Risk Factors Comparison 2024-02-20 to 2023-02-23 Form: 10-K

Legend: **New Text** ~~Removed Text~~ Unchanged Text Moved Text Section

Our business, as well as an investment in our common stock, is highly speculative in nature and involves a high degree of risk. Our securities should be purchased only by persons who can afford to lose their entire investment. Carefully consider the risks and uncertainties described below together with all of the other information included herein, including the financial statements and related notes, before deciding to invest in our common stock. If any of the following risks actually occur, they could adversely affect our business, prospects, financial condition and results of operations. In such event (s), the market price of our common stock could decline and result in a loss of part or all of your investment. Accordingly, prospective investors should carefully consider, along with other matters referred to herein, the following risk factors in evaluating our business before purchasing any shares of our common stock. Risks Related to the Commercialization of Our Products Our future prospects are highly dependent upon our ability to successfully develop and execute commercialization strategies for our products, including FILSPARI, and to attain market acceptance among physicians, patients and healthcare payers. Our ability to generate significant product revenues and to achieve commercial success in the near- term will depend almost entirely on our ability to successfully commercialize our products in the United States, including FILSPARI (sparsentan) to reduce proteinuria in adults with primary IgAN at risk of rapid disease progression, which was approved by the FDA in February 2023 under the FDA' s accelerated approval regulations. As a newly- approved product for a rare disease that had no previously- approved non-immunosuppressive treatment, the successful launch and commercialization of FILSPARI is subject to many risks. There are numerous examples of unsuccessful product launches and failures to meet high expectations of market potential, including by pharmaceutical companies with more experience and resources than we have. While we have established our commercial team and U. S. sales force, we will need to continue to train and further develop the team in order to successfully coordinate the **ongoing** launch and commercialization of FILSPARI in the United States. There are many factors that could cause the launch and commercialization of FILSPARI to be unsuccessful, including a number of factors that are outside our control. Because no non- immunosuppressive product has previously been approved by the FDA for the treatment of IgAN, it is difficult to estimate FILSPARI' s market potential or the time it will take to increase patient and physician awareness of FILSPARI and change current treatment paradigms **. In September 2023, we announced topline two- year confirmatory secondary endpoint results from the PROTECT Study. While FILSPARI demonstrated long- term kidney function preservation and achieved a clinically meaningful difference in estimated glomerular filtration rate (eGFR) total and chronic slope versus irbesartan as well as statistical significance in eGFR chronic slope for purposes of regulatory review in the EU., the PROTECT Study narrowly missed statistical significance in eGFR total slope, which was the pre- specified confirmatory endpoint in the U. S. In December 2023, we announced the completion of a successful pre- NDA meeting with the FDA for FILSPARI in IgAN. We plan to submit a supplemental New Drug Application (sNDA) in the first quarter of 2024 for conversion of the existing U. S. accelerated approval of FILSPARI to full approval. However, there is no guarantee that the FDA will accept our sNDA submission for filing, that the FDA' s accelerated approval of FILSPARI will continue, or that FILSPARI will receive full approval for IgAN. Further, if the FDA grants full approval of FILSPARI for IgAN, there is no guarantee that the FDA will approve an expanded label** . The commercial success of FILSPARI depends on the extent to which patients and physicians accept and adopt FILSPARI for IgAN patients. For example, if the addressable patient population suffering from primary IgAN is smaller than we estimate, if it proves difficult to educate physicians as to the availability and potential benefits of FILSPARI, or if physicians are unwilling to prescribe or patients are unwilling to take FILSPARI, the commercial potential of FILSPARI will be limited. We also do not know how physicians, patients and payers will respond to the pricing of FILSPARI **, the confirmatory endpoint data from the Phase 3 PROTECT Study, the results of our ongoing interactions with regulators, and any future publications** . Physicians may not prescribe FILSPARI and patients may be unwilling to use FILSPARI if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. Thus, significant uncertainty remains regarding the commercial potential of FILSPARI. If the launch or commercialization of FILSPARI is unsuccessful or perceived as disappointing, the price of our common stock could decline significantly and long- term success of the product and our company could be harmed. In order to operate our business and increase adoption and sales of our products, we need to continue to develop our commercial organization, including maintaining ~~and growing~~ a highly experienced and skilled workforce with qualified sales representatives. In order to successfully commercialize our products in the United States, we have built a specialized sales force. In order to successfully commercialize any approved products, we must continue to build our sales, marketing, distribution, managerial and other non- technical capabilities. Factors that may hinder our ability to successfully market and commercially distribute our products include: • inability of sales personnel to obtain access to or educate adequate numbers of physicians on the benefits and safety of prescribing our products; • inability to recruit, retain and effectively manage adequate numbers of effective sales personnel; • lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies that have more extensive product lines; and • unforeseen delays, costs and expenses associated with maintaining our sales organization. If we are unable to maintain an effective sales force for our products, including the recently expanded sales force for FILSPARI or any other potential future approved products, we may not be able to generate sufficient product revenue in the United States. In addition, **until the commencement of our commercial launch in February 2023,** no one in our sales force ~~has~~ **had** promoted FILSPARI or any other medicine for the treatment of IgAN patients. We are required to expend significant time and resources to train our sales force to be credible ~~and persuasive~~ in ~~convincing~~ **educating** physicians ~~to~~

~~prescribe~~ and pharmacists ~~to dispense~~ **on the benefits of** our products. In addition, we must continually train our sales force to ensure that a consistent and appropriate message about our products is being delivered to our potential customers. We currently have limited resources compared to some of our competitors, and the continued development of our own commercial organization to market our products and any additional products we may develop or acquire will be expensive and time-consuming. We also cannot be certain that we will be able to continue to successfully develop this capability. ~~Similarly, if CSL~~ **We have granted exclusive licenses to third parties** ~~Vifor -- for does~~ **the commercialization of sparsentan in certain territories outside of the United States, including Europe, Australia, New Zealand, Japan, South Korea, Taiwan and the ASEAN member states. If these third parties do** not effectively engage or maintain ~~its~~ **their** sales force for sparsentan if approved in the ~~Licensed~~ **applicable** ~~Territories~~ **territories**, our ability to recognize milestone payments and royalties from the ~~Licensed~~ **sales in such** ~~Territories~~ **territories** will be adversely affected. We will need to continue to expend significant time and resources to train our sales forces to be credible ~~and persuasive~~ in discussing our products with the specialists treating the patients indicated under the product' s label. In addition, if we are unable to effectively train our sales force and equip them with effective marketing materials our ability to successfully commercialize our products could be diminished, which would have a material adverse effect on our business, results of operations and financial condition. We are dependent on ~~CSL Vifor~~ **third parties** for the successful commercialization of sparsentan in certain key territories outside of the United States, if approved, and ~~CSL Vifor~~ **such third parties**' ~~s~~ commercialization efforts may fail to meet our expectations. We may not be able to establish additional collaborations or other arrangements for sparsentan in other territories, which may adversely impact our ability to generate product revenue in additional jurisdictions. **We have** ~~Pursuant to the terms of the License Agreement, we~~ granted ~~an~~ exclusive ~~license~~ **licenses** to ~~CSL Vifor~~ **third parties** for the commercialization of sparsentan in **certain** ~~the Licensed Territories~~ **territories outside**, ~~which consist~~ of **the United States, including** Europe, Australia ~~and~~, New Zealand **, Japan, South Korea, Taiwan and the ASEAN member states**. Consequently, the commercial success of sparsentan in ~~the~~ **these** ~~Licensed Territories~~ **territories** will depend in significant part on the efforts of ~~CSL Vifor~~ **such third parties**, over which we will have limited control. In August 2022, Vifor Pharma Group was acquired by CSL Limited, parent company to CSL Behring and is now operating under the brand CSL Vifor. We do not currently know what effect, if any, this acquisition will ultimately have on our relationship with CSL Vifor. While our agreement with CSL Vifor remains in place following the acquisition, there is no guarantee that our collaboration with CSL Vifor will not be affected, adversely or otherwise, by the change in ownership. Moreover, in connection with the acquisition of CSL Vifor and related restructuring, substantially less resources could be devoted to the commercialization of sparsentan in the ~~Licensed Territories~~ **territories licensed to CSL Vifor**, or such efforts could be discontinued entirely. If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell sparsentan in territories outside of the United States, if approved, our ability to generate product revenue outside of the United States ~~and the Licensed Territories~~ may be limited. The commercial success of our products depends on them being considered to be effective drugs with advantages over other therapies. The commercial success of our products FILSPARI ~~,~~ **and** Thiola ~~, Chenodal and Cholbam~~, and, if approved, sparsentan for the treatment of FSGS, depends on them being considered to be effective drugs with advantages over other therapies. A number of factors, as discussed in greater detail below, may adversely impact the degree of acceptance of these products, including their efficacy, safety, price and benefits over competing therapies, as well as the coverage and reimbursement policies of third- party payers, such as government and private insurance plans. If unexpected adverse events are reported in connection with the use of any of these products, physician and patient acceptance of the product could deteriorate and the commercial success of such product could be adversely affected. We are required to report to the FDA events associated with our products relating to death or injury. Adverse events could result in additional regulatory controls, such as a requirement for costly post- approval clinical studies or revisions to our approved labeling which could limit the indications or patient population for a product or could even lead to the withdrawal of a product from the market. We face substantial generic and other competition, and our operating results will suffer if we fail to compete effectively. Under the Hatch- Waxman Amendments of the Federal Food, Drug, and Cosmetic Act, a pharmaceutical manufacturer may file an ANDA seeking approval of a generic copy of an approved innovator product or an NDA under Section 505 (b) (2) that relies on the FDA' s prior findings of safety and effectiveness in approving the innovator product. A Section 505 (b) (2) NDA may be for a new or improved version of the original innovator product. ~~Certain of our~~ **Our product Thiola, and** products ~~,~~ **from which we may receive milestone payments** including ~~Thiola, Cholbam and~~ Chenodal ~~and Cholbam~~, are subject to immediate competition from compounded and generic entrants, as the ANDA and **/ or** NDA for these drug products have no remaining or current patent or non- patent exclusivity. In April 2021, a generic option for the 100 mg version of the original formulation of Thiola (tiopronin tablets) was approved by the FDA and an additional generic option of the original formulation of Thiola (tiopronin tablets) was approved in June 2022 **and** ~~. Additional generic versions of Thiola may be approved in the future. During~~ **during** the year ended December 31, 2022, we experienced a decrease in total net product revenues compared to the year ended December 31, 2021, which was due in part to competition from generic tiopronin tablets (100 mg version of the original formulation). **Additional generic versions of Thiola may be approved in the future. In February 2023, August 2023 and January 2024, generic versions of Thiola EC (100 mg and 300 mg) were approved by the FDA.** Our future net product revenues from Thiola **and / or Thiola EC** may be materially impacted by competition from existing or additional generic versions of Thiola ~~. In addition, our -~~ **or** ~~future net product revenues from Thiola EC may also be materially impacted by competition from existing or additional generic versions of Thiola, as well as any generic versions of~~ Thiola EC. In addition, there have been a number of recent regulatory and legislative initiatives designed to encourage generic competition for pharmaceutical products, including expedited review procedures for generic manufacturers and incentives designed to spur generic competition of branded drugs. In particular, the FDA and the U. S. Federal Trade Commission (" FTC ") have been focused on brand companies' denial of drug supply to potential generic competitors for testing. In December 2019, the CREATES Act was enacted, which provides a legislatively defined private right of action under which generic companies

