or all of the revenue we may generate through our expanded access or compassionate use programs if the appropriate foreign regulatory authority ultimately does not approve our products or product candidates for marketing in the jurisdiction of our expanded access or compassionate use programs. If this were to occur, it could materially and adversely affect our business operations and financial performance. Delays, suspensions and terminations in our clinical trials for our product candidates** could result in increased costs to us and delay our ability to generate product revenues. The commencement of clinical trials can be delayed for a variety of reasons, including delays in: • demonstrating sufficient safety and efficacy to obtain regulatory approval to commence a clinical trial; • reaching agreement on acceptable terms with prospective contract research organizations (CROs) and clinical trial sites; • manufacturing sufficient quantities of a product candidate; • obtaining clearance from the FDA to commence clinical trials pursuant to an Investigational New Drug application; • obtaining approval to conduct clinical trials in countries **or jurisdictions** outside the United States pursuant to evolving regional and local regulations (e. g., EU Clinical Trials Regulation (EU No. 536 / 2014)); • obtaining institutional review board approval to conduct a clinical trial at a prospective clinical trial site; and • patient recruitment, which is a function of many factors, most of which is outside our control, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical trial sites, the availability of effective treatments for the relevant disease and the eligibility criteria for the clinical trial. Once a clinical trial has begun, it may be delayed, suspended or terminated due to a number of factors, including: • competition for internal and external resources, including clinical sites and study patients, that we may choose to allocate to other programs; • ongoing discussions with regulatory authorities regarding the scope or design of our clinical trials or requests by them for supplemental information with respect to our clinical trial results; • imposition of clinical holds by regulatory authorities or institutional review boards; • failure to conduct clinical trials in accordance with regulatory requirements; • inability to monitor patients adequately during or after

treatment; • difficulty monitoring multiple study sites; • patient enrollment, which is a function of many factors, most of which is outside our control, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical trial sites, the availability of effective treatments for the relevant disease and the eligibility criteria for the clinical trial; • lower than anticipated screening or retention rates of patients in clinical trials; • serious adverse events or side effects experienced by participants; and • insufficient supply or deficient quality of product candidates or other materials necessary for the conduct of our clinical trials. In addition, enrollment and retention of patients in, or the ability to receive results from, clinical trials could be disrupted by geopolitical or macroeconomic developments. For example, as a result of the ~~ongoing~~ conflict between Ukraine and Russia, we experienced temporary delays in accessing historical records of certain clinical trial sites located in Russia. It is possible that ~~future enrollment in these studies, or~~ enrollment in future studies, could be impacted due to the same or similar geopolitical or macroeconomic developments. If patients withdraw from our trials, miss scheduled doses or follow- up visits or otherwise fail to follow trial protocols, or if our trial results are otherwise disrupted or disputed due to such developments, the integrity of data from our trials may be compromised or not accepted by the FDA or other regulatory authorities, which would represent a significant setback for the applicable program. Many of these factors may also ultimately lead to denial of regulatory approval of a current or potential future product candidate. If we experience delays, suspensions or terminations in a clinical trial, clinical trial materials or investigational products, the commercial prospects for the related product candidate will be harmed, and our ability to generate product revenues will be delayed. If we are unable to attract, retain, and motivate key management, research and development, and sales and marketing personnel, our drug development programs, our research and discovery efforts, and our commercialization plans may be delayed and we may be unable to successfully commercialize our products, or develop our product candidates. Our success depends on our ability to attract, retain, and motivate highly qualified management, scientific, and commercial personnel. In particular, our development programs depend on our ability to attract and retain highly skilled development personnel, especially in the fields of CNS disorders ~~, including neuropsychiatric~~ and ~~related disorders~~ **rare diseases** . We are currently hiring, and in the future we expect to need to continue to hire, additional personnel as we expand our research and development efforts for ~~pimavanserin~~ **our products** and ~~trofinetide~~ **product candidates** , and commercial activities for **our products** ~~NUPLAZID and DAYBUE~~ . We face competition for experienced management, scientists, clinical operations personnel, commercial and other personnel from numerous companies and academic and other research institutions across **all** ~~the U. S. and other~~ jurisdictions in which ~~DAYBUE~~ **our products** may be commercialized ~~, if approved~~ . Many of the other biotechnology and pharmaceutical companies with whom we compete for qualified personnel have greater financial and other resources, different risk profiles and longer histories in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than that which we have to offer. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can develop and commercialize products and product candidates, if approved, will be limited. If we are unable to attract and retain the necessary personnel, it will significantly impede our commercialization efforts for **our products** ~~NUPLAZID and DAYBUE~~ , and the achievement of our research and development objectives **. In September 2024, Catherine Owen Adams became our new Chief Executive Officer (CEO), replacing our former CEO, Stephen R. Davis. Our new CEO will be critical to executing on and achieving our strategy. Further, our new CEO may bring different perspectives, and the future strategy and direction of our business may differ materially from those of the past. If we are unable to execute an orderly transition and successfully integrate our new CEO into our leadership team, we may experience material disruptions to our operations and our financial condition and results of operations may be adversely affected** . All of our employees are " at will " employees, which means that any employee may quit at any time and we may terminate any employee at any time. We do not carry " key person " insurance covering members of senior management. **Risks Related** ~~If we receive approval of NUPLAZID or DAYBUE in additional indications or in jurisdictions outside the U. S., we may need~~ to ~~continue to increase the size of our organization. We may encounter difficulties with managing our growth, which could adversely affect our results of operations. As of December 31, 2023, we employed 598 employees.~~ Our ~~current infrastructure may be inadequate to support our development and commercialization efforts and expected growth. Future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, and integrate additional employees and retain existing employees, and may take time away from running other aspects of our business~~ **Business** ~~, including development and commercialization of our products and product candidates, if approved. Our future financial performance and our ability to commercialize NUPLAZID, DAYBUE and any product candidates that receive regulatory approval and to compete effectively will depend, in part, on our ability to manage any future growth effectively. In particular, we will need to support the training and ongoing activities of our sales forces. To that end, we must be able to: • manage our development efforts effectively; • integrate additional management, administrative and manufacturing personnel; • develop our marketing and sales organization; and • maintain sufficient administrative, accounting and management information systems and controls. We may not be able to accomplish these tasks or successfully manage our operations and, accordingly, may not achieve our research, development, and commercialization goals. Our failure to accomplish any of these goals could harm our business, results of operations, financial condition and prospects.~~ If we fail to develop, acquire or in- license other product candidates or products, our business and prospects would be limited. Even if we obtain rights to other product candidates or products, we will incur a variety of costs and may never realize the anticipated benefits. **Part** ~~A key element~~ of our **corporate** strategy is to develop, acquire or in- license businesses, technologies, product candidates or products that we believe are a strategic fit with our business. The success of this strategy depends in large part on the combination of our regulatory, development and commercial capabilities and expertise and our ability to identify, select and acquire or in- license clinically- enabled product candidates for the treatment of ~~neurological~~ **CNS** disorders **and rare diseases** , or for therapeutic indications that complement or augment our current products and product candidates, or that otherwise fit into our development or strategic plans on terms that are acceptable to us. Identifying, selecting and acquiring or in- licensing

promising product candidates requires substantial technical, financial and human resources expertise, and we may not be successful in identifying acquisition targets, completing proposed acquisitions and integrating any acquired businesses, technologies, services or products into our current infrastructure. Efforts to do so may not result in the actual acquisition or in-license of a particular product candidate, potentially resulting in a diversion of our management' s time and the expenditure of our resources with no resulting benefit. If we are unable to identify, select and acquire or license suitable product candidates from third parties on terms acceptable to us, our business and prospects will be limited. ~~In particular, if we are unable to add additional commercial products to our portfolio, we may not be able to successfully leverage our commercial organization that we have assembled for the marketing and sale of NUPLAZID and DAYBUE.~~ The process of integrating any acquired business, technology, service, or product may result in unforeseen operating difficulties and expenditures and may divert significant management attention from our ongoing business operations. As a result, we will incur a variety of costs in connection with an acquisition and may never realize its anticipated benefits. Moreover, any product candidate we identify, select and acquire or license may require additional, time- consuming development or regulatory efforts prior to commercial sale, including preclinical studies, if applicable, and extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to the risk of failure that is inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and / or effective for approval by regulatory authorities. In addition, ~~we cannot assure you that~~ any such products that are approved ~~will~~ **may not** be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective or desired than other commercially available alternatives ~~. In addition, if we fail to successfully commercialize and further develop NUPLAZID, DAYBUE or our product candidates, if approved, there is a greater likelihood that we will fail to successfully develop a pipeline of other product candidates, and our business and prospects would therefore be harmed~~ . We have a history of net losses and we may not be able to predict the extent of future losses. We have experienced significant net losses since our inception. As of December 31, ~~2023~~ **2024** , we had an accumulated deficit of approximately $ 2. ~~4~~ **2** billion. We expect to increase our expenses and other investments in the coming years as we fund our operations, in- licensing or acquisition opportunities, and capital expenditures. Thus, our future operating results, profitability and other financial metrics may fluctuate from period to period, and we will need to generate significant revenues to achieve and maintain profitability and / or positive cash flow on a sustained basis. We expect that our revenues over the next few years will be entirely dependent on our ability to generate product sales. Substantially all of our revenues since May 2016 were from **U. S.** net product sales of NUPLAZID and DAYBUE. To the extent that we cannot generate significant revenues from the sale of **our products** ~~NUPLAZID and DAYBUE~~ to cover our expenses, including the significant expenses associated with commercializing **our products** ~~NUPLAZID and DAYBUE~~ and continuing to develop ~~pimavanserin and~~ trofinetide in additional indications and jurisdictions outside the U. S., we may not achieve profitability and / or may have to reduce our commercialization and / or research and development activities to become profitable, which would harm our future growth prospects. Additionally, to obtain revenues from our product candidates, if approved, we must succeed, either alone or with others, in developing, obtaining regulatory approval for, manufacturing and marketing compounds with significant market potential. We may never succeed in these activities and may never generate revenues that are significant enough to achieve profitability. **We may require additional financing in the future to fund our operations.** If we **cannot raise additional financing in** ~~fail to generate capital, or otherwise obtain~~ the **future** ~~capital necessary to fund our operations~~ , we ~~will~~ **may** be unable to ~~successfully continue the~~ **fund our business plan and our future research,** development **,** ~~and commercialization of NUPLAZID and DAYBUE or successfully develop and commercialize~~ --- **commercial and manufacturing efforts. We have funded** our **operations primarily with revenues from sales of our products since their approvals, and through sales of our equity securities and interest income. We anticipate that the level of cash used in our operations will fluctuate in future periods depending on the levels of spending required for our ongoing and planned commercial activities for our products, our ongoing and planned development activities for pimavanserin for the negative symptoms of schizophrenia, ACP- 101 as a treatment for PWS and ACP- 204 as a treatment for ADP, studies to be conducted pursuant to our PMRs, our ongoing and planned development activities for other early- and late- stage** product candidates ~~, if approved~~ **and strategic business development to further expand our portfolio** . We **expect that** ~~have consumed substantial amounts of capital since~~ our ~~inception. Our~~ cash, cash equivalents ~~,~~ and investment securities ~~totaled $ 438. 9 million at December 31~~ , ~~2023. While we believe that~~ **as well as funds generated by anticipated sales of** our **products,** ~~existing cash resources~~ will be sufficient to fund our ~~cash requirements~~ **planned operations** through ~~at least~~ **and beyond** the next ~~twelve~~ **12** months ~~, we~~ **. We** may require additional financing in the future ~~to continue~~ to fund our operations. Our future capital requirements will depend on, and could increase significantly as a result of, many factors **,** including: **• the costs of acquiring additional product candidates or research and development programs; • the scope, prioritization and number of our research and development programs; • the ability of our collaborators and us to reach the milestones and other events or developments triggering payments under our collaboration or license agreements, or our collaborators' ability to make payments under these agreements; • our ability to enter into new collaboration and license agreements;** • the progress in, and the costs of, our ongoing and planned development activities for pimavanserin ~~and trofinetide~~ **, post- marketing studies for DAYBUE to be conducted over the next several years** , and ongoing and planned commercial activities for **our products** ~~NUPLAZID and DAYBUE~~ ; • the costs of our development activities for ~~our early-stage pipeline programs and any~~ our product candidates; • the costs of commercializing **our products** ~~NUPLAZID and DAYBUE~~ , including the maintenance and development of our sales and marketing capabilities; • the costs of establishing, or contracting for, sales and marketing capabilities for our product candidates ~~, if approved~~ ; • the amount of U. S. product sales from **our products** ~~NUPLAZID and DAYBUE~~ ; • the costs of preparing applications for regulatory approvals for DAYBUE in jurisdictions other than the U. S. ~~and~~ **, for NUPLAZID** in additional indications other than **PDP and** ~~Rett syndrome, for NUPLAZID in additional indications~~ other ~~than in PDP, and for our~~ product candidates, as well as the costs required to support