can bring suit against companies who refuse access to product for the bioequivalence testing needed to support approval of a generic product. We have completed our response to a civil investigative demand from the FTC related to the marketing, sale, distribution and pricing of our products, including Thiola. While the investigation remains open, at this time the FTC has not indicated that it has additional questions for us ~~,~~ and has not initiated any claim or proceeding against us relating to these matters. We cannot currently predict the specific outcome or impact on our business of such regulatory and legislative initiatives, litigation or investigation. However, it is our policy, which is in compliance with the CREATES Act, to evaluate requests for samples of our branded products, and to provide samples in response to bona fide requests from qualified third parties, including generic manufacturers, subject to specified conditions. We have provided ~~and are in the process of providing~~ samples to certain generic manufacturers. If additional generic versions of Thiola **or Thiola EC** , any generic versions of ~~Thiola EC~~ **FILSPARI following the expiration of patent or regulatory exclusivity for the product** , ~~any~~ **or** generic versions of ~~FILSPARI following the expiration of patent or regulatory exclusivity for the product, or generic versions of Cholbam or Chenodal or~~ any ~~of our~~ other current or future products are approved, sales of that product likely would be negatively impacted, which could have a material adverse impact on our ~~sales~~ **revenue** and profitability **. If generic versions of Cholbam or Chenodal are approved, our potential to receive milestone payments from the sale of our bile acid product portfolio may be negatively impacted** . In addition, the defense of litigation and response to investigation requests could result in substantial costs, reputational impact, and the diversion of management attention and resources. The Drug Price Competition and Patent Term Restoration Act (commonly referred to as the" Hatch- Waxman Act") requires an ANDA applicant seeking FDA approval of its proposed generic product prior to the expiration of an Orange Book- listed patent (as defined below) to certify that the applicant believes that the patent is invalid, unenforceable and / or will not be infringed by the manufacture, use or sale of the drug for which the application has been submitted (a paragraph IV certification) and notify the NDA and patent holder of such certification (a paragraph IV notice). Upon receipt of a paragraph IV notice, the Hatch- Waxman Act allows the patent holder, with proper basis, to bring an action for patent infringement against the ANDA filer, asking that the proposed generic product not be approved until after the patent expires. For ANDAs that are filed (“ received ”) after the listing of the patent in the Orange Book, if the patent holder commences a lawsuit within 45 days from receipt of the paragraph IV notice, the Hatch- Waxman Act provides a 30- month stay during which time the FDA cannot finally approve the generic’ s application. If the litigation is resolved in favor of the ANDA applicant during the 30- month stay period, the stay is lifted and the FDA may finally approve the ANDA if it is otherwise ready for approval. For ANDAs that are filed (“ received ”) before the listing of the patent in the Orange Book, the 30- month stay provision of the Hatch- Waxman Act does not apply. It also may be possible, depending on the approved label, for an ANDA applicant to elect to submit a section viii statement certifying that its proposed ANDA label does not contain (or carves out) any language regarding the patented method- of- use rather than certify to a listed method- of- use patent. In October 2022, our licensor, Mission Pharmacal Company, was granted a patent covering the treatment of cystinuria by administering Thiola EC with food (US Patent No. 11, 458, 104, “ the ‘ 104 patent ”) and ~~has~~ listed this patent in the FDA’ s Approved Drug Products with Therapeutic Equivalence Evaluations (the **"** Orange Book **"**). Following Mission’ s listing of the' 104 patent in the Orange Book, and as of December 31, ~~2022~~ **2023** , Mission has received three paragraph IV notice letters from three generic manufacturers notifying Mission that each has filed an ANDA seeking approval of a proposed generic version of Thiola EC (tiopronin) 100 mg and 300 mg oral tablets before expiration of the' 104 patent and asserting that the' 104 patent is not infringed and / or is invalid, with each such ANDA having been filed prior to the granting and listing of the ‘ 104 patent. **The ANDAs filed by Par Pharmaceutical Inc. (Par) and Amneal EU, Limited (Amneal) for generic versions of Thiola EC (100 mg and 300 mg) were approved by the FDA in February and August 2023, respectively.** Under our agreement with Mission, we have the right to enforce the' 104 patent. We ~~are evaluating these paragraph IV notices,~~ and **Mission have entered into agreements with each of Par and Amneal** ~~will evaluate any other paragraph IV notices received, on a case by case basis~~ in order to **settle** ~~determine whether to initiate~~ patent **invalidity and infringement disputes related to** ~~litigation against any such generic manufacturer. Through Mission, we have received notice that at least one of these~~ -- **the'** ~~generic manufacturers may challenge the ‘~~ 104 patent ~~through~~ **and providing for a license entry date of April 1, 2026 for** ~~the~~ **their generic versions of Thiola EC (100mg** ~~Patent Appeals Board procedures at the United States Patent~~ and ~~Trademark Office~~ **300mg), or earlier under certain circumstances** . There is no guarantee that the ‘ 104 patent will withstand any challenge at the Patent and Trademark Office or in litigation, if initiated. Patent litigation is expensive and time consuming, requires significant resources, may absorb significant time of our management and has an unpredictable outcome. If ~~these or any other ANDAs were to be approved and either~~ we determine not to pursue patent litigation or the patent is not upheld in litigation or administrative review or if a generic competitor ~~were~~ **is** found not to infringe this patent, the resulting generic competition ~~would~~ **will** likely negatively affect our business, financial condition and results of operations **. Following the FDA’ s approval in January 2024 of an ANDA for a generic version of Thiola EC (100 mg and 300 mg), Thiola EC is subject to immediate generic competition** . Healthcare reform initiatives, unfavorable pricing regulations, and changes in reimbursement practices of third- party payers or patients' access to insurance coverage could affect the pricing of and demand for our products. The business and financial condition of healthcare- related businesses will continue to be affected by efforts of governments and third- party payers to contain or reduce the cost of healthcare through various means. In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval for **our current product candidates** ~~sparsentan for the treatment of FSGS, pegtibatinase (TVT- 058),~~ or any ~~other~~ **future** product candidate that we develop, restrict or regulate post- approval activities and affect our ability to profitably sell sparsentan, pegtibatinase ~~(TVT- 058)~~ , or any other product candidate for which we obtain marketing approval. Our products are sold to patients whose healthcare costs are met by third- party payers, such as government programs, private insurance plans and managed- care programs. These third- party payers are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement for medical products and

services. Levels of reimbursement, if any, may be decreased in the future, and future healthcare reform legislation, regulations or changes to reimbursement policies of third- party payers may otherwise adversely affect the demand for and price levels of our products, which could have a material adverse effect on our sales and profitability. Economic, social, and congressional pressure may result in individuals and government entities increasingly seeking to achieve cost savings through mechanisms that limit coverage or payment for our products. For example, state Medicaid programs are increasingly requesting manufacturers to pay supplemental rebates and **are** requiring prior authorization for use of drugs. Managed care organizations continue to seek price discounts and, in some cases, to impose restrictions on the coverage of particular drugs. Government efforts to reduce Medicaid expenses may lead to increased use of managed care organizations by Medicaid programs. This may result in managed care organizations influencing prescription decisions for a larger segment of the population and a corresponding constraint on prices and reimbursement for our products. In addition, patients' access to employer sponsored insurance coverage may be negatively impacted by economic factors that result in increased rates of unemployment. To the extent patients taking our approved therapies become unemployed and experience a reduction to, or increased costs associated with, their insurance coverage, demand for our products could decline, which could have a material adverse effect on our sales and profitability, either as a result of decreased sales of our products and / or increased provision by us of free product to uninsured or commercially insured patients. The extent and duration of this potential impact on our business is currently unknown. We are dependent on third parties to manufacture and distribute our products. We have no manufacturing capabilities and rely on third-party manufacturers who are sole source suppliers for manufacturing of FILSPARI ~~,~~ **and** Thiola ~~, Chenodal and Cholbam~~ . The facilities used by our third- party manufacturers must be approved by the FDA **and comparable foreign regulatory authorities** . Our dependence on third parties for the manufacture of our products may harm our profit margin on the sale of products and our ability to deliver products on a timely and competitive basis. Because we are ultimately responsible for ensuring that our API and finished products are manufactured in accordance with cGMP regulations and similar regulatory requirements outside the United States, it is critical that we maintain effective management practices and oversight with respect to our third- party manufacturers, including routine auditing. If our third- party manufacturers are unable to manufacture to specifications or in compliance with applicable regulatory requirements, our ability to commercialize our products will be adversely impacted and could affect our ability to gain market acceptance for our products and negatively impact our revenues. We currently have no in- house distribution channels for FILSPARI ~~,~~ **or** Thiola ~~, Chenodal or Cholbam~~ and we are dependent on third- party distributors to distribute such products. The outsourcing of our distribution function is complex, and we may experience difficulties that could reduce, delay or stop shipments of such products. If we encounter such distribution problems, and we are unable to quickly enter into a similar agreement with another distributor on substantially similar terms, distribution of FILSPARI ~~,~~ **and / or** Thiola ~~, Chenodal and / or Cholbam~~ could become disrupted, resulting in lost revenues, provider dissatisfaction, and / or patient dissatisfaction. Governments outside the United States tend to impose strict price controls and reimbursement approval policies, which may adversely affect our prospects for generating revenue. **Outside the United States, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.** In some countries, particularly EU **Member States and EFTA** countries ~~and EFTA member states~~ , the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time (6 to 12 months or longer) after the receipt of marketing approval for a product. ~~To~~ **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, to** obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of our product candidate to other available therapies **. This Health Technology Assessment (" 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 amending Directive 2011 / 24 / EU, was adopted in the EU. This Regulation, which entered into force in January 2022 and will apply as of January 2025, 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. The Regulation foresees a three- year transitional period and will permit 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 will continue to be responsible for assessing non- clinical (e. g., economic, social, ethical) aspects of health technologies, and making decisions on pricing and reimbursement. If we or our partners are unable to maintain favorable pricing and reimbursement status in EU Member States for product candidates that we or our partners may successfully develop and for which we or our partners may obtain regulatory approval, any anticipated revenue from and growth prospects for those products in the**

EU could be negatively affected . In addition, certain governmental authorities may conduct reviews of reimbursement previously provided and assert for various reasons that amounts need to be repaid. For example, in October 2021 our distributor / exploitant in France for our previously marketed product Kolbam **(which has since been divested)** informed us that they had received a notice that the price previously paid for Kolbam during its period on the market in France had been recalculated by the agency responsible for pharmaceutical pricing in France, with such notice asserting amounts owed for repayment. **Based on the ongoing review process, we expect that we will need to repay the amounts being asserted prior to pursuing a formal appeal, which we currently estimate to be approximately $ 5 million.** While we cannot **predict** ~~currently estimate~~ the ~~likelihood~~ **amount** that **we may** ~~any of such asserted amount will~~ ultimately need to ~~be repaid~~ **repay,** following ~~the currently~~ ongoing review ~~process~~ and ~~any applicable~~ **future potential** appeal ~~procedures~~ **proceedings** , ~~we may ultimately determine the need to repay all or a portion of the amounts being asserted. From~~ **from** 2015 through 2020, the period during which we had sales of Kolbam in France, our aggregate revenues from sales of Kolbam in France attributable to all purchasers / payers were approximately $ 8 million. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels or subject to re- assessment and recoupment procedures, our prospects for generating revenue outside of the United States, if any, could be adversely affected and our business may suffer. We may not be able to rely on orphan drug exclusivity for our products. Regulatory authorities in some jurisdictions, including the United States and ~~Europe~~ **the EU** , may designate drugs for relatively small patient populations as orphan drugs, providing eligibility for orphan drug exclusivity upon regulatory approval if certain jurisdictional- specific conditions are met. For example, FILSPARI has been granted orphan drug designation for the treatment of IgAN and **has been** ~~in light of its regulatory approval we expect that it will be~~ awarded seven years of orphan drug exclusivity **in the United States** to reduce proteinuria in adults with primary IgAN at risk of rapid disease progression, **generally a urinary protein- to- creatinine ratio (" UPCR") ≥ 1. 5 gram / gram** ~~and Cholbam was granted orphan drug designation in the United States and upon FDA approval of the marketing application in March 2015 was awarded seven years of orphan drug exclusivity, which expired in March 2022~~ . Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, that product is entitled to a period of marketing exclusivity, which precludes the applicable regulatory authority from approving another marketing application for the same drug for the same indication for that time period. The applicable period is seven years in the United States and ten years in ~~Europe~~ **the EU** or, in the case of orphan drugs for which a pediatric investigation plan has been completed, 12 years. Even though we have been awarded orphan drug designation in the United States and ~~Europe~~ **the EU** for sparsentan for the treatment of IgAN and FSGS and for pegtibatinase for the treatment of HCU, we may not be able to maintain it in ~~Europe~~ **the EU** and the orphan drug designation may not result in orphan drug exclusivity in the United States ~~or~~ **for** ~~Europe upon~~ **FSGS or the EU if** ~~approval~~ **approved** . For example, if a competitive product that contains the same active moiety and treats the same disease as our product is shown to be clinically superior to our product, any orphan drug exclusivity we have obtained will not block the approval of such competitive product and we may effectively lose orphan drug exclusivity. Similarly, if a competitive product that contains the same active moiety and treats the same disease as our product candidate is approved for orphan drug exclusivity before our product candidate, we may not be able to obtain approval for our product candidate until the expiration of the competitive product' s orphan drug exclusivity unless our product candidate is shown to be clinically superior to the competitive product. Risks Related to the Development of our Product Candidates Our clinical trials are expensive and time- consuming and may fail to demonstrate the safety and efficacy of our product candidates. Before obtaining regulatory approval for the sale of any of our current or future product candidates, ~~including sparsentan for the treatment of FSGS and pegtibatinase (TVT- 058),~~ we must subject these product candidates to extensive nonclinical and clinical testing to demonstrate their safety and efficacy for humans. Clinical trials are expensive, time- consuming and may take years to complete. We may experience numerous unforeseen events during, or as a result of, preclinical or nonclinical testing and the clinical trial process that could delay or prevent our ability to obtain, or impact our willingness to pursue, regulatory approval or commercialize our product candidates, including: • our preclinical or nonclinical tests or clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional nonclinical testing or clinical trials or we may abandon projects that we expect to be clinically promising in light of cost or strategic considerations; • regulators may require us to conduct studies of the long- term effects associated with the use of our product candidates; • regulators ~~or~~ **,** institutional review boards **or ethics committees** may not authorize us to commence a clinical trial or conduct a clinical trial at a prospective trial site; • the FDA or any non- United States regulatory authority may impose conditions on us regarding the scope or design of our clinical trials or may require us to resubmit our clinical trial protocols to institutional review boards **or ethics committees** for re- inspection due to changes in the regulatory environment; • the number of patients required for our clinical trials may be larger than we anticipate or participants may drop out of our clinical trials at a higher rate than we anticipate; • our third- party contractors or clinical investigators may fail to comply with regulatory requirements or fail to meet their contractual obligations to us in a timely manner; • we might have to suspend **, vary** or terminate one or more of our clinical trials if we, regulators or institutional review boards **or ethics committees** determine that the participants are being exposed to unacceptable health risks; • regulators ~~or~~ **,** institutional review boards **or ethics committees** may require that we hold, suspend **, vary** or terminate clinical research for various reasons, including noncompliance with regulatory requirements; • the cost of our clinical trials or the anticipated commercialization costs may be greater than we anticipate; • the supply or quality of our product candidates or other materials necessary to conduct our clinical trials may be insufficient or inadequate, or more expensive than we originally anticipated, or we may not be able to reach agreements on acceptable terms with prospective suppliers or clinical research organizations; and • the effects of our product candidates may not be the desired effects or may include undesirable side effects or the product candidates may have other unexpected characteristics. We will only obtain regulatory approval to commercialize a product candidate if we can demonstrate to the satisfaction of the FDA, and in the case of foreign commercialization, to the applicable foreign regulatory authorities, in well- designed and conducted clinical trials, that our