review of such applications; • the costs of manufacturing and distributing **our products** ~~NUPLAZID and DAYBUE~~ for commercial use in the U. S.; • our ability to obtain regulatory approval for, and subsequently generate product sales from, NUPLAZID **for** ~~in additional indications other~~ -- **the** ~~than in PDP~~ **negative symptoms of schizophrenia** , or from DAYBUE **, and** ~~in jurisdictions other than the U. S. or~~ **our** ~~in additional indications other than Rett syndrome, our early- stage pipeline programs and any~~ product candidates ~~, if approved; • the costs of acquiring additional products, product candidates or research and development programs; • the scope, prioritization and number of our research and development programs; • the ability of our collaborators and us to reach the milestones and other events or developments triggering payments under our collaboration or license agreements, or our collaborators' ability to make payments under these agreements; • our ability to enter into new collaboration and license agreements~~ ; • the extent to which we are obligated to reimburse collaborators or collaborators are obligated to reimburse us for costs under collaboration agreements; • the costs involved in filing, prosecuting, enforcing, and defending patent claims and other intellectual property rights; • the costs of maintaining or securing manufacturing arrangements ~~and supply~~ for clinical or commercial production of pimavanserin, trofinetide or other product candidates; and • the costs associated with litigation, including the costs incurred in defending against any product liability claims that may be brought against us related to ~~NUPLAZID and DAYBUE or~~ **our** ~~our product~~ **products** ~~candidates. Unless and until we can generate significant cash from our operations, we expect to satisfy our future cash needs through our existing cash, cash equivalents and investment securities, strategic collaborations, public or private sales of our securities, debt financings, grant funding, or by licensing all or a portion of our product candidates or technology~~ . In the past, periods of turmoil and volatility in the financial markets have adversely affected the market capitalizations of many biotechnology companies, and generally made equity and debt financing more difficult to obtain. For example, as a result of geopolitical and macroeconomic developments ~~, including the ongoing conflict between Ukraine and Russia and related sanctions, and the ongoing conflict in Israel and the surrounding areas~~ , the global credit and financial markets have experienced extreme volatility and disruptions, including diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. These events, coupled with other factors, may limit our access to additional financing in the future ~~. This~~ **if needed, and** could have a material adverse effect on our ability to access sufficient funding. We cannot be certain that additional funding will be available to us on **a timely basis, on** acceptable terms, or at all. If **additional** funds are not available, we will be required to delay, reduce the scope of, or eliminate one or more of our research or development programs or our commercialization efforts. We also may be required to relinquish greater or all rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose. Additional funding, if **necessary and** obtained, may significantly dilute existing stockholders and could negatively impact the price of our stock. We expect that our results of operations will fluctuate, which may make it difficult to predict our future performance from period to period. Our operating results have fluctuated in the past and are likely to do so in future periods. Some of the factors that could cause our operating results to fluctuate from period to period include: • the success of our commercialization of **our products** ~~NUPLAZID in the U. S. for the treatment of hallucinations and delusions associated with PDP and DAYBUE in the U. S. for the treatment of Rett syndrome~~ ; • the impact of geopolitical and macroeconomic developments, general political, health and economic conditions ~~, including military conflicts such as the ongoing Ukraine- Russia conflict and the conflicts in Israel and the surrounding areas~~ , as well as any related political or economic responses and counter- responses or otherwise by various global actors or the general effect on the global economy and supply chain, pandemics or epidemics, economic slowdowns, recessions, inflation, ~~rising~~ **high** interest rates and tightening of credit markets on our business; • the status and cost of our **PMRs** ~~post-marketing commitments~~ for ~~NUPLAZID or~~ DAYBUE; • the variation in our gross- to- net adjustments from quarter to quarter, primarily because of the fluctuation in our share of the donut hole for Medicare Part D patients; • the status and cost of development and commercialization of ~~pimavanserin for indications other than for the treatment of hallucinations and delusions associated with PDP, and the status and cost of development and commercialization of~~ trofinetide for indications other than for the treatment of Rett syndrome; • the status and cost of development and commercialization of our product candidates, if approved, including compounds being developed under our collaborations; • whether we acquire or in- license additional product candidates or products, and the status of development and commercialization of such product candidates, if approved **,** or products; • whether we generate revenues or reimbursements by achieving specified research, development or commercialization milestones under any agreements or otherwise receive potential payments under these agreements; • whether we are required to make payments due to achieving specified milestones under any licensing or similar agreements or otherwise make payments under these agreements; • the incurrence of preclinical or clinical expenses that could fluctuate significantly from period to period, including reimbursement obligations pursuant to our collaboration agreements; • the initiation, termination, or reduction in the scope of our collaborations or any disputes regarding these collaborations; • the timing of our satisfaction of applicable regulatory requirements; • the rate of expansion of our clinical development, other internal research and development efforts, and pre- commercial and commercial efforts; • the effect of competing technologies and products and market developments; • the costs associated with litigation, including the costs incurred in defending against any product liability claims that may be brought against us related to **our products** ~~NUPLAZID, DAYBUE~~ or our product candidates; and • general and industry- specific economic conditions. We believe that comparisons from period to period of our financial results are not necessarily meaningful and should not be relied upon as indications of our future performance. From time to time, we provide guidance relating to our expectations for net sales of **our products** ~~NUPLAZID and DAYBUE~~ and certain expense line items based on estimates and the judgment of management. If, for any reason, our actual net sales or expenses differ materially from our guidance, we may have to revise our previously announced financial guidance. If we change, update or fail to meet any element of such guidance, our stock price could decline. Changes in tax laws or regulations that are applied adversely to us or our customers may have a material adverse effect on our business, cash flow, financial condition or results of operations. New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could

adversely affect our business operations and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, legislation enacted in 2017 informally titled the Tax Cuts and Jobs Act, the Coronavirus Aid, Relief, and Economic Security Act and the Inflation Reduction Act enacted many significant changes to the U. S. tax laws. **For example,** ~~Effective~~ **effective** January 1, 2022, the Tax Cuts and Jobs Act eliminated the option to deduct research and development expenses for tax purposes in the year incurred and requires taxpayers to capitalize and subsequently amortize such expenses over five years for research activities conducted in the United States and over 15 years for research activities conducted outside the United States. Although there have been legislative proposals to repeal or defer the capitalization requirement to later years, the provision may not actually be repealed or otherwise modified. Future guidance from the Internal Revenue Service and other tax authorities with respect to such legislation may affect us, and certain aspects of such legislation could be repealed or modified in future legislation. In addition, it is uncertain if and to what extent various states will conform to federal tax laws. Future tax reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one- time charges, and could increase our future U. S. tax expense. Our ability to use net operating ~~losses~~ -- **loss carryforwards** and certain other tax attributes to offset future taxable income or taxes may be limited. Portions of our net operating loss carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under current law, federal net operating losses incurred in tax years beginning after December 31, 2017, may be carried forward indefinitely, but the deductibility of such federal net operating ~~losses~~ -- **loss carryforwards in a taxable year** is limited to 80 % of taxable income **in such year** . ~~It is uncertain if and to what extent various states will conform to federal tax laws~~ . In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the Code), and corresponding provisions of state law, if a corporation undergoes an " ownership change, " which is generally defined as a greater than 50 percent change, by value, in its equity ownership over a three- year period, the corporation' s ability to use its pre- change net operating loss carryforwards and other pre- change tax attributes to offset its post- change income or taxes may be limited. We have experienced ownership changes in the past and we may experience additional ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If an ownership change occurs and our ability to use our net operating loss carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations. In addition, at the state level, there may be periods during which the use of net operating loss carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. **For example, California imposed limits on the usability of California state net operating losses to offset taxable income in tax years beginning after 2023 and before 2027.** As a result, if we earn net taxable income, we may be unable to use all or a material portion of our net operating loss carryforwards and other tax attributes, which could potentially result in increased future tax liability to us and adversely affect our future cash flows. Tax authorities could reallocate our taxable income among our subsidiaries, which could increase our overall tax liability. The amount of taxes we pay in different jurisdictions depends on the application of the tax laws of various jurisdictions, including the United States, to our international business activities, tax rates, new or revised tax laws, or interpretations of tax laws and policies, and our ability to operate our business in a manner consistent with our corporate structure and intercompany arrangements. In 2015, we licensed worldwide intellectual property rights related to pimavanserin in certain indications to Acadia Pharmaceuticals GmbH, our wholly owned Swiss subsidiary (Acadia GmbH), and in July 2020 we licensed additional related rights to Acadia GmbH. Our goals for the establishment of Acadia GmbH, and the licensing of worldwide intellectual property rights for pimavanserin, include building a platform for long- term operational and financial efficiencies, including tax-related efficiencies. The taxing authorities of the jurisdictions in which we operate may challenge our methodologies for pricing intercompany transactions pursuant to our intercompany arrangements or disagree with our determinations as to the income and expenses attributable to specific jurisdictions. In addition, future changes in U. S. and non- U. S. tax laws, including implementation of international tax reform relating to the tax treatment of multinational corporations, if enacted, may reduce or eliminate any potential financial efficiencies that we hoped to achieve by establishing this operational structure. Additionally, taxing authorities, such as the U. S. Internal Revenue Service, may audit and otherwise challenge these types of arrangements, and have done so with other companies in the pharmaceutical industry. If any such challenge or disagreement were to occur or change in tax law were enacted, we could be required to pay additional taxes, interest and penalties, which could result in one-time tax charges, higher effective tax rates, reduced cash flows and lower overall profitability of our operations. Our financial statements could fail to reflect adequate reserves to cover such a contingency. Similarly, a taxing authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a " permanent establishment " under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations. Our results of operations could be adversely affected by general conditions in the U. S. and global economies, the U. S. and global financial markets and adverse macroeconomic developments. U. S. and global market and economic conditions have been, and continue to be, disrupted and volatile due to many factors, including material shortages and related manufacturing and supply chain challenges, geopolitical developments ~~such as ongoing military the conflict between Ukraine and Russia and related sanctions, and the ongoing conflict in Israel and the surrounding areas~~ (as well as any related political or economic responses and counter- responses or otherwise by various global actors or the general effect on the global economy and manufacturing and supply chain), and the responses by central banking authorities to control inflation, among others. General business and economic conditions that could affect our business, financial condition or results of operations include fluctuations in economic growth, debt and equity capital markets, liquidity of the global financial markets, the availability and cost of credit, investor and consumer confidence, and the strength of the economies in which we, our collaborators, our manufacturers and our suppliers operate. A severe or prolonged global economic downturn could result in a variety of risks to our business. For example, **high** ~~inflation rates, particularly in the United States, have increased recently to~~