product candidates are safe and effective and otherwise meet the appropriate standards required for approval for a particular indication. Conducting clinical trials effectively in pursuit of regulatory approval requires significant resources, and the costs of conducting clinical trials varies depending on a number of factors, including the dosage of the study ~~drug~~ **therapy** , trial size and duration. These costs may prove greater than we originally anticipated, which may result in us choosing to abandon or forgo clinical trials that we deem clinically promising as we actively strategize over time with respect to the allocation of our resources. Our product development costs will also increase if we experience delays in testing or approvals. We do not know whether any nonclinical tests or clinical trials will be initiated as planned, will need to be restructured or will be completed on schedule, if at all. Significant nonclinical or clinical trial delays also could shorten the patent protection period during which we may have the exclusive right to commercialize our product candidates. In addition, such delays could allow our competitors to bring products to market before we do and impair our ability to commercialize our products or product candidates. If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete our clinical trials or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may: • be delayed in obtaining, or may not be able to obtain, marketing approval for one or more of our product candidates; • obtain approval for indications that are not as broad as intended or entirely different than those indications for which we sought approval; and • have the product removed from the market after obtaining marketing approval. **For example** ~~In February 2021~~ , **in** ~~we announced that~~ our ~~ongoing~~ pivotal Phase 3 DUPLEX Study of sparsentan in FSGS **, although we** achieved ~~its~~ **the** pre- specified interim FSGS partial remission of proteinuria endpoint ~~(" FPRE ")~~ after 36 weeks of treatment ~~and in August 2021~~ , **the study did not achieve the primary efficacy eGFR slope endpoint over 108 weeks of treatment. While** we ~~announced~~ **intend to continue to engage with the FDA to explore a potential path forward for a supplemental New Drug Application (sNDA) in the U. S. and work with our collaborator CSL Vifor to engage with the European Medicines Agency (" EMA") to also explore a potential regulatory path forward in FSGS in the EU based on the DUPLEX data, there is no guarantee** that **we will be able to establish a pathway to a potential submission of sparsentan for FSGS based on the results from the DUPLEX Study, that the FDA and /** ~~our~~ **or** ~~ongoing~~ **EMA will support an application for sparsentan in FSGS, or that sparsentan will be approved for FSGS. Also, in our** pivotal Phase 3 PROTECT Study of sparsentan in IgAN **, although we** achieved ~~its~~ **the** pre-specified primary efficacy **proteinuria** endpoint after 36 weeks of treatment **,** ~~. Pursuant to the DUPLEX~~ and ~~PROTECT~~ **after 110 weeks of treatment, FILSPARI demonstrated long- term kidney function preservation and achieved a clinically meaningful difference in estimated glomerular filtration rate (eGFR) total and chronic slope versus irbesartan, the** ~~Study~~ **study** ~~protocols~~ **narrowly missed statistical significance in eGFR total slope while achieving statistical significance in eGFR chronic slope for purposes of regulatory review in the EU. In December 2023** , ~~patients are~~ **we announced the completion of a successful pre- NDA meeting with the FDA for FILSPARI in IgAN. We plan** to **submit a supplemental New Drug Application (sNDA) in the first quarter of 2024 for conversion of the existing U. S. accelerated approval of FILSPARI to full approval. However, there is no guarantee that the FDA will accept our sNDA submission for filing, that the FDA' s accelerated approval of FILSPARI will** continue **, or** ~~in a blinded manner to assess the treatment effect on eGFR slope over two years in the confirmatory endpoint analyses of the studies. Given~~ that ~~interim results from~~ **FILSPARI will receive full approval for IgAN. Furthermore, if the FDA grants full approval for FILSPARI for IgAN,** ~~the~~ **there** ~~studies have been publicly announced, it~~ is ~~possible~~ **no guarantee** that ~~we may see a higher than anticipated attrition rate in one or both of these~~ -- **the FDA will approve** ~~studies. To the extent that~~ an **expanded label** ~~insufficient number of patients choose to remain in either study for the full two years, it could jeopardize our ability to complete the studies and submit for traditional regulatory approval for sparsentan in FSGS and / or IgAN~~ . We may not be able to initiate or continue clinical trials in the rare diseases on which we are focused if we are unable to locate a sufficient number of eligible patients willing and able to participate in the clinical trials required by the FDA or foreign regulatory ~~agencies~~ **authorities** . In addition, as other companies and researchers may be concurrently developing therapies for the same or similar indications that we are focused on, we could face competition for a limited number of patients, investigators and clinical trial sites willing to participate in clinical trials. Our inability to enroll and maintain a sufficient number of patients for any of our current or future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether ~~. In January 2020, we randomized the first patients in a Phase 3 clinical trial to evaluate the effects of Chenodal in adult and pediatric patients with CTX. The pivotal study, known as the RESTORE study, is intended to support an NDA submission for marketing authorization of Chenodal for CTX in the United States. While Chenodal has been used as the standard of care for CTX for over three decades, it is not labeled for CTX and as such we cannot market this drug candidate for the treatment of CTX unless and until it receives FDA approval for this indication. If we experience delays in obtaining approval or if we fail to obtain approval of Chenodal for the treatment of CTX, our business, financial condition and results of operations could be adversely affected~~ . Success in nonclinical testing and early clinical trials does not ensure that later clinical trials will be successful. Success in nonclinical testing and early clinical trials does not ensure that later clinical trials will be successful. For example, ~~although~~ **while** we ~~observed favorable responses with~~ **saw trends in favor of sparsentan in** the ~~physician~~ **two** ~~- initiated treatment of fosmetpantotenate~~ **year confirmatory endpoint analysis** in ~~PKAN patients outside~~ the **DUPLEX** ~~United States, the Phase 3 FORT~~ Study ~~evaluating the safety and efficacy of fosmetpantotenate compared to placebo~~ in **FSGS** ~~patients with PKAN did not meet its primary endpoint~~ , ~~did not demonstrate a difference between treatment groups, and did not meet its secondary endpoint. In addition, there can be no assurance that~~ the positive eGFR results from the open- label portion of the DUET study of sparsentan in FSGS ~~will be~~ **were not** ~~repeated~~ **replicated** in the Phase 3 clinical trial **with statistical significance. Similarly, while the Phase 3 PROTECT Study of FILSPARI in IgAN demonstrated long- term kidney function preservation in IgAN and met the endpoint for eGFR chronic slope for the purposes of regulatory review in the EU, and all topline efficacy endpoints favored FILSPARI as compared to the active control (irbesartan), the study narrowly missed statistical significance with respect to the eGFR**

total slope endpoint . Similarly, the positive nonclinical data we have seen from pegtibatinase ~~(TVT- 058)~~ being tested in a mouse model of homocystinuria and the positive topline results we reported in December 2021 **and May 2023** from the ongoing Phase 1 / 2 clinical trial of pegtibatinase ~~(TVT- 058)~~ may not be replicated in future studies. We cannot assure that any current or future clinical trials of sparsentan or pegtibatinase ~~(TVT- 058)~~ will ultimately be successful. Before obtaining regulatory approval to conduct clinical trials of our product candidates, we must conduct extensive nonclinical tests to demonstrate the safety of our product candidates in animals. Nonclinical testing is expensive, difficult to design and implement, and can take many years to complete. In addition, during the clinical development process, additional nonclinical toxicology studies are routinely conducted concurrently with the clinical development of a product candidate. If any of our product candidates show unexpected findings in concurrent toxicology studies, we could experience potentially significant delays in, or be required to abandon, development of that product candidate. A failure of one or more of our nonclinical studies can occur at any stage of testing. Communications and / or feedback from regulatory authorities related to our current or planned future clinical trials does not guarantee any particular outcome from or timeline for regulatory review, and expedited regulatory review pathways may not actually lead to faster development or approval. Communications and / or feedback from regulatory authorities, including the FDA or EMA, related to our current or future clinical trials does not guarantee any particular outcome from or timeline for regulatory review for such clinical trials, and expedited regulatory review pathways may not actually lead to faster development or approval. In 2018 we initiated the ~~following~~ Phase 3 **DUPLEX Study and the** ~~clinical trials of sparsentan: 1) a single~~ Phase 3 ~~clinical trial designed to serve as the basis for an NDA and MAA filing for sparsentan for the treatment of FSGS (the " DUPLEX Study "), and 2) a single Phase 3 clinical trial designed to serve as the basis for an NDA and MAA filing for sparsentan for the treatment of IgAN (the "~~ PROTECT Study ~~")~~ . We initiated the DUPLEX Study and the PROTECT Study under the Subpart H pathway for potential accelerated approval in the United States, and potential conditional marketing authorization in ~~Europe~~ **the EU** , in both jurisdictions based on change in proteinuria. Recognition of change in proteinuria as a surrogate endpoint in kidney disease is a relatively new regulatory development, and, as the field continues to evolve, new learnings may impact regulatory viewpoints. In February 2023, the FDA granted accelerated approval to FILSPARI (sparsentan) to reduce proteinuria in adults with primary IgAN at risk of rapid disease progression, generally a UPCR ≥ 1. 5 gram / gram. **In September 2023** ~~As a postmarketing requirement~~ , we ~~must complete~~ **announced topline two- year confirmatory secondary endpoint results from** the PROTECT Study ~~and fulfill other post~~ **. While FILSPARI demonstrated long** ~~marketing requirements. The EMA~~ **term kidney function preservation and achieved a clinically meaningful difference in estimated glomerular filtration rate (eGFR) total and chronic slope versus irbesartan** ~~has~~ **as** ~~accepted~~ **well as statistical significance in eGFR chronic slope** for **purposes of regulatory** review **in the EU, the PROTECT Study narrowly missed statistical significance in eGFR total slope, which was the pre- specified confirmatory endpoint in the U. S. In December 2023, we announced the completion of a successful pre- NDA meeting with the FDA for FILSPARI in IgAN. We plan to submit a supplemental New Drug Application (sNDA) in the first quarter of 2024 for conversion of the existing U. S. accelerated approval of FILSPARI to full approval. However,** ~~the~~ **there is no guarantee that the FDA will accept our sNDA submission for filing, that the FDA' s accelerated approval of FILSPARI will continue, or that FILSPARI will receive full approval for IgAN. In January 2024, we announced that, following submission of the two- year results from the PROTECT Study of FILSPARI in IgAN and a corresponding procedural review clock- stop, we and our collaborator CSL Vifor anticipate an opinion by the Committee for Medicinal Products for Human Use (CHMP) on our** conditional marketing authorization **(CMA)** application ~~of~~ **for** sparsentan for the treatment of IgAN in ~~Europe, and a review decision is expected in~~ the **EU** ~~second half of 2023. In August 2022, following engagements with the FDA around the potential to file an NDA under Subpart H for accelerated approval of sparsentan for the treatment of FSGS, and feedback from the FDA instead indicating support solely for filing for traditional approval pending completion of the DUPLEX Study, we announced our updated plan (i) to pursue traditional approval for FSGS~~ in the **first** ~~United States following receipt of the full two- year eGFR data from the DUPLEX Study, which is expected in the second~~ quarter of ~~2023~~ **2024** ~~and (ii) that we and CSL Vifor are submitting an application for CMA of sparsentan for the treatment of IgAN in Europe, and that pending completion of the DUPLEX Study and data supportive of approval, we and CSL Vifor are targeting to submit by the end of 2023 a subsequent variation of sparsentan for the treatment of FSGS in Europe~~ . There is no guarantee that **sparsentan** ~~the data from the DUPLEX Study will support a regulatory submission or approval in the United States or Europe. We expect that the EMA' s determination as to whether the sufficiency of the data from the PROTECT Study supports a conditional marketing authorization (EMA) in Europe~~ will be **approved** ~~made during the application review process based on the totality of the data, including eGFR data available for review from the relevant studies. There can be no assurance that the EMA will deem our achievement of any interim endpoint or measurement in the PROTECT Study to be sufficient to grant conditional marketing authorization for sparsentan~~ for the treatment of IgAN **in the EU** , or that our timelines will not be delayed notwithstanding the availability of an expedited regulatory review pathway. **In May 2023, we announced that the DUPLEX Study did not achieve its two- year primary endpoint with statistical significance over the active control irbesartan.** Although **we are encouraged by** ~~the EMA has accepted our conditional marketing authorization application for review, there~~ -- **the topline results for** ~~can be no assurance that the study will proceed as planned and there~~ -- **the** ~~can be no guarantee that the EMA will grant conditional marketing authorization in the EU~~ **secondary endpoints on proteinuria and topline exploratory endpoints, including renal outcomes, which trended favorably** for sparsentan ~~for IgAN. Furthermore~~ , **and we are continuing to analyze** ~~even though sparsentan was granted accelerated approval for IgAN, there can be no assurance that~~ the data ~~from~~ **to further evaluate** the **potential for** ~~ongoing PROTECT Study will support traditional approval of~~ sparsentan as a treatment for **FSGS** ~~IgAN. Although the FDA has granted Fast Track~~ and **are engaging with** ~~Breakthrough Therapy designations to pegtibatinase (TVT- 058) for~~ the ~~treatment of HCU~~ **regulators to explore a potential path to a submission for sparsentan in FSGS** , there is no guarantee that we **or our collaborator CSL Vifor** will be able to ~~reach agreement with~~ **establish a pathway**