~~levels not seen in years, and increased~~ inflation may result in increases in our operating costs (including our labor costs), reduced liquidity and limits on our ability to access credit or otherwise raise capital on acceptable terms, if at all. In addition, ~~the U. S. Federal Reserve has raised, and may again raise, interest rates in response to concerns about inflation, which coupled with~~ reduced government spending and volatility in financial markets may have the effect of further increasing economic uncertainty and heightening these risks. Risks of a prolonged global economic downturn are particularly true in Europe, which is undergoing a continued severe economic crisis. A weak or declining economy could also strain our suppliers and manufacturers, possibly resulting in supply and clinical trial disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business. ~~The geo- political turmoil resulting~~ **We or the third parties upon whom we depend may be adversely affected by catastrophic events, such as earthquakes, fires or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us** from ~~Russia' s invasion~~ **a serious disaster. We depend on our employees, consultants, and CROs, as well as regulatory agencies and other parties, for the continued operation** of ~~Ukraine~~ **our business. While we maintain disaster recovery plans, those plans may not adequately protect us. Despite any precautions that we or any third parties on whom we depend take for catastrophic events** , including **earthquakes, fires or** ~~the~~ **other natural disasters** ~~widespread and significant economic sanctions imposed on Russia~~ , ~~has caused~~ **these events could result in** significant disruptions ~~of our clinical trial activities in Russia and Ukraine. We have engaged CROs~~ to ~~conduct~~ **our research and development,** clinical trials ~~worldwide. Certain~~ **, manufacturing and the commercialization** of **our products. Long-term disruptions in the infrastructure caused by these types of events, particularly involving geographies in which we** ~~our~~ - **or** ~~trials~~ **third parties on whom we depend** have **offices** ~~a limited number of clinical sites in Russia and Ukraine where patient recruiting and screening were not complete at the time of Russia' s military aggression in Ukraine. The resulting geo-political turmoil has caused significant disruptions, including the suspension of further new enrollment of patients at our~~ - **or manufacturing, distribution or** clinical trial sites ~~in Ukraine and Russia~~ **, could adversely affect our businesses** . ~~Existing patients may~~ **Although we carry business interruption insurance policies and typically** have ~~been~~ **provisions in our contracts that protect us in certain events, our coverage might not include or be adequate to compensate us for all losses that may occur. Any catastrophic event affecting us or the third parties on whom we depend could have a material adverse effect on our business, results of operations, financial condition and prospect. We have incurred, and expect to continue to incur, significant costs as a result of laws and regulations relating to corporate governance and other matters. Laws and regulations affecting public companies, including provisions of the Dodd- Frank Wall Street Reform and Consumer Protection Act that was enacted in July 2010, the provisions of the Sarbanes- Oxley Act of 2002 (SOX), and rules adopted or proposed by the SEC and by The Nasdaq Stock Market, have resulted in, and will continue to result in, significant costs to us as we** ~~evacuated~~ - **evaluate the implications of these rules and respond to their requirements. In the future, if we are not able to issue an evaluation of** ~~or our relocated far~~ **internal control over financial reporting, as required, or we or our independent registered public accounting** ~~from~~ - **firm** ~~clinical sites~~ **determine that our internal control over financial reporting is not effective** , ~~making~~ **this shortcoming could have an adverse effect on our business and financial results and the price of our common stock could be negatively affected. New rules could make** it **more difficult or more costly for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the coverage that is the same or similar to our current coverage. The impact of these events could also make it more** difficult for **us to attract and retain qualified** ~~participation in our clinical trials. Site personnel~~ **persons** ~~and / or CRO personnel may be unavailable or otherwise unable~~ to **serve** ~~conduct clinical trial activities. Furthermore, the widespread sanctions imposed~~ on ~~Russia have affected clinical sites in Russia managed by~~ **our board of directors and board committees, and as our executive officers. We cannot predict** ~~our~~ - **or estimate** ~~CRO. In addition, clinical sites, their~~ -- **the total amount** ~~personnel and patients may not be able to continue in the trials and therefore we have terminated the trials in Russia. While we have a limited number~~ of ~~clinical sites in Ukraine,~~ **the costs we may incur or the timing of such costs to comply with** these **rules** ~~significant disruptions and the suspension / termination of clinical trial activities could potentially delay the completion of enrollment in our clinical trials and complicate the analysis of data, as affected clinical sites might not be able to have their data be validated or protocol assessments may be missed. Even if data collection can be completed, the FDA may be unable to audit clinical trial sites in Ukraine or Russia. Interruptions of clinical trials may further delay our clinical development and the potential authorization or approval of our product candidates, which could materially increase our costs and adversely affect our ability to commence product sales and generate revenues. Earthquake or fire damage to our facilities could delay our research and development efforts and adversely affect our business. Our headquarters and research and development facilities in San Diego are located in a seismic zone, and we face the possibility of one or more earthquakes, which could be disruptive to our operations and result in delays in our research and development efforts. In addition, while our facilities have not been adversely impacted by local wildfires, there is the possibility of future fires in the area. In the event of an~~ **and regulations** ~~earthquake or fire, if our facilities or the equipment in our facilities is significantly damaged or destroyed for any reason, we may not be able to rebuild or relocate our facilities or replace any damaged equipment in a timely manner and our business, financial condition, and results of operations could be materially and adversely affected. We do not have insurance for damages resulting from earthquakes. While we do have fire insurance for our property and equipment located in San Diego, any damage sustained in a fire could cause a delay in our research and development efforts and our results of operations could be materially and adversely affected~~ . Our business involves the use of hazardous materials, and we and our third- party manufacturers and suppliers must comply with environmental, health and safety laws and regulations, which can be expensive and restrict how we do, or interrupt our, business. Our research and development activities and our third- party manufacturers' and suppliers' activities involve the generation, storage, use and disposal of hazardous materials, including the components of our products and product candidates

and other hazardous compounds and wastes. We and our manufacturers and suppliers are subject to environmental, health and safety laws and regulations governing, among other matters, the use, manufacture, generation, storage, handling, transportation, discharge and disposal of these hazardous materials and wastes and worker health and safety. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination or injury, which could result in an interruption of our commercialization efforts, research and development efforts and business operations, damages and significant cleanup costs and liabilities under applicable environmental, health and safety laws and regulations. We also cannot guarantee that the safety procedures utilized by our third- party manufacturers for handling and disposing of these materials and wastes generally comply with the standards prescribed by these laws and regulations. We may be held liable for any resulting damages costs or liabilities, which could exceed our resources, and state or federal or other applicable authorities may curtail our use of certain materials and / or interrupt our business operations. Furthermore, environmental, health and safety laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. Failure to comply with these environmental, health and safety laws and regulations may result in substantial fines, penalties or other sanctions. We do not currently carry hazardous waste insurance coverage **. Our management has broad discretion over the use of our cash and we may not use our cash effectively, which could adversely affect our results of operations. Our management has significant flexibility in applying our cash resources and could use these resources for corporate purposes that do not increase our market value, or in ways with which our stockholders may not agree. We may use our cash resources for corporate purposes that do not yield a significant return or any return at all for our stockholders, which may cause our stock price to decline** . Risks Related to Our Relationships with Third Parties We depend on collaborations with third parties to develop certain of our product candidates and may need to enter into future collaborations to develop and commercialize certain of our product candidates. We depend on collaborations with third parties to develop certain of our product candidates and may need to enter into future collaborations to develop and commercialize certain of our product candidates. ~~For example, in July 2023, we entered into an expanded license agreement with Neuren under which we have the exclusive worldwide rights to develop and commercialize trofinetide for Rett syndrome and other indications and NNZ- 2591 for Rett syndrome and Fragile X syndrome. In January 2022, we entered into a license and collaboration agreement with Stoke to discover, develop and commercialize novel RNA- based medicines for the potential treatment of severe and rare genetic neurodevelopmental diseases of the CNS.~~ In addition, we may choose to rely on collaborations in the future for ~~certain portions of~~ our **products** ~~pimavanserin and trofinetide programs~~ or other product candidates, ~~or~~ **including** for the commercialization of DAYBUE in selected markets outside of the U. S. Our collaborators may fail to develop or effectively commercialize products using our product candidates, if approved, or technologies because they: • do not have sufficient resources or decide not to devote the necessary resources due to internal constraints such as limited cash or human resources or a change in strategic focus; • may not properly maintain, enforce or defend our intellectual property rights or may use our proprietary information in a manner that could jeopardize or invalidate our proprietary information or expose us to potential litigation; • terminate the arrangement or allow it to expire, which would delay the development and commercialization and may increase the cost of developing and commercializing our products or product candidates, if approved; • may sell, transfer or divest assets or programs related to our partnered product or product candidates; • may not pursue further development and commercialization of products resulting from the strategic collaboration arrangement; • decide to pursue a competitive product developed outside of the collaboration; or • cannot obtain the necessary regulatory approvals. Collaborations are complex and time- consuming to negotiate and document. ~~We also will face competition in our search for new collaborators, if we seek a new partner for our pimavanserin or trofinetide programs or other programs.~~ Given the current economic and industry environment, it is possible that competition for new collaborators may increase ~~. 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. If we are unable to find new collaborations, we may not be able to continue advancing our programs alone. Our collaborations may be subject to conflicts or disputes, which could have a material adverse effect on our business, results of operations and financial condition. Conflicts may arise in our collaborations due to one or more of the following: • disputes or breaches with respect to payments that we believe are due under the applicable agreements, particularly in the current environment when companies, including large established ones, may be seeking to reduce external payments; • disputes on strategy as to what development or commercialization activities should be pursued under the applicable agreements; • disputes as to the responsibility for conducting development and commercialization activities pursuant to the applicable collaboration, including the payment of costs related thereto; • disagreements with respect to ownership of intellectual property rights; • unwillingness on the part of a collaborator to keep us informed regarding the progress of its development and commercialization activities, or to permit public disclosure of these activities; • delay or reduction of a collaborator' s development or commercialization efforts with respect to our product candidates, if approved; or • termination or non- renewal of the collaboration. Conflicts arising with our collaborators could impair the progress of our product candidates, harm our reputation, result in a loss of revenues, reduce our cash position, and cause a decline in our stock price. In addition, in our past collaborations, from time to time, we have agreed not to conduct independently, or with any third party, any research that is directly competitive with the research conducted under the applicable program. Any collaborations we establish in the future may have the effect of limiting the areas of research that we may pursue, either alone or with others. Conversely, the terms of any collaboration we may establish in the future might not restrict our collaborators from developing, either alone or with others, products or product candidates in related fields that are competitive with the products or product candidates that are the subject of these collaborations. Competing products and product candidates, either developed by our collaborators or to which our collaborators have rights, may result in the allocation of resources by our collaborators to competing products and product candidates, and their withdrawal of support for our products

and product candidates or may otherwise result in lower demand for our potential products and product candidates. In addition, 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 patents and other rights to third parties; • our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, if approved, and what activities satisfy those diligence obligations; • our right to transfer or assign the license; 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 not be able to successfully develop and commercialize the related product candidates, if approved, which would have a material adverse effect on our business **.** We rely on third parties to conduct our clinical trials and perform data collection and analysis, which may result in costs and delays that prevent us from successfully commercializing product candidates, if approved. Although we design and manage our current preclinical studies and clinical trials, we currently do not have the ability to conduct clinical trials for our product candidates on our own. We rely on CROs, medical institutions, clinical investigators, and contract laboratories to perform data collection and analysis and other aspects of our clinical trials. In addition, we also rely on third parties to assist with our preclinical studies, including studies regarding biological activity, safety, absorption, metabolism, and excretion of product candidates. Some of these third parties may experience shutdowns or other disruptions as a result of adverse geopolitical or macroeconomic developments and therefore may be unable to provide the level of service that we have received in the past. Our preclinical activities or clinical trials may be delayed, suspended, or terminated if: • these third parties do not successfully carry out their contractual duties or fail to meet regulatory obligations or expected deadlines; • these third parties need to be replaced; or • the quality or accuracy of the data obtained by these third parties is compromised due to their failure to adhere to our clinical protocols or regulatory requirements or for other reasons. Failure to perform by these third parties may increase our development costs, delay our ability to obtain regulatory approval, and delay or prevent the commercialization of our product candidates, if approved. We currently use several CROs to perform services for our preclinical studies and clinical trials. While we believe that there are numerous alternative sources to provide these services, in the event that we seek such alternative sources, we may not be able to enter into replacement arrangements without delays, additional expenditures, or at all, any of which could negatively affect our business, results of operations, financial condition and prospects. Even if we or our collaborators successfully..... or other treatments commercialized by competitors. We currently depend, and in the future will continue to depend, on third parties to manufacture **our products** ~~NUPLAZID, DAYBUE~~ and ~~any~~ product candidates. If these manufacturers fail to provide us or our collaborators with adequate supplies of clinical trial materials and commercial product or fail to comply with the requirements of regulatory authorities, we may be unable to develop or commercialize ~~NUPLAZID, DAYBUE or~~ **our** ~~any~~ **products or** product candidates, if approved. We have no manufacturing facilities and only limited experience as an organization in the manufacturing of drugs or in designing drug- manufacturing processes. We have contracted with third- party manufacturers to produce, in collaboration with us, ~~NUPLAZID, DAYBUE and~~ our **products and** product candidates. We have contracted with Patheon Pharmaceuticals Inc. **(Patheon)** to manufacture NUPLAZID 10 mg tablet and 34 mg capsule drug product and DAYBUE for commercial use in the U. S **. and Canada** . We have also contracted with a second contract manufacturing organization to manufacture NUPLAZID 34 mg drug product for commercial use in the U. S. Additionally, we have contracted with Siegfried AG to manufacture API to be used in the manufacture of NUPLAZID drug product for commercial use, Corden **Pharma Bergamo S. p. A. (Corden)** and **F. I. S. Fabbrica Italiana Sintetici S. p. A. (** FIS **)** to manufacture API to be used in the manufacture of DAYBUE drug product for commercial use, and Patheon and CoreRx **Inc. (CoreRx)** to manufacture DAYBUE for commercial use. However, we have not entered into any agreements with any alternate suppliers for 10 mg NUPLAZID drug product or NUPLAZID API. We may face delays or increased costs in our supply chain that could jeopardize the commercialization of ~~NUPLAZID or~~ **our** ~~DAYBUE~~ **products** . While we currently have sufficient API for both NUPLAZID and DAYBUE and NUPLAZID and DAYBUE finished products on hand to continue our commercial and clinical operations as planned, depending on the effects of geopolitical and macroeconomic developments and whether such developments cause disruptions, we may face such delays or costs in future years. If any third party in our supply or distribution chain for materials or finished product is adversely impacted by geopolitical and macroeconomic developments, ~~such as the ongoing military conflict between Ukraine and Russia and related sanctions, and the ongoing conflict in Israel and the surrounding areas, as well as any related political or~~ **our** ~~economic responses and counter- responses or otherwise by various global actors or the general effect on the global economy and~~ supply chain ~~, our supply chain~~ may be disrupted, limiting our ability to manufacture, test and distribute ~~NUPLAZID or~~ **our** ~~DAYBUE~~ **products** for commercial sales and our product candidates for our clinical trials and research and development operations. For example, it takes approximately two years for our third- party manufacturers to produce DAYBUE API, and a supply chain disruption in DAYBUE API would cause delays or increased costs to us that could jeopardize the commercialization of DAYBUE. ~~Additionally, if NUPLAZID is approved for commercial sale in jurisdictions outside the U. S., we will need to contract with a third party to manufacture such products for commercial sale in the U. S. and / or in such other jurisdictions. We may not be able to enter into such contracts in a timely manner or on acceptable terms, if at all.~~ Even though we have agreements with third parties for the manufacture of **our products** ~~NUPLAZID and DAYBUE~~ , the FDA may not approve the facilities of such manufacturers, the manufacturers may not perform as agreed, or the manufacturers may terminate their agreements with us. If any of the foregoing circumstances occur, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, maintain or obtain, as applicable, regulatory approval for or market ~~NUPLAZID, DAYBUE or~~ **our** ~~any~~ **products or** product candidates. While we believe that there will be alternative sources available to manufacture **our products** ~~NUPLAZID, DAYBUE~~ and ~~any~~ product candidates, in the event that we seek such

alternative sources, we may not be able to enter into replacement arrangements without delays or additional expenditures. We cannot estimate these delays or costs with certainty but, if they were to occur, they could cause a delay in our development and commercialization efforts, which would have a negative effect on our business, results of operations, financial condition and prospects. The manufacturers of **our products** ~~NUPLAZID, DAYBUE~~ and ~~any other~~ product candidates, including Patheon, Siegfried, Corden, FIS and CoreRx, are obliged to operate in accordance with FDA- mandated **current good manufacturing practices (** cGMPs **)** , and we have limited control over the ability of third- party manufacturers to maintain adequate quality control, quality assurance and qualified personnel to ensure compliance with cGMPs. In addition, the facilities used by our third-party manufacturers to manufacture ~~NUPLAZID~~ **our products** and ~~DAYBUE and any~~ product candidates must be approved by the FDA pursuant to inspections that will be conducted prior to any grant of regulatory approval by the FDA. If any of our third-party manufacturers are unable to successfully manufacture material that conforms to our specifications and the FDA' s strict regulatory requirements, or pass regulatory inspection, they will not be able to secure or maintain approval for the manufacturing facilities. Additionally, a failure by any of our third- party manufacturers to establish and follow cGMPs or to document their adherence to such practices may lead to significant delays in clinical trials or in obtaining regulatory approval of product candidates, or result in issues maintaining regulatory approval of **our products** ~~NUPLAZID, DAYBUE~~ and any product candidate that receives regulatory approval, negatively impact our commercialization of ~~NUPLAZID or~~ **our** ~~DAYBUE~~ **products** , or lead to significant delays in the launch and commercialization of any other products we may have in the future. Failure by our third- party manufacturers or us to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure of regulatory authorities to grant pre- market approval of drugs, delays, suspension or withdrawal of approvals, seizures or recalls of products, operating restrictions, and criminal prosecutions. The manufacture of pharmaceutical products requires significant capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. We cannot assure you that any issues relating to the manufacture of ~~NUPLAZID, DAYBUE or~~ **our** ~~any~~ **products or** product candidates will not occur in the future. Additionally, our manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations, our ability to commercialize ~~NUPLAZID or~~ **our** ~~DAYBUE~~ **products** , or provide ~~pimavanserin, trofinetide or~~ **our** ~~any other~~ **products or** product candidates to patients in clinical trials, would be jeopardized. Any delay or interruption in our ability to meet commercial demand for **our products** ~~NUPLAZID, DAYBUE~~ and any other approved products will result in the loss of potential revenues and could adversely affect our ability to gain market acceptance for these products. In addition, any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely. Failures or difficulties faced at any level of our supply chain could materially adversely affect our business and delay or impede the development and commercialization of ~~NUPLAZID, DAYBUE or~~ **our** ~~any~~ **products or** product candidates, if approved, and could have a material adverse effect on our business, results of operations, financial condition and prospects. **Further, changes in federal policy could affect the geopolitical landscape and could give rise to circumstances that negatively affect our business. The third parties that manufacture our products and product candidates have manufacturing activities located in Canada, Europe and Switzerland. The U. S. has implemented, and has proposed to further implement, tariffs that may increase the costs of our third- party manufacturers and the expense to us to produce our products and product candidates. If such actions were to materially affect us or our third- party manufacturers, we may not be able to successfully commercialize our products, which would have an adverse effect on our results of operations.** We may not be able to continue or fully exploit our collaborations with outside scientific and clinical advisors, which could impair the progress of our clinical trials and our research and development efforts. We work with scientific and clinical advisors at academic and other institutions who are experts in the field of CNS disorders **and rare diseases** . They assist us in our research and development efforts and advise us with respect to our clinical trials. These advisors are not our employees and may have other commitments that would limit their future availability to us. Although our scientific and clinical advisors generally agree not to engage in competing work, if a conflict of interest arises between their work for us and their work for another entity, we may lose their services, which may impair our reputation in the industry and delay the development or commercialization of our product candidates, if approved. Risks Related to Our Intellectual Property Our ability to compete may decline if we do not adequately protect our proprietary rights. Our commercial success depends on obtaining and maintaining intellectual property rights to our products and product candidates ~~, including NUPLAZID and DAYBUE,~~ and technologies, as well as successfully defending these rights against third- party challenges. Successful challenges to, or misappropriation of, our intellectual property could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. To protect our intellectual property, we rely on a combination of patents, trade secret protection and contracts requiring confidentiality and nondisclosure. If our patents are successfully challenged, we may face generic competition prior to the expiration dates of our U. S. Orange Book listed patents. In addition, potential competitors have in the past and may in the future file an Abbreviated New Drug Application (ANDA) with the FDA for generic versions of NUPLAZID, seeking approval prior to the expiration of our patents. In response, we have filed complaints against these companies alleging infringement of certain of our Orange Book- listed patents covering NUPLAZID. For a more detailed description of these matters, see **the** section captioned " Legal Proceedings " elsewhere in this report. While we intend to defend the validity of such patents vigorously, and will seek to use all appropriate methods to prevent their infringement, such efforts are expensive and time consuming. Any substantial decrease in the revenue

and income derived from ~~NUPLAZID or~~ **our** ~~DAYBUE~~ **products** would have an adverse effect on our results of operations. With regard to patents, although we have filed numerous patent applications worldwide with respect to pimavanserin, not all of our patent applications resulted in an issued patent, or they resulted in an issued patent that is susceptible to challenge by a third party. Our ability to obtain, maintain, and / or defend our patents covering our product candidates and technologies is uncertain due to a number of factors, including: • we may not have been the first to make the inventions covered by our pending patent applications or issued patents; • we may not have been the first to file patent applications for our product candidates or the technologies we rely upon; • others may develop similar or alternative technologies or design around our patent claims to produce competitive products that fall outside of the scope of our patents; • our disclosures in patent applications may not be sufficient to meet the statutory requirements for patentability; • we may not seek or obtain patent protection in all countries that will eventually provide a significant business opportunity; • any patents issued to us or our collaborators may not provide a basis for commercially viable products, may not provide us with any competitive advantages, or are easily susceptible to challenges by third parties; • our proprietary technologies may not be patentable; • changes to patent laws that limit the exclusivity rights of patent holders or make it easier to render a patent invalid; • recent decisions by the U. S. Supreme Court limiting patent- eligible subject matter; • litigation regarding our patents may include challenges to the validity, enforceability, scope and term of one or more patents; • the passage of The Leahy- Smith America Invents Act (the America Invents Act), introduced new procedures for challenging pending patent applications and issued patents; and • technology that we may in- license may become important to some aspects of our business; however, we generally would not control the patent prosecution, maintenance or enforcement of any such in- licensed technology. Even if we have or obtain patents covering our product candidates or technologies, we may still be barred from making, using and selling our product candidates or technologies because of the patent rights of others. Others have or may have filed, and in the future are likely to file, patent applications covering compounds, assays, genes, gene products or therapeutic products that are similar or identical to ours. There are many issued U. S. and foreign patents relating to genes, nucleic acids, polypeptides, chemical compounds or therapeutic products, and some of these may encompass reagents utilized in the identification of candidate drug compounds or compounds that we desire to commercialize. Numerous U. S. and foreign issued patents and pending patent applications owned by others exist in the area of CNS disorders and the other fields in which we are developing products. These could materially affect our freedom to operate. Moreover, because patent applications can take many years to issue, there may be currently pending applications, unknown to us, that may later result in issued patents that our product candidates or technologies may infringe. These patent applications may have priority over patent applications filed by us. We regularly conduct searches to identify patents or patent applications that may prevent us from obtaining patent protection for our proprietary compounds or that could limit the rights we have claimed in our patents and patent applications. Disputes may arise regarding the ownership or inventorship of our inventions. For applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third- party or instituted by the U. S. Patent and Trademark Office (U. S. PTO), to determine who was the first to invent the invention at issue. It is difficult to determine how such disputes would be resolved. Applications containing a claim not entitled to priority before March 16, 2013, are not subject to interference proceedings due the change brought by the America Invents Act to a " first- to- file " system. However, a derivation proceeding can be brought by a third- party alleging that the inventor derived the invention from another. Periodic maintenance fees on any issued patent are due to be paid to the U. S. PTO and foreign patent agencies in several stages over the lifetime of the patent. The U. S. PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non- compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non- payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business. Some of our academic institutional licensors, research collaborators and scientific advisors have rights to publish data and information to which we have rights. We generally seek to prevent our collaborators from disclosing scientific discoveries until we have the opportunity to file patent applications on such discoveries, but in some cases, we are limited to relatively short periods to review a proposed publication and file a patent application. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborations, then our ability to receive patent protection or protect our proprietary information may be impaired. Confidentiality agreements with employees and others may not adequately prevent disclosure of our trade secrets and other proprietary information and may not adequately protect our intellectual property, which could limit our ability to compete. Because we operate in the highly technical field of drug discovery and development of small molecule drugs, we rely in part on trade secret protection in order to protect our proprietary technology and processes. However, trade secrets are difficult to protect. We enter into confidentiality, nondisclosure, and intellectual property assignment agreements with our corporate partners, employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors. These agreements generally require that the other party keep confidential and not disclose to third parties all confidential information developed by the party or made known to the party by us during the course of the party' s relationship with us. These agreements also 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 may not effectively assign intellectual property rights to us. Enforcing a claim that a party illegally obtained and is using our trade secrets is difficult, expensive and time consuming and the outcome is unpredictable. In addition, courts outside the U. S. may be less willing to protect trade secrets. We also have not entered into any noncompete agreements with any of our employees. Although each of our employees is required to sign a confidentiality agreement with us at the time of hire, we cannot guarantee that the confidential nature of our

proprietary information will be maintained in the course of future employment with any of our competitors. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results and financial condition. A dispute concerning the infringement or misappropriation of our proprietary rights or the proprietary rights of others could be time- consuming and costly, and an unfavorable outcome could harm our business. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including post- issuance review proceedings before the U. S. PTO or oppositions and other comparable proceedings in foreign jurisdictions. Central provisions of the America Invents Act went into effect on September 16, 2012 and on March 16, 2013. The America Invents Act includes a number of significant changes to U. S. patent law. These changes include provisions that affect the way patent applications are being filed, prosecuted and litigated. For example, the America Invents Act enacted proceedings involving post- issuance patent review procedures, such as inter partes review (IPR), and post- grant review, that allow third parties to challenge the validity of an issued patent in front of the U. S. PTO Patent Trial and Appeal Board. Each proceeding has different eligibility criteria and different patentability challenges that can be raised. IPRs permit any person (except a party who has been litigating the patent for more than a year) to challenge the validity of the patent on the grounds that it was anticipated or made obvious by prior art. Patents covering pharmaceutical products have been subject to attack in IPRs from generic drug companies and from hedge funds. If it is within nine months of the issuance of the challenged patent, a third party can petition the U. S. PTO for post- grant review, which can be based on any invalidity grounds and is not limited to prior art patents or printed publications. In post- issuance proceedings, U. S. PTO rules and regulations generally tend to favor patent challengers over patent owners. For example, unlike in district court litigation, claims challenged in post- issuance proceedings are given their broadest reasonable meaning, which increases the chance a claim might be invalidated by prior art or lack support in the patent specification. As another example, unlike in district court litigation, there is no presumption of validity for an issued patent, and thus, a challenger' s burden to prove invalidity is by a preponderance of the evidence, as opposed to the heightened clear and convincing evidence standard. As a result of these rules and others, statistics released by the U. S. PTO show a high percentage of claims being invalidated in post- issuance proceedings. Moreover, with few exceptions, there is no standing requirement to petition the U. S. PTO for inter partes review or post- grant review. In other words, companies that have not been charged with infringement or that lack commercial interest in the patented subject matter can still petition the U. S. PTO for review of an issued patent. Thus, even where we have issued patents, our rights under those patents may be challenged and ultimately not provide us with sufficient protection against competitive products or processes. We may be exposed to future litigation by third parties based on claims that our product candidates, technologies or activities infringe the intellectual property rights of others. In particular, there are many patents relating to specific genes, nucleic acids, polypeptides or the uses thereof to identify product candidates. Some of these may encompass genes or polypeptides that we utilize in our drug development activities. If our drug development activities are found to infringe any such patents, and such patents are held to be valid and enforceable, we may have to pay significant damages or seek licenses to such patents. A patentee could prevent us from using the patented genes or polypeptides for the identification or development of drug compounds. There are also many patents relating to chemical compounds and the uses thereof. If our compounds are found to infringe any such patents, and such patents are held to be valid and enforceable, we may have to pay significant damages or seek licenses to such patents. A patentee could prevent us from making, using or selling the patented compounds. In addition to the patent infringement lawsuits ~~that we have recently initiated~~ against the filers of ANDAs pertaining to NUPLAZID, we may need to resort to litigation to enforce other patents issued to us, protect our trade secrets or determine the scope and validity of third- party proprietary rights. From time to time, we may hire scientific personnel formerly employed by other companies involved in one or more areas similar to the activities conducted by us. Either we or these individuals may be subject to allegations of trade secret misappropriation or other similar claims as a result of their prior affiliations. If we become involved in litigation, it could consume a substantial portion of our managerial and financial resources, regardless of whether we win or lose. We may not be able to afford the costs of litigation. Any legal action against us or our collaborators could lead to: • payment of damages, which could potentially be trebled if we are found to have willfully infringed a party' s patent rights; • injunctive or other equitable relief that may effectively block our ability to further develop, commercialize, and sell products; or • we or our collaborators having to enter into license arrangements that may not be available on commercially acceptable terms, or at all. As a result, we could be prevented from commercializing current or future products. Furthermore, because of the substantial amount of pre- trial document and witness 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. In addition, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. ~~If securities~~ **Securities** analysts ~~or~~ **and** investors **have in the past, and may again in the future** perceive these results to be negative, it could have a substantial adverse effect on the trading price of our common stock. The patent applications of pharmaceutical and biotechnology companies involve highly complex legal and factual questions, which, if determined adversely to us, could negatively impact our patent position. The strength of patents in the pharmaceutical and biotechnology field can be highly uncertain and involve complex legal and factual questions. The U. S. PTO' s interpretation of the Supreme Court' s decisions and the standards for patentability it sets forth are uncertain and could change in the future. Consequently, the issuance and scope of patents cannot be predicted with certainty. Patents, if issued, may be challenged, invalidated or circumvented. U. S. patents and patent applications may also be subject to interference proceedings as mentioned above, and U. S. patents may be subject to reexamination and post- issuance proceedings in the U. S. PTO (and foreign patents may be subject to opposition or comparable proceedings in the corresponding foreign patent office), which 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. Similarly, opposition or invalidity proceedings