to a potential submission of sparsentan for FSGS based on the results from the DUPLEX Study, that the FDA **and /** ~~on the final study design for~~ **or EMA will support an application for sparsentan in FSGS** ~~a proposed Phase 3 trial of pegtibatinase (TVT- 058)~~ **, or** that **sparsentan** ~~we will ultimately proceed with the proposed Phase 3 trial, or that pegtibatinase (TVT- 058)~~ will be approved for **FSGS. In December 2023, we initiated the pivotal Phase 3 HARMONY Study to support the potential approval of pegtibatinase for the treatment of classical** HCU ~~in the future~~ **. The HARMONY Study is a global** , ~~on~~ **randomized, multi- center, double- blind, placebo- controlled Phase 3 clinical trial designed to evaluate the efficacy** ~~an~~ **and safety of pegtibatinase as** ~~expedited timeline or at all. We intend to use~~ a **novel treatment to reduce** ~~surrogate endpoint, change in~~ total homocysteine (tHcy) ~~level~~ **levels** ~~,~~ **. Topline results from the HARMONY Study are expected in 2026. Although the FDA** ~~as~~ **has granted Fast Track** ~~a biomarker to demonstrate efficacy in the proposed Phase 3 pivotal trial~~ and **Breakthrough Therapy designations** to **pegtibatinase** ~~support a future marketing application for TVT- 058~~ for the treatment of HCU ~~. While we have commenced discussions with the FDA regarding the use of this biomarker to support a future approval under the traditional or accelerated approval pathway, we will need to have further interactions with the FDA as part of the routine regulatory advancement of the program and will need to confirm with the FDA the use of total homocysteine as the pivotal endpoint for the study, align with the FDA on the details of the study, as well as on other elements of the program such as matters related to chemistry, manufacturing and controls. Prior to initiating the proposed Phase 3 trial, we will need to evaluate the clinical / regulatory pathway and the drug supply and product profile against the backdrop of the commercial landscape and opportunity to confirm strategic alignment within the program. Due to the inherent complexities of drug development~~ , there is no guarantee that **our pivotal** ~~these factors will align in support of the proposed~~ Phase 3 **Harmony** ~~program. Similarly, while we were granted Fast Track designation by the FDA for the investigation of Chenodal for CTX in September 2022, the Phase 3 RESTORE study~~ **Study will be successful** ~~may not ultimately support an NDA submission and the Fast Track designation may not ultimately lead to FDA approval of Chenodal for~~ **or** ~~CTX~~ **that pegtibatinase will be approved for HCU in the future,** on an expedited timeline or at all. Obtaining access to an expedited program (such as Fast Track and Breakthrough Therapy designations) may not in fact lead to faster development timelines or achieve faster review or approval than conventional FDA procedures. We may experience delays in approval timelines attributable to, among other things, acquiring sufficient supply of our product to conduct clinical trials, identifying and resolving issues relating to chemistry, manufacturing and controls, or conducting additional nonclinical or clinical studies. In addition, the FDA may withdraw access to an expedited program if it believes the access or designation is no longer supported by the data from our program. Interim, topline and preliminary data from our clinical trials that we announce or publish may change materially as more patient data become available and audit and verification procedures are complete. From time to time, we may publicly disclose preliminary or topline or interim data from our clinical studies, which is based on a preliminary analysis of then- available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution. From time to time, we may also disclose interim data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment and dosing continues and more patient data become available. Adverse differences between preliminary or interim data and final or confirmatory data could significantly harm our business prospects. Further, others, including regulatory ~~agencies~~ **authorities** , may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular ~~drug~~ **therapy** , ~~drug~~ **therapeutic** candidate or our business. If the topline data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition. We and / or a collaborative partner are or will be subject to ongoing regulatory obligations and continued regulatory review for our approved products and any product candidates that receive regulatory approval. The FDA' s accelerated approval of FILSPARI is limited to adults with primary IgAN who are at risk of rapid disease progression, generally a UPCR ≥ 1. 5 gram / gram **. The continued approval** ~~, and is subject to our completion~~ of **FILSPARI may be contingent upon confirmation of a clinical benefit in** the **Phase 3** PROTECT Study. **In September 2023, we announced data from the Phase 3 PROTECT Study as further described herein, including in the risk factor titled " Our future prospects are highly dependent upon our ability to successfully develop and execute commercialization strategies for our products, including FILSPARI, and to attain market acceptance among physicians, patients and healthcare payers. "** Any future regulatory approvals that sparsentan or any of our other product candidates receives may be subject to significant limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post- marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. In addition, our products, including FILSPARI, and any of our product candidates that are approved by the FDA or a comparable foreign regulatory authority, are or will be subject to extensive and ongoing regulatory requirements, including for the manufacturing,

labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export, recordkeeping, conduct of potential post- marketing studies and post- market submission requirements. These requirements include submissions of safety and other post- marketing information and reports, registration, as well as continued compliance with current good manufacturing practices and good clinical practices, for any clinical trials that we conduct post- approval. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, undesirable side effects caused by the product, problems encountered by our third- party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, either before or after product approval, may result in, among other things: • restrictions on the marketing, manufacturing, or distribution of the product; • requirements to include additional warnings on the label; • requirements to create or enhance a medication guide outlining the risks to patients; • withdrawal of the product from the market; • voluntary or mandatory product recalls; • requirements to change the way the product is administered or for us to conduct additional clinical trials; • fines, warning or untitled letters or holds on clinical trials; • refusal by the FDA **or comparable foreign regulatory authorities** to approve pending applications or supplements to approved applications filed by us or our strategic partners, or suspension **, variation** or revocation of product license approvals; • product seizure or detention, or refusal to permit the import or export of products; • injunctions or the imposition of civil or criminal penalties; and • harm to our reputation. For example, we have certain post- marketing requirements and commitments associated with FILSPARI ~~and Cholbam~~ . Further, we face risks relating to those post- marketing obligations, as well as the commercial acceptance of FILSPARI ~~and Cholbam~~ . If the regulatory approval for FILSPARI ~~,~~ **and / or** Thiola ~~, Chenodal and / or Cholbam~~ are withdrawn for any reason, it would have a material adverse impact on our sales and profitability **. Furthermore, if the regulatory approval for Chenodal and / or Cholbam are withdrawn for any reason, it would reduce the chance that we will receive any or all of the milestone payments from the sale of our bile acid product portfolio in August 2023** . The third- party clinical investigators and contract research organizations that we rely upon to conduct our clinical trials may not be diligent, careful or timely, and may make mistakes, in the conduct of our trials. We depend on third- party clinical investigators and contract research organizations (" CROs ") to conduct our clinical trials under agreements with us. The CROs play a significant role in the conduct of our clinical trials. Failure of the CROs to meet their obligations could adversely affect clinical development of our product candidates. The third- party clinical investigators are not our employees and we cannot control the timing or amount of resources they devote to our studies. If their performance is substandard, it could delay or prevent approval of our FDA applications. Moreover, these third- party investigators and CROs may also have relationships with other commercial entities, some of which may compete with us. If third- party investigators and CROs allocate their resources to assist our competitors at our expense, it could harm our competitive position ~~. In response to COVID- 19, we have engaged providers of home health and remote monitoring services to assist with the ongoing conduct of our clinical trials in an effort to mitigate disruption caused by COVID- 19 related issues~~ . The introduction of new third parties into our ongoing clinical trials increases the risks associated with our dependence on third parties, including the risk that substandard performance by, or competing interests of, such third parties could have a negative impact on our clinical trials. Risks Related to our Products and Product Candidates Our products may not achieve or maintain expected levels of market acceptance or commercial success. The success of our products is dependent upon achieving and maintaining market acceptance. Commercializing products is time consuming, expensive and unpredictable. There can be no assurance that we will be able to, either by ourselves or in collaboration with our partners or through our licensees, successfully commercialize new products or current products or gain market acceptance for such products. New product candidates that appear promising in development may fail to reach the market or may have only limited or no commercial success. Further, the discovery of significant problems with a product similar to one of our products that implicate (or are perceived to implicate) an entire class of products could have an adverse effect on sales of the affected products. Accordingly, new data about our products, or products similar to our products, could negatively impact demand for our products due to real or perceived side effects or uncertainty regarding efficacy and, in some cases, could result in product withdrawal. Our current products, including FILSPARI, and any product candidates that receive marketing approval, that we or a collaboration partner bring to the market may not gain market acceptance by physicians, patients, third- party payers, and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and we may not become profitable. The degree of market acceptance of our current products and product candidates, if approved for commercial sale, will depend on a number of factors, including: • the prevalence and severity of any side effects, including any limitations or warnings contained in a product' s approved labeling; • the efficacy and potential advantages over alternative treatments; • the pricing of our product candidates; • **the** relative convenience and ease of administration; • the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies; • the strength of marketing and distribution support and timing of market introduction of competitive products; • publicity concerning our products or competing products and treatments; and • sufficient third- party insurance coverage and reimbursement. As part of the NDA review process for sparsentan for IgAN, the FDA required us to include a REMS and a boxed warning on the label regarding mandatory birth control for patients of child- bearing potential regarding risk of embryo- fetal toxicity, as has been required for other approved endothelin antagonists, and a REMS and boxed warning on the label for liver monitoring regarding potential risk of hepatotoxicity, as has been required for certain other approved endothelin antagonists. As part of the liver monitoring REMS, monthly monitoring of each patient is required for the first year the patient is on treatment, and quarterly thereafter. While we have taken efforts to streamline the REMS with the cadence of typical patient monitoring and have implemented convenience- focused features within the REMS program, the existence of monthly liver monitoring has the potential to be viewed as an impediment to prescribing FILSPARI. Also, while we intend to utilize our continued clinical trial experience with FILSPARI and post- marketing data gathering commitment to potentially support **modifying or** lifting of the liver monitoring REMS in the future following sufficient experience with FILSPARI and if supported by the data, there is no guarantee that the data will support this endeavor, or even if we believe it