could result in loss of rights or reduction in the scope of one or more claims of a patent in foreign jurisdictions. In addition, such interference, reexamination, post- issuance and opposition proceedings may be costly. Accordingly, rights under any issued patents may not provide us with sufficient protection against competitive products or processes. In addition, changes in or different interpretations of patent laws in the U. S. and foreign countries may permit others to use our discoveries or to develop and commercialize our technology and products without providing any compensation to us or may limit the number of patents or claims we can obtain. In particular, there have been proposals to shorten the exclusivity periods available under U. S. patent law that, if adopted, could substantially harm our business. The product candidates that we are developing are protected by intellectual property rights, including patents and patent applications. If any of our product candidates becomes a marketable product, we will rely on our exclusivity under patents to sell the compound and recoup our investments in the research and development of the compound. If the exclusivity period for patents is shortened, then our ability to generate revenues without competition will be reduced and our business could be materially adversely impacted. The laws of some countries do not protect intellectual property rights to the same extent as U. S. laws and those countries may lack adequate rules and procedures for defending our intellectual property rights. For example, some countries, including many in Europe, do not grant patent claims directed to methods of treating humans and, in these countries, patent protection may not be available at all to protect our **products and** product candidates. In addition, U. S. patent laws may change which could prevent or limit us from filing patent applications or patent claims to protect our products and / or technologies or limit the exclusivity periods that are available to patent holders. For example, the America Invents Act (2012) included a number of significant changes to U. S. patent law. These included changes to transition from a " first- to- invent " system to a " first- to- file " system and to the way issued patents are challenged. These changes may favor larger and more established companies that have more resources to devote to patent application filing and prosecution. It is still not clear what, if any, impact the America Invents Act will ultimately have on the cost of prosecuting our patent applications, our ability to obtain patents based on our discoveries and our ability to enforce or defend our issued patents. If we fail to obtain and maintain patent protection and trade secret protection of our product candidates, proprietary technologies and their uses, we could lose our competitive advantage and competition we face would increase, reducing our potential revenues and adversely affecting our ability to attain or maintain profitability. Risks Related to Government Regulation and Our Industry Healthcare reform measures may negatively impact our ability to sell NUPLAZID, DAYBUE or our product candidates, if approved, profitably. In both the U. S. and certain foreign jurisdictions, there have been a number of legislative and regulatory proposals to change the healthcare system in ways that could impact our ability to sell **our** ~~NUPLAZID, DAYBUE and any other potential~~ products, as described in greater detail in the Government Regulation section of this ~~Annual Report~~ **report** . For example, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the ACA), as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we may receive for any **of our** approved ~~product, including NUPLAZID and DAYBUE. With respect to pharmaceutical~~ products ~~, the~~ **. The** ACA, among other things, expanded and increased industry rebates for drugs covered by Medicaid ~~and~~ **,** made changes to the coverage requirements under Medicare Part D, Medicare' s prescription drug benefits program **and broadened access to health insurance** . There have been legal and political challenges **and amendments** to certain aspects of the ACA. ~~Furthermore, on June 17, 2021, the U. S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the " individual mandate " was repealed by Congress. Moreover, prior to the U. S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which began on February 15, 2021 and remained open through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or~~ **For example** ~~the ACA. Further~~ , on August 16, 2022, ~~President Biden signed~~ the Inflation Reduction Act of 2022 (IRA) **was signed** into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the " donut hole " under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out- of- pocket cost and through a newly established manufacturer discount program. It is possible that the ACA will be subject to **additional** ~~judicial or Congressional~~ challenges in the future. It is unclear how any such challenges and additional healthcare reform measures of the ~~Biden~~ **current** administration will impact the ACA and our business. Other legislative changes have been proposed and adopted in the U. S. since the ACA. Through the process created by the Budget Control Act of 2011, there are automatic reductions of Medicare payments to providers up to 2 % per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments, including the Infrastructure Investment and Jobs Act and the Consolidated Appropriations Act of 2023, will remain in effect through 2032 unless additional Congressional action is taken. ~~Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100 % of a drug' s average manufacturer price, for single source and innovator multiple source drugs, effective January 1, 2024. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to certain providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. In addition, Congress is considering additional health reform measures as part of the budget reconciliation process.~~ An expansion in the government' s role in the U. S. healthcare industry may increase existing congressional or governmental agency scrutiny on price increases, such as the ones we have implemented for NUPLAZID, cause general downward pressure on the prices of prescription drug products, lower reimbursements for providers using ~~NUPLAZID, DAYBUE or~~ **our** ~~any other product~~ **products** ~~for which we obtain regulatory approval~~ , reduce product utilization and adversely affect our business and results of

operations. There have been several recent U. S. presidential executive orders, Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. For example, **the IRA** ~~in July 2021~~ , **among** ~~the~~ **other things** ~~Biden administration released an executive order that included multiple provisions aimed at prescription drugs. In response to Biden' s executive order~~ , **(1) directs** ~~on September 9, 2021,~~ the **U. S.** Department of Health and Human Services (HHS) ~~released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform. The plan sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. In addition, the IRA, among other things, (1) directs HHS~~ to negotiate the price of certain single-source drugs ~~and biologics~~ **that have been on the market for at least 7 years** covered under Medicare **(the Medicare Drug Price Negotiation Program)** and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. ~~The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.~~ HHS has and will continue to issue and update guidance as these programs are implemented. These provisions ~~will~~ **began to take** effect progressively ~~starting~~ in fiscal year 2023. On August ~~29~~ **15** , ~~2023~~ **2024** , HHS announced the ~~list~~ **agreed- upon reimbursement prices** of the first ten drugs that **were** ~~will be~~ subject to price negotiations, although the Medicare ~~drug~~ **Drug** ~~price~~ **Price** ~~negotiation~~ **Negotiation** ~~program~~ **Program** is currently subject to legal challenges. **HHS** ~~It is currently unclear how the IRA~~ will **select up** ~~be implemented but is likely~~ to **fifteen additional drugs covered under Part D** ~~have a significant impact on the pharmaceutical industry. Further, in response to the Biden administration' s October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models~~ for ~~testing by~~ **negotiation in 2025. Each year thereafter more Part B and Part D products will become subject to** the ~~Centers for~~ Medicare **Drug Price Negotiation Program** ~~and Medicaid Services (CMS) Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future~~ . On December 7, 2023, ~~the Biden administration announced~~ an initiative to control the price of prescription drugs through the use of march- in rights under the Bayh- Dole Act **was announced** . On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March- In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march- in rights. While march- in rights have not previously been exercised, it is uncertain if that will continue under the new framework. **Further, the overall funding of certain government programs such as Medicaid and Medicare is uncertain and there is no guarantee that funds approved by the U. S. Congress will be made available by the current administration. We expect additional health reform measures may be implemented in the future, particularly in light of the recent U. S. Presidential and Congressional elections.** Individual states in the U. S. have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, on January 5, 2024, the FDA approved Florida' s proposal to import certain drugs from Canada for specific state healthcare programs. It is unclear if and how this program will be implemented and whether it will be subject challenges in the United States or Canada. Other states have also submitted proposals that are pending review by the FDA. Any such approved importation plans, if implemented, may result in lower drug prices for products covered by those programs. The implementation of cost- containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize ~~NUPLAZID, DAYBUE or~~ **our** ~~any other~~ products ~~for which we may receive regulatory approval~~ . We are subject, directly and indirectly, to federal, state and foreign healthcare laws and regulations, including healthcare fraud and abuse laws, false claims laws, physician payment transparency laws and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties. Our operations are directly, and indirectly through our customers and third- party payors, subject to various U. S. federal and state healthcare laws and regulations, including, without limitation, the U. S. federal Anti- Kickback Statute, the U. S. federal False Claims Act, and physician payment sunshine laws and regulations. These laws may impact, among other things, our clinical research, sales, marketing, grants, charitable donations, and education programs and constrain the business or financial arrangements with healthcare providers, physicians, charitable foundations that support Parkinson' s disease patients generally, and other parties that have the ability to directly or indirectly influence the prescribing, ordering, marketing, or distribution of our products for which we obtain marketing approval. In addition, we and any current or potential future collaborators, partners or service providers are or may become subject to data privacy and security regulation by both the U. S. federal government and the states in which we conduct our business, including laws and regulations that apply to our processing of personal data or the processing of personal data on our behalf. Finally, we may be subject to additional healthcare, statutory and regulatory requirements and enforcement by foreign regulatory authorities in jurisdictions in which we conduct our business. The laws that may affect our ability to operate include: • the U. S. federal Anti- Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe, or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service, for which payment may be made, in whole or in part, under U. S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation; • the U. S. federal civil and criminal false claims laws, including the civil False Claims Act, which can be enforced through civil whistleblower or qui tam actions, and civil monetary penalties laws, which impose criminal and civil penalties on individuals or entities for, among other things, knowingly presenting, or causing to be presented to the U. S. federal government, claims for

payment or approval that are false or fraudulent or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U. S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U. S. federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act; • the U. S. federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e. g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U. S. federal Anti- Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation; • HIPAA, and its implementing regulations, and as amended again by the Final HIPAA Omnibus Rule, Modifications to the HIPAA Privacy, Security, Enforcement and Breach Notification Rules Under the Health Information Technology for Economic and Clinical Health Act (HITECH) and the Genetic Information Nondiscrimination Act; Other Modifications to the HIPAA Rules, published in January 2013, which imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information on covered entities subject to the rule, such as health plans, healthcare clearinghouses and certain healthcare providers as well as their business associates, individuals or entities that perform certain services involving the use or disclosure of individually identifiable health information on behalf of a covered entity and their subcontractors that use, disclose or otherwise process individually identifiable health information; • the U. S. Federal Food, Drug and Cosmetic Act (FDCA), which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices; • the U. S. federal physician payment transparency requirements, sometimes referred to as the " Physician Payments Sunshine Act ", which was enacted as part of the ACA and its implementing regulations and requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children' s Health Insurance Program to report annually to the CMS information related to certain payments and other transfers of value made to physicians (as defined to include doctors of medicine, dentists, optometrists, podiatrists and chiropractors under such law), other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members; and • analogous state and local laws and regulations, including: state anti- kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third- party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry' s voluntary compliance guidelines and the relevant compliance guidance promulgated by the U. S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state and local laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities and / or the registration of pharmaceutical sales representatives; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. For example, contributions to third- party charitable foundations are a current area of significant governmental and congressional scrutiny, and we could face action if a federal or state governmental authority were to conclude that our charitable contributions to foundations that support Parkinson' s disease patients generally are not compliant. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from U. S. government- funded healthcare programs, such as Medicare and Medicaid, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits, additional reporting requirements and / or oversight, and the curtailment or restructuring of our operations. Moreover, while we do not bill third- party payors directly and our customers make the ultimate decision on how to submit claims, from time- to- time, for **our** ~~NUPLAZID, DAYBUE and any product~~ **products** ~~candidates that may be approved~~ , we may provide reimbursement guidance to patients and healthcare providers. If a government authority were to conclude that we provided improper advice and / or encouraged the submission of a false claim for reimbursement, we could face action against us by government authorities. If any of the physicians **, healthcare professions,** or other providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government- funded healthcare programs and imprisonment. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations. ~~In addition~~ **Outside the U. S.** , **interactions between pharmaceutical companies and health care professionals are also governed by strict laws, such as national anti- bribery laws of European countries, national sunshine rules, regulations, industry self- regulation codes of conduct and physicians' codes of professional conduct. Failure to comply with** ~~the~~ **these** ~~approval and commercialization of NUPLAZID~~ **requirements could result in reputational risk** , ~~DAYBUE~~ **public reprimands, administrative penalties, fines** or **imprisonment,** any ~~product candidates that may be approved, outside the U. S. will also likely subject us to foreign equivalents~~ of ~~the healthcare laws mentioned above, among other foreign laws~~ **which could adversely affect our ability to operate our business and our results of operations** . We **and the third parties with whom we work** are subject to stringent and evolving U. S. and foreign laws, regulations and rules, contractual obligations, industry