does, that the FDA will agree with it. Even if a potential or current product displays a favorable efficacy and safety profile in nonclinical and clinical trials, market acceptance of the product will not be known until after it is launched. The efforts by us or any applicable collaboration partner to educate patients, the medical community, and third- party payers on the benefits of our products may require significant resources and may never be successful. Such efforts to educate the marketplace may require more resources than are required by the conventional marketing technologies employed by our competitors. The market opportunities for our products and product candidates may be smaller than we believe they are. Certain of the diseases that our current and future product candidates are being developed to address, such as IgAN, FSGS and HCU, are relatively rare. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, may not be accurate. Currently, most reported estimates of the prevalence of IgAN, FSGS and HCU are based on studies of small subsets of the population of specific geographic areas, which are then extrapolated to estimate the prevalence of the diseases in the broader world population. As new studies are performed the estimated prevalence of these diseases may change. There can be no assurance that the prevalence of IgAN, FSGS or HCU in the study populations accurately reflect the prevalence of these diseases in the broader world population. The FDA- approved label of FILSPARI is currently limited to adult patients with IgAN at risk of rapid disease progression, generally a UPCR ≥ 1. 5 gram / gram. Based on our interactions with the FDA, we believe that the FDA has imposed the rapid disease progression limitation on the FILSPARI label because of the accelerated approval pathway under which the product has been approved, and that there ~~should~~ **may** be an opportunity to further expand the label to cover a broader population of IgAN patients **based on** ~~following the conclusion of~~ the confirmatory ~~portion of~~ **data from** the PROTECT Study, pending ~~supportive data~~ **favorable regulatory review** . However, there can be no guarantee that this will be the case. **For additional information, see the risk factor titled " Our future prospects are highly dependent upon our ability to successfully develop and execute commercialization strategies for our products, including FILSPARI, and to attain market acceptance among physicians, patients and healthcare payers. "** If our estimates of the prevalence of IgAN, FSGS or HCU or of the number of patients who may benefit from treatment with sparsentan or pegtibatinase prove to be incorrect or if regulatory approval is conditioned on label restrictions that limit the approved patient population, the market opportunities for our product candidates may be smaller than we believe they are, our prospects for generating revenue may be adversely affected and our business may suffer. Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval or commercialization. Undesirable side effects caused by our product candidates could interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, and in turn prevent us from commercializing our product candidates and generating revenues from their sale. In addition, if any of our product candidates receive marketing approval and we or others later identify undesirable side effects caused by the product: • regulatory authorities may require the addition of restrictive labeling statements; • regulatory authorities may withdraw **, suspend or vary** their approval of the product; and • we may be required to change the way the product is administered or conduct additional clinical trials. Any of these events could prevent us from achieving or maintaining market acceptance of the affected product or could substantially increase the costs and expenses of commercializing the product candidate, which in turn could delay or prevent us from generating significant revenues from its sale or adversely affect our reputation. We do not currently have patent protection for certain of our commercial products. If we are unable to obtain and maintain protection for the intellectual property relating to our technology and products, their value will be adversely affected. Our success will depend in large part on our ability to obtain and maintain protection in the United States and other countries for the intellectual property covering, or incorporated into, our technology and products. The patent situation in the field of biotechnology and pharmaceuticals generally is highly uncertain and involves complex legal, technical, scientific and factual questions. We do not have, and do not expect to obtain, patent protection for **the original formulation of** Thiola ~~, Chenodal or Cholbam~~ . Additionally, although we have a license to a granted U. S. patent covering the treatment of cystinuria by administering Thiola EC with food (U. S. Patent No. 11, 458, 104," the' 104 patent "), as well as a pending U. S. patent application directed to Thiola EC, we do not know whether the pending U. S. patent application or any future patent application will result in a granted patent covering Thiola EC. More generally, we may not be able to obtain additional issued patents relating to our technology or products. Even if issued, patents issued to us or our licensors ~~, including for example the 104 patent,~~ may be challenged, narrowed, invalidated, held to be unenforceable or circumvented, which could limit our ability to stop competitors from marketing similar products or reduce the term of patent protection we may have for our products **. In addition, in certain circumstances with respect to method of use patents, an ANDA applicant may certify that its proposed ANDA label does not contain (or carves out) any language regarding the patented method- of- use rather than certify to a listed method- of- use patent. On January 30, 2024, the FDA approved Torrent Pharmaceuticals Limited' s (Torrent) ANDA for Thiola EC (100mg and 300mg), and accordingly, Thiola EC is now subject to immediate generic competition** . Changes in either patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection. Patent laws vary by country. Some countries have compulsory licensing laws under which a patent owner may be required to grant licenses to third parties. Some countries do not grant or enforce patents related to medical treatments, or limit enforceability in the case of a public emergency. In addition, many countries limit the enforceability of patents against government agencies or government contractors. If we are unable to obtain or enforce patents related to medical treatments in certain countries, or we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our business may be adversely affected. The intellectual property systems in other countries can be destabilized as a result of political events, during which the ability to obtain, maintain and enforce intellectual property protection in the affected country may be uncertain and evolving. For example, as a result of the ongoing war between Ukraine and Russia, Russian officials have suggested that they may treat patents or patent applications owned by parties from certain countries, including the United States, as unenforceable and / or

provide for zero compensation compulsory licenses to such patents or patent applications. Recent court decisions in Russia have raised questions about the strength of trademark protections in Russia. The U. S. government' s response to political events may also negatively affect our ability to obtain, maintain and enforce intellectual property protection in the affected country. For example, the U. S. government has issued sanctions against Russia related to the ongoing war in Ukraine, and as a result of these sanctions, it may not be possible to pay fees necessary for prosecution and maintenance of Russian patent applications and patents in the absence of licenses or exclusions set forth by the U. S. government authorizing transactions in connection with intellectual property. Payments for trademark protection may be similarly impacted. The U. S. Department of the Treasury has issued General License No. 31, authorizing such transactions to allow filing, prosecution and maintenance of Russian patents and trademarks. Uncertainties regarding political events, including the ongoing war between Ukraine and Russia, as well as any resulting losses of intellectual property protection, could harm our business. Our product FILSPARI is covered by U. S. Patent No. 6, 638, 937, which expired in 2019 and to which we have an exclusive license. In addition, U. S. Patent No. 9, 662, 312, to which we also have an exclusive license and which was granted on May 30, 2017 and expires in 2030, covers the use of sparsentan for treating glomerulosclerosis, including FSGS. U. S. Patent No. 9, 993, 461, to which we also have an exclusive license and which was granted on June 12, 2018 and expires in 2030, covers the use of sparsentan for treating IgAN as well as glomerulosclerosis, including FSGS. For products we develop based on a new chemical entity not previously approved by the FDA, we expect that in addition to the protection afforded by our patent filings that we will be able to obtain five years regulatory exclusivity via the provisions of the Food, Drug, and Cosmetic **Act** (" FDC **Act** ") ~~Act~~ and possibly seven years regulatory exclusivity via the orphan drug provisions of the FDC Act. In the case of sparsentan, the periods of regulatory exclusivity may, if certain conditions are satisfied, be extended by six months on the basis of pediatric exclusivity, thereby resulting in exclusivity periods of 5. 5 years and 7. 5 years, respectively. In addition, we may be able to obtain up to five years patent term extension (to compensate for regulatory approval delay) for one patent covering such a product for its FDA-approved use. Such a patent, like the periods of regulatory exclusivity, also may be extended by a further six months on the basis of pediatric exclusivity if certain conditions are satisfied. The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that: • we or our licensors were the first to make the inventions covered by each of our pending patent applications; • we or our licensors were the first to file patent applications for these inventions; • others will not independently develop similar or alternative technologies or duplicate any of our technologies; • any patents issued to us or our licensors that provide a basis for commercially viable products will provide us with any competitive advantages or will not be challenged by third parties; • we will develop additional proprietary technologies that are patentable; • we will file patent applications for new proprietary technologies promptly or at all; • the claims we make in our patents will be upheld by patent offices in the United States and elsewhere; • our patents will not expire prior to or shortly after commencing commercialization of a product; and • the patents of others will not have a negative effect on our ability to do business. We have negotiated a license agreement with Ligand Pharmaceuticals for the rights to sparsentan which we are initially developing for the treatment of IgAN and FSGS. This license subjects us to various commercialization, reporting and other obligations. If we were to default on our obligations, we and CSL Vifor could lose our rights to sparsentan. We have obtained a U. S. patent and European patent each covering the use of sparsentan for treating glomerulosclerosis, including FSGS, as well as a second U. S. patent and a second European patent each covering both the use of sparsentan for treating IgAN and the use of sparsentan for treating glomerulosclerosis, including FSGS. In ~~addition, in 2020 we obtained a U. S. patent covering the use of sparsentan for the treatment of Alport syndrome. However, we cannot be certain that we will be able to obtain patent protection for various other potential indications for sparsentan, or whether, if granted, we would be able to enforce such patents. Additionally, in~~ November 2020, a third party filed an opposition to our second European patent (European Patent No. EP3222277, " the ' 277 EP Patent "), in the European Patent Office (" EPO"). While we are vigorously defending the ' 277 EP Patent against the opposition, there is no guarantee that we will be successful in doing so. Our patents also may not afford us protection against competitors with similar technology. Because patent applications in the United States and many other jurisdictions are typically not published until 18 months after filing, or in some cases not at all, and because publications of discoveries in the scientific literature often lag behind the actual discoveries, neither we nor our licensors can be certain that we or they were the first to make the inventions claimed in our or their issued patents or pending patent applications, or that we or they were the first to file for protection of the inventions set forth in these patent applications. If a third party has also filed a United States patent application prior to the effective date of the relevant provisions of the America Invents Act (i. e. before March 16, 2013) covering our product candidates or a similar invention, we may have to participate in an adversarial proceeding, known as an interference, declared by the USPTO to determine priority of invention in the United States. The costs of these proceedings could be substantial, and it is possible that our efforts could be unsuccessful, resulting in a loss of our United States patent position. We cannot assure you that third parties will not assert patent or other intellectual property infringement claims against us with respect to technologies used in our products. If patent infringement suits were brought against us, we may be unable to commercialize some of our products which could severely harm our business. Litigation proceedings, even if not successful, could result in substantial costs and harm our business. We expect to rely on orphan drug status to develop and commercialize certain of our products and product candidates, but our orphan drug designations may not confer marketing exclusivity or other expected commercial benefits. We expect to rely on orphan drug exclusivity for sparsentan and potential future product candidates that we may develop. Orphan drug status currently confers seven years of marketing exclusivity in the United States under the FDC Act, and up to ten years of marketing exclusivity in ~~Europe~~ **the EU** for a particular product in a specified indication or, in the case of orphan drugs for which a pediatric investigation plan has been completed, 12 years. The FDA and ~~EMA~~ **European Commission** have granted orphan designation for ~~Chenodal,~~ sparsentan **for the treatment of IgAN and FSGS** , and pegtibatinase ~~(TVT- 058)~~ for the treatment of ~~CTX, IgAN and FSGS and~~ homocystinuria ~~, respectively~~ . While we have been granted these orphan designations, we will not be able to rely on these designations to exclude other companies from