standards, policies and other obligations related to data privacy and security. Our **(or the third parties with whom we work)** actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; and other adverse business consequences. In the ordinary course of business, we collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, process) personal data and other sensitive information, including proprietary and confidential business data, trade secrets, intellectual property, data we collect about trial participants in connection with clinical trials, sensitive third- party data, business plans, transactions, financial information and medical information collected by our patient access management team (collectively, sensitive data). Our data processing activities may subject us to numerous data privacy and security obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contractual requirements, and other obligations relating to data privacy and security. In the United States, federal, state, and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal data privacy laws, consumer protection laws (e. g., Section 5 of the Federal Trade Commission Act), and other similar laws (e. g., wiretapping laws). For example, HIPAA, as amended by HITECH, imposes specific requirements relating to the privacy, security, and transmission of individually identifiable health information. Additionally, ~~in the past few years,~~ numerous U. S. states ~~— including California, Virginia, Colorado, Connecticut, and Utah —~~ have enacted comprehensive privacy laws that impose certain obligations on covered businesses, including providing specific disclosures in privacy notices and affording residents with certain rights concerning their personal data. As applicable, such rights may include the right to access, correct, or delete certain personal data, and to opt- out of certain data processing activities, such as targeted advertising, profiling, and automated decision- making. The exercise of these rights may impact our business and ability to provide our products and services. Certain states also impose stricter requirements for processing certain personal data, including sensitive information, such as conducting data privacy impact assessments. These state laws allow for statutory fines for noncompliance. For example, the California Consumer Privacy Act of 2018 ~~, as amended by the California Privacy Rights Act of 2020~~ (~~CPRA) (collectively,~~ CCPA) requires businesses to provide specific disclosures in privacy notices and honor requests of California residents to exercise certain privacy rights. The CCPA provides for fines **for** ~~of up to $ 7, 500 per~~ intentional ~~violation~~ **violations** and allows private litigants affected by certain data breaches to recover significant statutory damages. Although some U. S. comprehensive privacy laws exempt some data processed in the context of clinical trials, these laws may increase compliance costs and potential liability with respect to other personal data we may maintain about California residents. Similar laws are being considered in several other states, as well as at the federal and local levels, and we expect more jurisdictions to pass similar laws in the future. Outside the United States, an increasing number of laws, regulations, and industry standards may govern data privacy and security. For example, the European Union' s General Data Protection Regulation (EU GDPR), United Kingdom' s GDPR (UK GDPR) (collectively, the GDPR), Brazil' s General Data Protection Law (Lei Geral de Proteção de Dados Pessoais, or LGPD) (Law No. 13, 709 / 2018), and China' s Personal Information Protection Law (PIPL) impose strict requirements for processing personal data. For example, under the GDPR, companies may face temporary or definitive bans on data processing and other corrective actions; fines of up to 20 million Euros under the EU GDPR / 17. 5 million pounds sterling under the UK GDPR or 4 % of annual global revenue, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests. The Swiss Federal Act on Data Protection, or the FADP, also applies to the collection and processing of personal data, including health- related information, by companies located in Switzerland, or in certain circumstances, by companies located outside of Switzerland. ~~The FADP has been revised and adopted by the Swiss Parliament. Companies must comply with the revised version of the FADP and its revised ordinances from September 1, 2023, which may result in an increase of costs of compliance, risks of noncompliance and penalties for noncompliance.~~ In addition, we may be unable to transfer personal data from Europe and other jurisdictions to the United States or other countries due to data localization requirements or limitations on cross- border data flows. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the European Economic Area (EEA) and the UK have significantly restricted the transfer of personal data to the United States and other countries whose privacy laws it believes are inadequate. Other jurisdictions **have adopted and** may **continue to** adopt similarly stringent ~~interpretations of their~~ data localization and cross- border data transfer laws. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the United States in compliance with law, such as the EEA standard contractual clauses, the UK' s International Data Transfer Agreement / Addendum, and the EU- U. S. Data Privacy Framework and the UK extension thereto (which allows for transfers to relevant U. S.- based organizations who self- certify compliance and participate in the Framework), these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. If there is no lawful manner for us to transfer personal data from the EEA, the UK, or other jurisdictions to the United States, or if the requirements for a legally- compliant transfer are too onerous, we could face significant adverse consequences, including by limiting our ability to conduct clinical trial activities in Europe and elsewhere, the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions (such as Europe) at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers of personal data to recipients outside Europe for allegedly violating the GDPR' s cross- border data transfer limitations. Additionally, companies that transfer personal data to recipients outside of the EEA and / or UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators individual litigants and activist groups. Our employees and personnel use generative artificial intelligence (AI) technologies to perform their work, and the disclosure and use of personal data in generative AI technologies is

subject to various privacy laws and other privacy obligations. Governments have passed and are likely to pass additional laws regulating generative AI. Our use of this technology could result in additional compliance costs, regulatory investigations and actions, and lawsuits. If we are unable to use generative AI, it could make our business less efficient and result in competitive disadvantages. In addition to data privacy and security laws, we may be contractually subject to industry standards adopted by industry groups and may become subject to **additional** such obligations in the future. We are also bound by other contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. We publish privacy policies, marketing materials, and other statements, such as **statements related to** compliance with certain certifications or self- regulatory principles, regarding **artificial intelligence,** data privacy and security. ~~If~~ **Regulators in the United States are increasingly scrutinizing these statements, and if** these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, **misleading** or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators, or other adverse consequences. Additionally, under various privacy laws and other obligations, we may be required to obtain certain consents to process personal data. For example, some of our data processing practices may be challenged under wiretapping laws, if we obtain consumer information from third parties through various methods, including chatbot and session replay providers, or via third- party marketing pixels. These practices may be subject to increased challenges by class action plaintiffs. Our inability or failure to obtain consent for these practices could result in adverse consequences, including class action litigation and mass arbitration demands. Obligations related to data privacy and security (and consumers' data privacy expectations) are quickly changing, becoming increasingly stringent, and creating uncertainty. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent or conflict among jurisdictions. Preparing for and complying with these obligations requires us to devote significant resources and may necessitate changes to our services, information technologies, systems, and practices and to those of any third parties that process personal data on our behalf. We may at times fail (or be perceived to have failed) in our efforts to comply with our data privacy and security obligations. Moreover, despite our efforts, our personnel or third parties ~~on~~ **with** whom we **work** ~~rely on~~ may fail to comply with such obligations, which could negatively impact our business operations. If we or the third parties ~~on which~~ **with whom** we ~~rely~~ **work** fail, or are perceived to have failed, to address or comply with applicable data privacy and security obligations, we could face significant consequences, including but not limited to: government enforcement actions (e. g., investigations, fines, penalties, audits, inspections, and similar); litigation (including class- action claims) and mass arbitration demands; additional reporting requirements and / or oversight; bans **or restrictions** on processing personal data; and orders to destroy or not use personal data. In particular, plaintiffs have become increasingly more active in bringing privacy-related claims against companies, including class claims. Some of these claims allow for the recovery of statutory damages on a per violation basis, and, if viable, carry the potential for monumental statutory damages, depending on the volume of data and the number of violations. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to loss of customers; inability to process personal data or to operate in certain jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or substantial changes to our business model or operations. If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs in the U. S., we could be subject to additional reimbursement requirements, fines, sanctions and exposure under other laws which could have a material adverse effect on our business, results of operations and financial condition. We participate in the Medicaid Drug Rebate Program, as administered by CMS, and other federal and state government pricing programs in the U. S., and we may participate in additional government pricing programs in the future. These programs generally require us to pay rebates or otherwise provide discounts to government payors in connection with drugs that are dispensed to beneficiaries / recipients of these programs. In some cases, such as with the Medicaid Drug Rebate Program, the rebates are based on pricing that we report on a monthly and quarterly basis to the government agencies that administer the programs. Pricing requirements and rebate / discount calculations are complex, vary among products and programs, and are often subject to interpretation by governmental or regulatory agencies and the courts. The requirements of these programs, including, by way of example, their respective terms and scope, change frequently. For example, ~~on March 11, 2021, President Biden signed the~~ American Rescue Plan Act of 2021 ~~into law, which eliminates~~ **eliminated** the statutory Medicaid drug rebate cap, ~~currently~~ **previously** set at 100 % of a drug' s average manufacturer price (AMP), for single source and innovator multiple source drugs, effective January 1, 2024. Responding to current and future changes may increase our costs, and the complexity of compliance will be time consuming. Invoicing for rebates is provided in arrears, and there is frequently a time lag of up to several months between the sales to which rebate notices relate and our receipt of those notices, which further complicates our ability to accurately estimate and accrue for rebates related to the Medicaid program as implemented by individual states. Thus, **we may** ~~there can be no~~ **not** ~~assurance that we will~~ be able to identify all factors that may cause our discount and rebate payment obligations to vary from period to period, and our actual results may differ significantly from our estimated allowances for discounts and rebates. Changes in estimates and assumptions may have a material adverse effect on our business, results of operations and financial condition. In addition, the HHS Office of Inspector General and other Congressional, enforcement and administrative bodies have recently increased their focus on pricing requirements for products, including, but not limited to the methodologies used by manufacturers to calculate AMP, and best price (BP), for compliance with reporting requirements under the Medicaid Drug Rebate Program. We are liable for errors associated with our submission of pricing data and for any overcharging of government payors. For example, failure to submit monthly / quarterly AMP and BP data on a timely basis could result in significant civil monetary penalties for each day the submission is late beyond the due date. Failure to make necessary disclosures and / or to identify overpayments could result in allegations against us under the civil False Claims Act and other laws and regulations. Any required refunds to the U. S. government or responding to a government investigation or enforcement action would be expensive and time consuming and could have a material adverse effect on our business, results of operations and financial condition. In addition, in the event that