manufacturing or selling these molecules for the same indication beyond these time frames. Furthermore, in ~~Europe~~ **the EU**, orphan drug status is re- evaluated in connection with the marketing authorization review process and a product candidate must re- qualify as of such time in order to maintain orphan drug status ~~. In addition, any~~ **and benefit from the potential regulatory exclusivity periods related to** marketing **authorizations granted to orphan products. The period of market** exclusivity in ~~Europe can~~ **the EU may, however,** be reduced ~~from ten years~~ to six years if **, at** the ~~initial designation~~ **end of the fifth year, it is established that the product no longer meets the** criteria **on** ~~have significantly changed since~~ the **basis of which it received orphan medicinal product destination, including where it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of** market **exclusivity or where the prevalence of the condition has increased above the threshold. Additionally, a marketing** authorization ~~of~~ **may be granted to a similar medicinal product with** the **same** orphan **indication during the 10 year period if: (i) the applicant consents to a second original orphan medicinal** product **application, (ii) the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities; or (iii) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior to the original orphan medicinal product. A company may voluntarily remove a product from the register of orphan products**. For any product candidate for which we have been granted orphan drug designation in a particular indication, it is possible that another company also holding orphan drug designation for the same product candidate will receive marketing approval for the same indication before we do. If that were to happen, our applications for that indication may not be approved until the competing company' s period of exclusivity expires. Even if we are the first to obtain marketing authorization for an orphan drug indication in the United States, there are circumstances under which a competing product may be approved for the same indication during the seven- year period of marketing exclusivity, such as if the later product is shown to be clinically superior to our orphan product, or if the later product is deemed a different product than ours. Further, the seven- year marketing exclusivity would not prevent competitors from obtaining approval of the same product candidate as ours for indications other than those in which we have been granted orphan drug designation, or for the use of other types of products in the same indications as our orphan product. Any ~~drugs~~ **therapies** we develop may become subject to unfavorable pricing regulations, third- party reimbursement practices or healthcare reform initiatives, thereby harming our business. In March 2010, President Obama signed the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the" PPACA"), a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The PPACA revised the definition of " average manufacturer price " for reporting purposes, which could increase the amount of Medicaid drug rebates to states. The PPACA also increased the mandated Medicaid rebate from 15. 1 % to 23. 1 % of the average manufacturer price, expanded the rebate to Medicaid managed care utilization and increased the types of entities eligible for the federal 340B drug discount program. Further, the law imposed a significant annual fee on companies that manufacture or import certain branded prescription drug products. There have been executive, judicial, Congressional, and political challenges to certain aspects of the PPACA. For example, on June 17, 2021 the U. S. Supreme Court dismissed a challenge on procedural grounds that argued the PPACA is unconstitutional in its entirety because the " individual mandate " was repealed by Congress. Further, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 (" IRA") into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in PPACA 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 PPACA will be subject to judicial or Congressional challenges in the future. It is unclear how any additional healthcare reform measures of the Biden administration will impact the PPACA and our business. In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. For example, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, includes aggregate reductions to Medicare payments to providers of up to 2 % per fiscal year, which went into effect beginning on April 1, 2013 and, due to subsequent legislative amendments, will stay in effect until ~~2031~~ **2032** unless additional Congressional action is taken ~~. Under current legislation, the actual reduction in Medicare payments will vary from 1 % in 2022 to up to 4 % in the final fiscal year of this sequester~~. Additionally, in January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals and imaging centers. If we are unable to obtain and maintain coverage and adequate reimbursement from governments or third- party payers for any products that we may develop or if we are unable to obtain acceptable prices for those products, our prospects for generating revenue and achieving profitability will suffer. Our prospects for generating revenue and achieving profitability will depend heavily upon the availability of coverage and adequate reimbursement for the use of our approved product candidates from governmental and other third- party payers, both in the United States and in other markets. Reimbursement by a third- party payer may depend upon a number of factors, including the third- party payer' s determination that use of a product is: • a covered benefit under its health plan; • safe, effective and medically necessary; • appropriate for the specific patient; • cost- effective; and • neither experimental nor investigational. Obtaining reimbursement approval for a product from each government or other third- party payer is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of our products to each payer. We may not be able to provide data sufficient to gain acceptance with respect to reimbursement. Additionally, we might need to conduct post- marketing studies in order to demonstrate the cost- effectiveness of any future products to such payers' satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Even when a payer determines that a product is eligible for reimbursement, the payer may impose coverage limitations that preclude payment for some uses that are approved by the FDA or non- United States regulatory authorities. Also, prior authorization for a product

may be required. In addition, there is a risk that full reimbursement may not be available for high- priced products. Moreover, eligibility for coverage does not imply that any product will be reimbursed in all cases or at a rate that allows us to make a profit or even cover our costs. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Further, coverage policies and third- party payer reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained, less favorable coverage policies and reimbursement rates may be implemented in the future. A primary trend in the United States healthcare industry and elsewhere is toward cost containment. We expect the changes made by PPACA, other legislation impacting the Medicare program and the 340B program, and the increasing emphasis on managed care to continue to put pressure on pharmaceutical product pricing. As these concerns continue to grow over the need for tighter oversight, there remains the possibility that the Heath Resources and Services Administration or another agency under the U. S. Department of Health and Human Services (" HHS") will propose regulations or that Congress will explore changes to the 340B program through legislation. There have also been a number of initiatives pending at the state and federal level that could negatively impact the reimbursement for products approved under the accelerated approval pathway in the United States by restricting patient access or establishing differential payment models. Certain states are also in the process of establishing Patient Drug Affordability Boards with the authority in some cases to set upper payment limits. Further, there has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices, including several recent U. S. congressional inquiries and federal and state legislation designed to, among other things, increase drug pricing transparency, expedite generic competition, review relationships between pricing and manufacturer patient assistance programs, and reform government program drug reimbursement methodologies. At the federal level, in July 2021, the Biden administration released an executive order that included multiple provisions aimed at prescription drugs. In response to Biden' s executive order, on September 9, 2021, 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 (i) directs HHS to negotiate the price of certain high- expenditure, single- source drugs and biologics covered under Medicare and (ii) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions ~~will~~ take effect progressively starting in fiscal year 2023 **. On August 29** , ~~although~~ **2023, HHS announced** ~~they~~ **the** ~~may~~ **list of the first ten drugs that will** be subject to **price negotiations, although the Medicare drug price negotiation program is currently subject to** legal challenges **. HHS has and will continue to issue and update guidance as these programs are implemented** . It is currently unclear how the IRA will be implemented but it is likely to have a significant impact on the pharmaceutical industry. In addition, **in response to** the Biden administration ~~released an additional~~ **' s October 2022** executive order **,** on ~~October~~ **February** 14, ~~2022~~ **2023** , ~~directing~~ HHS ~~to~~ **released a** report ~~on how~~ **outlining three new models for testing by** the Center for Medicare and Medicaid Innovation **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. Further, 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. 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 ~~be further leveraged~~ **use when deciding** to ~~test~~ **exercise march- in rights. While march- in rights have not previously been exercised, it is uncertain if that will continue under the** new **framework** ~~models for lowering drug costs for Medicare and Medicaid beneficiaries~~ . At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. ~~Also~~ **For example** , **on January 5, 2024, the FDA approved Florida' s Section 804 Importation Program (SIP) proposal to import certain drugs from Canada for specific state healthcare programs. It is unclear how this program will be implemented, including which drugs will be chosen, and whether it will be subject to legal challenges in the United States or Canada.** ~~there~~ **Other states** have ~~been reports~~ **also submitted SIP proposals** that **are pending review by** the ~~U~~ **FDA** . **Any such approved importation plans** ~~S. government is considering targeted price controls and reference pricing based on foreign single- payer country access policies~~ , **when** ~~which, if~~ implemented, ~~could adversely affect our revenues~~ **may result in lower drug prices for products covered by those programs** . Any reduction in reimbursement from Medicare, Medicaid or other government- funded programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our ~~drugs~~ **therapies** . Additionally, we are currently unable to predict what additional legislation or regulation, if any, relating to the healthcare industry may be enacted in the future or what effect recently enacted federal legislation or any such additional legislation or regulation would have on our business. We face potential product liability exposure far in excess of our limited insurance coverage. The use of any of our potential products in clinical trials, and the sale of any approved products, may expose us to liability claims. These claims might be made directly by consumers, health care providers, pharmaceutical companies or others selling our products. We have obtained limited product liability insurance coverage for our clinical trials in the amount of $ 10 million per occurrence and $ ~~25~~ **30** million in the aggregate. However, our insurance may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. We intend to expand our insurance coverage as we obtain marketing approval for additional product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance. On occasion, juries have awarded large judgments in class action lawsuits based on drugs that had