the CMS were to terminate our rebate agreement, no federal payments would be available under Medicaid or Medicare for our covered outpatient drugs. We could face liability if a regulatory authority determines that we are promoting ~~NUPLAZID or~~ **our** ~~DAYBUE~~ **products** for any " off- label " uses. ~~A~~ **The FDA, Health Canada, the European Commission, competent authorities of individual EU Member States and other comparable foreign regulatory authorities and industry self-regulatory bodies strictly regulate the marketing and promotional claims that are made about drug and biologic products. In particular, a** company may not promote " off- label " uses for its drug products. An off- label use is the use of a product for an indication ~~or~~ **,** patient population **, or manner** that is not described in the product' s ~~FDA-~~ approved ~~label~~ **labeling and** ~~in the U. S. or for uses in other jurisdictions~~ that ~~differ~~ **differs** from those approved by the applicable regulatory ~~agencies~~ **authorities** . Physicians **and other persons qualified to prescribe medicinal products** , on the other hand, may **, in certain jurisdictions including the U. S.,** prescribe products for off- label uses. Although the FDA and ~~other~~ **certain comparable foreign** regulatory ~~agencies~~ **authorities** do not **generally** regulate a physician' s **or other person qualified to prescribe' s** choice of drug treatment made in the ~~physician~~ **such person** ' s independent medical judgment, they do restrict promotional communications from pharmaceutical companies or their sales force with respect to off- label uses of products for which marketing clearance has not been issued. A company that is found to have promoted off- label use of its product may be subject to significant liability, including civil and criminal sanctions. We intend to comply with the requirements and restrictions of the FDA **, Health Canada** and other **comparable foreign** regulatory ~~agencies~~ **authorities, governmental authorities and regulatory bodies in the jurisdictions that approve our products or product candidates** with respect to our promotion of **our** ~~NUPLAZID, DAYBUE and any other~~ products ~~we may be approved to market~~ , but ~~we cannot be sure that~~ **such authorities may nevertheless make us** the ~~FDA~~ **target of an investigation or prosecution based on** ~~or~~ **our marketing and promotional practices** ~~other regulatory agencies will agree that we have not violated their restrictions~~ . As a result, we may be subject to criminal and civil liability **for the promotion of off- label uses** . In addition, our management' s attention could be diverted to handle any such alleged violations **, all of which could have a material adverse effect on our business, results of operations, financial condition and reputation** . A significant number of pharmaceutical companies have been the target of inquiries and investigations by various U. S. federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including **by** the Department of Justice (DOJ), and various U. S. Attorneys' Offices, the HHS Office of Inspector General, the FDA, the Federal Trade Commission and various state Attorneys General offices. These investigations have alleged violations of various U. S. federal and state laws and regulations, including claims asserting antitrust violations, violations of the FDCA, the civil False Claims Act, the Prescription Drug Marketing Act, anti- kickback laws, and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and / or Medicaid reimbursement. If the FDA, DOJ, or any other governmental agency initiates an enforcement action against us, or if we are the subject of a qui tam suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects, and reputation. **In the EU, the advertising and promotion of medicinal products are subject to both EU and EU Member States' laws governing promotion of medicinal products, interactions with physicians and other healthcare professionals, misleading and comparative advertising and unfair commercial practices. General requirements for advertising and promotion of medicinal products, such as direct- to- consumer advertising of prescription medicinal products, are established in EU law. However, the details are governed by regulations in individual EU Member States and can differ from one country to another. If the EU or an applicable EU Member State were to determine that we violated an applicable law or regulation, we could be subject to lawsuits, regulatory actions, penalties and other adverse consequences that would have an adverse effect on our revenue, business, financial prospects, and reputation.** Changes at the FDA and other government agencies could delay or prevent new products from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal 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 payment of user fees, **layoffs** and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, **including executive and congressional priorities, the impacts of** which ~~is~~ **are** inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs 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, have had to furlough critical government employees and stop critical activities. **In addition, the current administration has proposed substantial reductions in force at various government agencies that, if applied in a material way, could significantly reduce the FDA' s and other agencies' capacities to perform their functions in a manner consistent with past practices and could negatively impact our business.** If repeated or prolonged government shutdowns **or material layoffs of agency personnel** occur, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, and negatively impact other government operations on which we rely, which could have a material adverse effect on our business. We are subject to stringent regulation in connection with the marketing of **our** ~~NUPLAZID, DAYBUE and any other~~ products ~~derived from our product candidates~~ , which could delay the development and commercialization of our products. The pharmaceutical industry is subject to stringent regulation by the FDA and other regulatory agencies in the U. S. and by comparable **foreign regulatory** authorities in other ~~countries~~

jurisdictions . Neither we nor our collaborators can market a pharmaceutical product ~~, including NUPLAZID and DAYBUE,~~ in the U. S. until it has completed rigorous preclinical testing and clinical trials and an extensive regulatory clearance process implemented by the FDA. Satisfaction of regulatory requirements typically takes many years, depends upon the type, complexity and novelty of the product, and requires substantial resources. Even if regulatory approval is obtained, the FDA and ~~other~~ **comparable foreign** regulatory ~~agencies~~ **authorities** may impose significant restrictions on the indicated uses, conditions for use, labeling, advertising, promotion, and / or marketing of such products, and requirements for post- approval studies, including additional research and development and clinical trials. These limitations may limit the size of the market for the product or result in the incurrence of additional costs. Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues from the particular product candidate, if approved. Outside the U. S., the ability to market a product is contingent upon receiving approval from the appropriate regulatory authorities. The requirements governing the conduct of clinical trials, marketing authorization, pricing, and reimbursement vary widely from country to country. Only after the appropriate regulatory authority is satisfied that adequate evidence of safety, quality, and efficacy has been presented will it grant a marketing authorization. Approval by the FDA does not automatically lead to the approval by regulatory authorities outside the U. S. and, similarly, approval by regulatory authorities outside the U. S. will not automatically lead to FDA approval. In addition, U. S. and foreign government regulations control access to and use of some human or other tissue samples in our research and development efforts. U. S. and foreign government agencies may also impose restrictions on the use of data derived from human or other tissue samples. Accordingly, if we fail to comply with these regulations and restrictions, the commercialization of our product candidates, if approved, may be delayed or suspended, which may delay or impede our ability to generate product revenues. If our competitors develop and market products that are more effective than ~~NUPLAZID, DAYBUE or~~ **our** ~~our product~~ **products** ~~candidates, if approved~~ , they may reduce or eliminate our commercial opportunity. Competition in the pharmaceutical and biotechnology industries is intense and expected to increase. We face, and will continue to face, intense competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies, both in the U. S. and abroad. We compete, or will compete, with existing and new products being developed by our competitors. Some of these competitors have products or are pursuing the development of pharmaceuticals that target the same diseases and conditions that our research and development programs target. For example, the use of NUPLAZID for the treatment of PDP competes with off- label use of various antipsychotic drugs, including the generic drugs quetiapine, clozapine, risperidone, aripiprazole, and olanzapine. ~~Pimavanserin for the treatment of negative symptoms of schizophrenia, if approved for that indication, would compete with off- label use of Vraylar, marketed by Allergan, Rexulti, marketed by Otsuka Pharmaceutical Co., Ltd., Latuda, marketed by Sunovion Pharmaceuticals Inc., Caplyta, marketed by IntraCellular Therapeutics and various generic drugs, including quetiapine, clozapine, risperidone, aripiprazole, and olanzapine. In addition, DAYBUE competes indirectly with off- label usage of branded and generic prescription medications targeted at individual symptoms of Rett syndrome, including antiepileptics, antipsychotics, antidepressants and benzodiazepines.~~ In addition, Anavex has a product, Anavex 2- 73, in development for the potential treatment of Rett syndrome and Taysha Gene Therapies ~~is~~ **and Neurogene are** conducting **Phase 1 / 2** clinical trials of ~~a~~ gene ~~therapy~~ **therapies** to treat Rett syndrome. Several academic institutions and pharmaceutical companies are currently conducting clinical trials for the treatment of various symptoms of Rett syndrome **, including Unravel Bio and Vanderbilt University Medical Center, which are jointly conducting an early stage study with vorinostat (RVL- 001)** . Other competitors may have a variety of drugs in development or awaiting approval from the FDA or comparable foreign regulatory authorities that could reach the market and become established before we have a product to sell for the applicable disorder. Our competitors may also develop alternative therapies that could further limit the market for any drugs that we may develop. Many of our competitors are using technologies or methods different or similar to ours to identify and validate drug targets and to discover novel small molecule drugs. Many of our competitors and their collaborators have significantly greater experience than we do in the following: • identifying and validating targets; • screening compounds against targets; • preclinical studies and clinical trials of potential pharmaceutical products; • obtaining FDA and other regulatory approvals; and • commercializing pharmaceutical products. In addition, many of our competitors and their collaborators have substantially greater advantages in the following areas: capital resources, research and development resources, manufacturing capabilities, sales and marketing, and production facilities. Smaller companies also may prove to be significant competitors, particularly through proprietary research discoveries and collaboration arrangements with large pharmaceutical and established biotechnology companies. Many of our competitors have products that have been approved or are in advanced development and may develop superior technologies or methods to identify and validate drug targets and to discover novel small molecule drugs. Our competitors, either alone or with their collaborators, may succeed in developing technologies or drugs that are more effective, safer, more affordable, or more easily administered than ours and may achieve patent protection or commercialize drugs sooner than us. Our competitors may also develop alternative therapies that could further limit the market for any drugs that we may develop. Our failure to compete effectively could have a material adverse effect on our business. If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of ~~NUPLAZID, DAYBUE or~~ **our** ~~any other product~~ **products** ~~for which we obtain regulatory approval~~ , or development or commercialization of our product candidates, if approved. We face an inherent risk of product liability as a result of the commercial sales of **our products** ~~NUPLAZID and DAYBUE in the U. S.~~ and the clinical testing of our product candidates ~~, and will face an even greater risk following commercial launch of NUPLAZID or DAYBUE in additional jurisdictions, if approved, or if we engage in the clinical testing of new product candidates or commercialize any additional products~~ . For example, we may be sued if ~~NUPLAZID, DAYBUE or~~ any ~~other~~ **of our** ~~product~~ **products** ~~we develop~~ allegedly ~~causes~~ **cause** injury or ~~is~~ **are** found to be otherwise unsuitable for administration in humans. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection

acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates, if approved. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in: • decreased demand for our products or product candidates, if approved ~~, that we may develop~~ ; • injury to our reputation; • withdrawal of clinical trial participants; • initiation of investigations by regulators; • costs to defend the related litigation; • a diversion of management' s time and our resources; • substantial monetary awards to trial participants or patients; • product recalls, withdrawals or labeling, marketing or promotional restrictions; • loss of revenue; • exhaustion of any available insurance and our capital resources; • the inability to commercialize our products or product candidates, if approved; and • a decline in our stock price. Although we currently have product liability insurance that covers our clinical trials and the commercialization of **our products** ~~NUPLAZID and DAYBUE~~ , we may need to increase and expand this coverage, including if we commence larger scale trials and if our product candidates are approved for commercial sale. This insurance may be prohibitively expensive or may not fully cover our potential liabilities. Inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of products that we or our collaborators develop. If we determine that it is prudent to increase our product liability coverage, we may be unable to obtain such increased coverage on acceptable terms or at all. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. Our liability could exceed our total assets if we do not prevail in a lawsuit from any injury caused by our drug products. Product liability claims could have a material adverse effect on our business and results of operations. If our information technology systems or data, or those of third parties ~~upon which~~ **with whom** we ~~rely~~ **work** , are or were compromised, we could experience adverse consequences resulting from such compromise, including but not limited to regulatory investigations or actions, interruptions to operations or clinical trials, reputational harm, litigation, fines and penalties, disruptions of our business operations, and a loss of customers or sales. In the ordinary course of our business, we, or the third parties ~~upon which~~ **with whom** we ~~rely~~ **work** , process proprietary, confidential, and sensitive data, including personal data (such as health- related data), intellectual property, and trade secrets. Cyberattacks, malicious internet- based activity, online and offline fraud and other similar activities threaten the confidentiality, integrity, and availability of our sensitive data and information technology systems, and those of the third parties ~~upon which~~ **with whom** we ~~rely~~ **work** . These threats are prevalent, continue to rise, and are becoming increasingly difficult to detect. These threats come from a variety of sources, including traditional computer " hackers, " hacktivists, threat actors, personnel misconduct or error (such as through theft or misuse), organized criminal threat actors, sophisticated nation- states, and nation- state- supported actors. Some actors now engage and are expected to continue to engage in cyber- attacks, including without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we and the third parties ~~upon which~~ **with whom** we ~~rely~~ **work** may be vulnerable to a heightened risk of these attacks, including retaliatory cyber- attacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our goods and services. We and the third parties ~~upon which~~ **with whom** we ~~rely~~ **work** are subject to a variety of evolving threats, including but not limited to, social engineering attacks (including through deep fakes, which may be increasingly more difficult to identify as fake, and phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial- of- service attacks, credential stuffing, credential harvesting, personnel misconduct or error, ransomware attacks, supply- chain attacks, software bugs, server malfunction, software or hardware failures, loss of data or other information technology assets, adware, attacks enhanced or facilitated by AI, telecommunications failures, earthquakes, fire, flood, and other similar threats. Ransomware attacks, including by organized criminal threat actors, nation- states, and nation- state- supported actors, are becoming increasingly prevalent and severe and can lead to significant interruptions, delays, or outages in our operations, disruption of clinical trials or otherwise affecting our ability to provide our products or product candidates, loss of sensitive data (including data related to clinical trials) and income, significant extra expenses to restore data or systems, reputational harm and the diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments (including, for example, if applicable laws or regulations prohibit such payments). Remote work has ~~become more common and has~~ increased risks to our information technology systems and data, as ~~more of~~ our employees work from home, utilizing network connections, computers and devices outside our premises, including at home, while in transit or in public locations. Future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program. We rely on third- party service providers and technologies to operate critical business systems to process sensitive data in a variety of contexts, including, without limitation, cloud- based infrastructure, drug suppliers, data center facilities, encryption and authentication technology, employee email, content delivery to customers, and other functions. Our ability to monitor these third parties' information security practices and posture (including whether any unremediated vulnerabilities exist or have been exploited) is limited, and these third parties may not have adequate information security measures in place. In addition, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third- party partners' supply chains have not been compromised. For example, ~~in May 2021,~~ **we were made aware of** a ~~key drug supplier~~ **cyberattack against one of the largest prescription processors in the country in February 2024 that impacted the ability for our specialty pharmacy partners to have payors provide authorizations for patient refills and new patient starts for certain of our products. In April 2024, we were** notified ~~us of a ransomware attack on our supplier' s systems; however, to date we found no indication that our personal data was exposed. Additionally, we have been notified in the past~~ by a third- party ~~identity~~ **patient support service provider of a data security incident that involved personal data of**

NUPLAZID patients. It may be difficult and / or costly to detect, investigate, mitigate, contain and remediate a security incident. Our efforts to investigate, mitigate, contain and remediate a security incident may not be successful. Actions taken by us or the third parties with whom we work to detect, investigate, mitigate, contain and remediate a security incident could result in outages, data losses and disruptions of our business. Threat actors may also gain access ~~provider of~~ **to other networks and systems after** a **compromise** ~~potential exposure to our administrative accounts. Similarly, in November 2023, we were notified~~ of ~~a ransomware attack on a drug substance supplier that interrupted their operations. We have also been made aware of a cyberattack against one of the largest prescription processors in the country as of February 21, 2024 that may impact the ability for~~ our **networks** ~~specialty pharmacy partners to have payers provide authorizations for patient refills~~ and **systems** ~~new patient starts for certain of our products~~ . While we have implemented security measures designed to protect against security incidents, there can be no assurance that these measures will be effective. We take steps designed to detect, mitigate, and remediate vulnerabilities in our information security systems (such as our hardware and / or software, including that of third parties ~~upon which~~ **with whom** we ~~rely~~ **work**). We and the third parties ~~upon which may rely~~ **with whom we work** may not, however, detect and remediate all such vulnerabilities including on a timely basis. For example, we have identified certain vulnerabilities in our information systems, and we take steps designed to mitigate the risks associated with known vulnerabilities. These steps include implementing compensating controls and other protective measures. Further, we and the third parties ~~upon which~~ **with whom** we ~~rely~~ **work** may experience delays in developing and deploying remedial measures and patches designed to address identified vulnerabilities. Vulnerabilities could be exploited and result in a security incident. Any of the previously identified or similar threats could cause **, and in some cases have in the past caused,** a security incident or other interruption that could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive information or our information technology systems, or those of the third parties ~~upon~~ **with** whom we ~~rely~~ **work** . A security incident or other interruption could disrupt our ability (and that of third parties ~~upon~~ **with** whom we ~~rely~~ **work**) to provide our products. We may expend significant resources or fundamentally change our business activities and practices (including our clinical trials) to try to protect against security incidents. Certain data privacy and security obligations may require us to implement and maintain specific security measures or industry- standard or reasonable security measures to protect our information technology systems and sensitive data. Applicable data privacy and security obligations may require us **, or we may choose,** to notify relevant stakeholders, including affected individuals, customers, regulators, and investors, of security incidents **, or to implement other requirements, such as providing credit monitoring or identity theft protection services** . Such disclosures **and related actions** are costly, and the disclosure or the failure to comply with ~~such~~ **applicable** requirements could lead to adverse consequences. If we (or a third party ~~upon~~ **with** whom we ~~rely~~ **work**) experience a security incident or are perceived to have experienced a security incident, we may experience adverse consequences. These consequences may include: government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and / or oversight; restrictions on processing sensitive data (including personal data); litigation (including class claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; diversion of management attention; interruptions in our operations (including availability of data); financial loss; and other similar harms. Security incidents and attendant consequences may prevent or cause customers to stop using our products, deter new customers from using our products, and negatively impact our ability to grow and operate our business. Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. In addition, our insurance coverage may not be adequate or sufficient in type or amount to protect us from or to mitigate liabilities arising out of our privacy and security practices. The successful assertion of one or more large claims against us that exceeds our available insurance coverage, or results in changes to our insurance policies (including premium increases or the imposition of large deductible or co- insurance requirements), could have an adverse effect on our business. In addition to experiencing a security incident, third parties may gather, collect, or infer sensitive data about us from public sources, data brokers or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position. Additionally, sensitive information of the Company could be leaked, disclosed, or revealed as a result of or in connection with our employees', personnel' s, or vendors' use of generative AI technologies. Risks Related to Our Common Stock Our stock price historically has been, and is likely to remain, highly volatile. The market prices for securities of biotechnology companies in general, and drug discovery and development companies in particular, have been highly volatile and may continue to be highly volatile in the future. From the period between January ~~3~~ **2** , ~~2023~~ **2024** to February ~~26~~ **18** , ~~2024~~ **2025** , the closing price of our common stock has ranged from a low of $ ~~16~~ **14** . ~~32~~ **29** per share to a high of $ ~~33~~ **30** . ~~47~~ **86** per share. Furthermore, especially as we and our market capitalization have grown, the price of our common stock has been increasingly affected by quarterly and annual comparisons with the valuations and recommendations of the analysts who cover our business. The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of our common stock: • the status and cost of development and commercialization of our products and product candidates, if approved, including compounds being developed under our collaborations; • ~~whether we acquire or in- license additional product candidates or products, and~~ the status **and cost** of development and commercialization of **trofinetide** ~~such product candidates, if approved, or products; • the status and cost of development and commercialization of pimavanserin~~ for indications other than **Rett syndrome** ~~in PDP, including ADP,~~ and in jurisdictions **outside North America** ~~other than the U. S.~~ ; • any other communications or guidance from the FDA or other regulatory authorities that pertain to ~~NUPLAZID, DAYBUE or~~ **our products** ~~our~~ - **or** product candidates; • the initiation, termination, or reduction in the scope of our collaborations or any disputes or developments regarding our collaborations; • market conditions or trends related to biotechnology and pharmaceutical industries, or the market in general; • announcements of technological innovations, new products, or other material events by our competitors or us, including any new products that we

may acquire or in- license; • disputes or other developments concerning our proprietary and intellectual property rights; • fluctuations in our operating results; • changes in, or failure to meet, securities analysts' or investors' expectations of our financial performance; • our failure to meet applicable Nasdaq listing standards and the possible delisting of our common stock from the Nasdaq Stock Market; • additions or departures of key personnel; • discussions of our business, products, financial performance, prospects, or stock price by the financial and scientific press and online investor communities such as blogs and chat rooms; • public concern as to, and legislative action with respect to, genetic testing or other research areas of biopharmaceutical companies, the pricing and availability of prescription drugs, or the safety of drugs and drug delivery techniques; • regulatory developments in the U. S. and in foreign countries; • changes in the structure of healthcare payment systems; • the announcement of, or developments in, any litigation matters; • disruptions caused by geopolitical or macroeconomic developments or other business interruptions ~~, including, for example, the ongoing military conflict between Ukraine and Russia and related sanctions and the ongoing conflict in Israel and the surrounding areas~~ , as well as any related political or economic responses and counter- responses or otherwise by various global actors or the general effect on the global economy and supply chain; and • economic and political factors, including but not limited to economic and financial crises, wars, terrorism, and political unrest. In the past, following periods of volatility in the market price of a particular company' s securities, securities class action litigation has often been brought against that company. For example, we, and certain of our current and former officers and directors, are subject to numerous lawsuits related to prior statements about NUPLAZID and our sNDA seeking approval of pimavanserin for the treatment of hallucinations and delusions associated with DRP, as described in " Legal Proceedings ". If we are not successful in defense of these claims, we may have to make significant payments to, or other settlements with, our stockholders and their attorneys. Even if such claims are not successful, the litigation has resulted in additional costs in the past and could result in further substantial costs and diversion of our management' s attention and resources in the future, which could have a material adverse effect on our business, operating results or financial condition. If we or our stockholders sell substantial amounts of our common stock, the market price of our common stock may decline. A significant number of shares of our common stock are held by a small number of stockholders. Sales of a significant number of shares of our common stock, or the expectation that such sales may occur, could significantly reduce the market price of our common stock. In connection with our March 2014 public offering of common stock, we agreed to provide resale registration rights for the shares of our common stock held by entities affiliated with one of our principal stockholders and two of our directors, Julian C. Baker and Dr. Stephen R. Biggar, which we refer to as the Baker Entities. In connection with our January 2016 public offering of common stock, we entered into a formal registration rights agreement with the Baker Entities to provide for these rights. Under the registration rights agreement, we have agreed that, if at any time and from time to time, the Baker Entities demand that we register their shares of our common stock for resale under the Securities Act, we would be obligated to effect such registration. On May 25, 2022, we filed a registration statement covering the sale of up to 42, 393, 855 shares of our common stock, which includes 489, 269 shares of our common stock issuable upon the exercise of warrants that were owned by the Baker Entities as of May 16, 2022, and which represented approximately 26 percent of our outstanding shares at the time. Our registration obligations under this registration rights agreement, which cover all shares now held or later acquired by the Baker Entities, will be in effect for up to 10 years, and include our obligation to facilitate certain underwritten public offerings of our common stock by the Baker Entities in the future. If the Baker Entities sell a large number of our shares, or the market perceives that the Baker Entities intend to sell a large number of our shares, this could adversely affect the market price of our common stock. We also may elect to sell from time to time an indeterminate number of shares on our own behalf pursuant to a registration statement or in a private placement. Our stock price may decline as a result of the sale of the shares of our common stock included in any of these registration statements or future financings. If our officers, directors, and largest stockholders choose to act together, they may be able to significantly influence our management and operations, acting in their best interests and not necessarily those of our other stockholders. Our directors, executive officers and holders of 5 % or more of our outstanding common stock and their affiliates beneficially own a substantial portion of our outstanding common stock. As a result, these stockholders, acting together, have the ability to significantly influence all matters requiring approval by our stockholders, including the election of all of our board members, amendments to our certificate of incorporation, going- private transactions, and the approval of mergers or other business combination transactions. The interests of this group of stockholders may not always coincide with our interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of our other stockholders. Anti- takeover provisions in our charter documents and under Delaware law may make an acquisition of us more complicated and may make the removal and replacement of our directors and management more difficult. Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may delay or prevent a change in control, discourage bids at a premium over the market price of our common stock and adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock. These provisions may also make it difficult for stockholders to remove and replace our board of directors and management. These provisions: • establish that members of the board of directors may be removed only for cause upon the affirmative vote of stockholders owning at least a majority of our capital stock; • authorize the issuance of " blank check " preferred stock that could be issued by our board of directors to increase the number of outstanding shares and prevent or delay a takeover attempt; • limit who may call a special meeting of stockholders; • establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings; • prohibit our stockholders from making certain changes to our amended and restated certificate of incorporation or amended and restated bylaws except with 662 / 3 % stockholder approval; and • provide for a board of directors with staggered terms. We are also subject to provisions of the General Corporation Law of the State of Delaware that, in general, prohibit any business combination with a beneficial owner of 15 % or more of our common stock for three years unless the holder' s acquisition of our stock was approved in advance by our board of directors. Although we believe these provisions collectively provide for an

opportunity to receive higher bids by requiring potential acquirors to negotiate with our board of directors, they would apply even if the offer may be considered beneficial by some stockholders. We do not intend to pay dividends on our common stock in the foreseeable future; as such, you must rely on stock appreciation for any return on your investment. To date, we have not paid any cash dividends on our common stock, and we do not intend to pay any dividends in the foreseeable future. Instead, we intend to retain any future earnings to fund the development and growth of our business. For this reason, the success of an investment in our common stock, if any, will depend on the appreciation of our common stock, which may not occur. There is no guarantee that our common stock will appreciate, and therefore, a holder of our common stock may not realize a return on his or her investment. ~~General Risk Factors Our management has broad discretion over the use of our cash and we may not use our cash effectively, which could adversely affect our results of operations. Our management has significant flexibility in applying our cash resources and could use these resources for corporate purposes that do not increase our market value, or in ways with which our stockholders may not agree. We may use our cash resources for corporate purposes that do not yield a significant return or any return at all for our stockholders, which may cause our stock price to decline. We have incurred, and expect to continue to incur, significant costs as a result of laws and regulations relating to corporate governance and other matters. Laws and regulations affecting public companies, including provisions of the Dodd- Frank Wall Street Reform and Consumer Protection Act that was enacted in July 2010, the provisions of the Sarbanes- Oxley Act of 2002 (SOX), and rules adopted or proposed by the SEC and by The Nasdaq Stock Market, have resulted in, and will continue to result in, significant costs to us as we evaluate the implications of these rules and respond to their requirements. In the future, if we are not able to issue an evaluation of our internal control over financial reporting, as required, or we or our independent registered public accounting firm determine that our internal control over financial reporting is not effective, this shortcoming could have an adverse effect on our business and financial results and the price of our common stock could be negatively affected. New rules could make it more difficult or more costly for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the coverage that is the same or similar to our current coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors and board committees, and as our executive officers. We cannot predict or estimate the total amount of the costs we may incur or the timing of such costs to comply with these rules and regulations. Adverse securities and credit market conditions may significantly affect our ability to raise capital. Historically, turmoil and volatility in the financial markets (including recent volatility as a result of geopolitical and macroeconomic developments such as the ongoing military conflict between Ukraine and Russia and related sanctions, and the ongoing conflict in Israel and the surrounding areas, as well as any related political or economic responses and counter- responses or otherwise by various global actors or the general effect on the global economy and supply chain) have adversely affected the market capitalizations of many biotechnology companies, and generally made equity and debt financing more difficult to obtain. These events, coupled with other factors, may limit our access to financing in the future. This could have a material adverse effect on our ability to access funding on acceptable terms, or at all, and our stock price may suffer further as a result.~~