unanticipated side effects. A successful product liability claim or series of claims brought against us would decrease our cash reserves and could cause our stock price to fall. We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do. Our operating results will suffer if we fail to compete effectively. Several of our competitors have substantially greater financial, research and development, distribution, manufacturing and marketing experience and resources than we do and represent substantial long- term competition for us. Other companies may succeed in developing and marketing products that are more effective and / or less costly than any products that may be developed and marketed by us, or that are commercially accepted before any of our products. Factors affecting competition in the pharmaceutical and ~~drug~~ **therapeutic** industries vary, depending on the extent to which a competitor is able to achieve a competitive advantage based on its proprietary technology and ability to market and sell ~~drugs~~ **therapeutics** . The industry in which we compete is characterized by extensive research and development efforts and rapid technological progress. Although we believe that our orphan drug status and proprietary position with respect to sparsentan may give us a competitive advantage, new developments are expected to continue and there can be no assurance that discoveries by others will not render **our** ~~such potential~~ products **and product candidates** noncompetitive. Furthermore, competitors could enter the market with generic versions of our products. For example, a generic option for the 100 mg version of the original formulation of Thiola (tiopronin tablets) was approved by the FDA in May 2021 and a second 100 mg version of the original formulation of Thiola (tiopronin tablets) was approved by the FDA in June 2022 **. Also, as of February 1, 2024, three generic options for the 100 mg and 300 mg versions of Thiola EC have been approved by the FDA** . Our competitive position also depends on our ability to enter into strategic alliances with one or more large pharmaceutical and contract manufacturing companies, attract and retain qualified personnel, develop effective proprietary products, implement development and marketing plans, obtain patent protection, secure adequate capital resources and successfully sell and market our approved products. There can be no assurance that we will be able to successfully achieve all of the foregoing objectives. Use of third parties to manufacture our products and product candidates may increase the risk that we will not have sufficient quantities of our product and product candidates or such quantities at an acceptable cost, and clinical development and commercialization of our product and product candidates could be delayed, prevented or impaired. We do not own or operate manufacturing facilities for clinical or commercial production of our products or product candidates. We have limited personnel with experience in drug manufacturing and we lack the resources and the capabilities to manufacture any of our product candidates on a clinical or commercial scale. We outsource all manufacturing and packaging of our nonclinical, clinical, and commercial products to third parties. The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up initial production and in maintaining required quality control. These problems include difficulties with production costs and yields and quality control, including stability of the product candidate. We intend to rely on third- party manufacturers for the long- term commercial supply of FILSPARI and for our development stage product candidates ~~, including sparsentan for the treatment of FSGS and pegtibatinase (TVT- 058)~~ . We expect the manufacturers of each product or product candidate to, at least initially and potentially for a significant period of time, be single source suppliers to us. Reliance on third- party manufacturers entails risks to which we may not be subject if we manufactured our product candidates or products ourselves, including: • reliance on the third party for regulatory compliance and quality assurance; • limitations on supply availability resulting from capacity and scheduling constraints of the third parties; • less control over cost increases resulting from inflationary pressures affecting raw materials and other supply chain components; • impact on our reputation in the marketplace if manufacturers of our products fail to meet the demands of our customers; • the possible breach of the manufacturing agreement by the third party because of factors beyond our control; and • the possible termination or nonrenewal of the agreement by the third party, based on its own business priorities, at a time that is costly or inconvenient for us. The failure of any of our contract manufacturers to maintain high manufacturing standards could result in injury or death of clinical trial participants or patients using our products. Such failure could also result in product liability claims, product recalls, product seizures or withdrawals, delays or failures in testing or delivery, cost overruns or other problems that could seriously harm our business or profitability. Our contract manufacturers are required to adhere to FDA regulations setting forth cGMP **and comparable foreign regulatory authority requirements** . These regulations cover all aspects of the manufacturing, testing, quality control and recordkeeping relating to our product candidates and any products that we may commercialize. Our manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our manufacturers are subject to unannounced inspections by the FDA, state regulators and similar regulators outside the United States **to monitor and ensure compliance with cGMP** . We are ultimately responsible for ensuring that our API and finished products are manufactured in accordance with cGMP regulations and similar regulatory requirements outside the United States, and it is therefore critical that we maintain effective management practices and oversight with respect to our third- party manufacturers, including routine auditing. Our failure, or the failure of our third- party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including **shutdown of the third- party vendor or invalidation of drug product lots or processes,** fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approval of our product candidates, delays, suspension **, variation** or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect regulatory approval and supplies of our product candidates. Our product and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that are both capable of manufacturing for us and willing to do so. A health epidemic or pandemic and associated vaccine or treatment development and manufacturing efforts may increase demand for the services supplied by many third- party manufacturers, including some of those that we utilize for our products and product candidates, which may result in decreased availability of manufacturing slots at many such facilities. If the third parties that we engage to

manufacture products for our developmental or commercial products should halt or cease to continue to do so for any reason, we likely would experience interruptions in cash flows and / or delays in advancing our clinical trials while we identify and qualify replacement suppliers, and we may be unable to obtain replacement supplies on terms that are favorable to us. Later relocation to another manufacturer will also require notification, review and other regulatory approvals from the FDA and other regulators and will subject our production to further cost and instability in the availability of our product candidates. In addition, if we are not able to obtain adequate supplies of our products and product candidates, or the drug substances used to manufacture them, it will be more difficult for us to sell our products and to develop our product candidates. This could greatly reduce our competitiveness and negatively affect our results of operations. Our current and anticipated future dependence upon others for the manufacture of our products and product candidates may adversely affect our future profit margins and our ability to develop product candidates and commercialize our marketed products and any other products that may obtain regulatory approval on a timely and competitive basis. Materials necessary to manufacture our products and product candidates may not be available on commercially reasonable terms, or at all, which may delay the development and commercialization of our products and product candidates. We rely on the manufacturers of our products and product candidates to purchase from third- party suppliers the materials necessary to produce the compounds for our nonclinical and clinical studies and rely on these other manufacturers for commercial distribution if we obtain marketing approval for any of our product candidates. Suppliers may not sell these materials to our manufacturers at the time we need them or on commercially reasonable terms and all such prices are susceptible to fluctuations in price and availability due to transportation costs, government regulations, price controls, and changes in economic climate or other foreseen circumstances. We do not have any control over the process or timing of the acquisition of these materials by our manufacturers. In addition, ~~significant increases in~~ inflation and global supply chain disruptions, as well as past **disruptions related to COVID- 19** and potential future disruptions related to **a** ~~COVID- 19 and potential~~ future ~~disruptions related to Russia' s invasion of Ukraine~~ **health epidemic or pandemic, wars, armed conflicts,** and global geopolitical tension, including between the U. S. and China, have had and may continue to have a negative impact on our manufacturers' ability to acquire the materials necessary for our business. Moreover, we currently do not have any agreements for the commercial production of these materials. If our manufacturers are unable to obtain these materials for our nonclinical and clinical studies, product testing and potential regulatory approval of our product candidates would be delayed, significantly impacting our ability to develop our product candidates. If our manufacturers or we are unable to purchase these materials after regulatory approval has been obtained for our product candidates, the commercial launch of our product candidates would be delayed or there would be a shortage in supply, which would materially affect our ability to generate revenues from the sale of our product candidates. For example, in 2021 a membrane used in pegtibatinase ~~(TVT- 058)~~ drug substance manufacturing became more difficult to acquire due to the same or similar membranes being used in certain of the COVID- 19 vaccine manufacturing ~~and we continue to see challenges with securing materials used in the pegtibatinase manufacturing process~~ **processes** ~~that are in short supply as a result of COVID- 19~~. While ~~we believe~~ our contingency plans ~~will enable~~ **enabled** us to ~~continue~~ **initiate** the ~~ongoing clinical~~ **Phase 3** study of pegtibatinase **on our desired timeline** ~~(TVT- 058) with the currently available clinical supplies~~, there is no guarantee that we will not **continue to** face ~~additional~~ **supply challenges or** shortages of ~~this membrane, or~~ other materials necessary to manufacture pegtibatinase ~~(TVT- 058)~~ or our other products and product candidates. If our risk mitigation plans are not successful in overcoming these challenges, our pegtibatinase program or other products and product candidates, could be delayed. Risks Related to Our Business Our limited operating history makes it difficult to evaluate our future prospects, and our profitability in the future is uncertain. We face the problems, expenses, difficulties, complications and delays, many of which are beyond our control, associated with any business in its early stages and have a limited operating history on which an evaluation of our prospects can be made. Such prospects should be considered in light of the risks, expenses and difficulties frequently encountered in the establishment of a business in a new industry, characterized by a number of market entrants and intense competition, and in the shift from development to commercialization of new products based on innovative technologies. We have experienced significant growth over the past five years in the number of our employees and the scope of our operations. We have expanded our sales and marketing, compliance and legal functions in addition to expansion of all functions to support a commercial organization. We have also expanded our operations in ~~anticipation of~~ **connection with** the commercial launch of FILSPARI in the United States, including by adding additional members to our sales force ~~, and expect to continue to hire additional staff in the coming months~~. To **appropriately** manage **for** our ~~anticipated~~ future ~~growth~~, we must continue to implement and improve our managerial, operational and financial systems, ~~expand our facilities,~~ continue to recruit ~~and~~ **,** train ~~additional~~ **and retain** qualified personnel **as needed**, and successfully integrate **any changes** ~~such expanded operations~~ into our existing business. To succeed, we must recruit, retain, manage and motivate qualified clinical, scientific, technical, commercial and management personnel, and we face significant competition for experienced personnel. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit ~~and~~ **,** train ~~additional~~ **and retain** qualified personnel, including in connection with the ~~planned~~ **ongoing** commercial launch of FILSPARI in the United States. The **management** ~~physical expansion~~ of **changes to** our operations may lead to significant costs and may divert our management and business development resources. Any inability on the part of our management to manage growth **or other changes in our organization** could delay the execution of our business plans or disrupt our operations. Factors that may inhibit our efforts to commercialize our products without strategic partners or licensees include: • our inability to recruit and retain adequate numbers of effective sales and marketing personnel; • the inability of sales personnel to obtain access to or educate adequate numbers of physicians to prescribe our products; • the lack of complementary products to be offered by our sales personnel, which may put us at a competitive disadvantage against companies with broader product lines; • unforeseen costs associated with expanding our own sales and marketing team for new products or with entering into a partnering agreement with an independent sales and marketing organization; and • efforts by our competitors to commercialize competitive products. Moreover, though we generate revenues from product sales arrangements, we may incur

significant operating losses over the next several years. Our ability to achieve profitable operations in the future will depend in large part upon successful in- licensing of products approved by the FDA, selling and manufacturing these products, completing development of our products, obtaining regulatory approvals for these products, and bringing these products to market. The likelihood of the long- term success of our company must be considered in light of the expenses, difficulties and delays frequently encountered in the development and commercialization of new **therapeutics** ~~drug products~~ , competitive factors in the marketplace, as well as the regulatory environment in which we operate. In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We depend on a highly experienced and skilled workforce to grow and operate our business. If we are unable to attract, retain and engage our employees, we may not be able to grow effectively. The execution of our strategic objectives and future success will depend upon our continued ability to identify, hire, develop, motivate and retain a highly qualified workforce. We depend on contributions from our employees, and, in particular, our senior management team, to execute efficiently and effectively. Our success further depends on our ability to attract, retain and motivate highly skilled mid- level and senior managers as well as team members at various levels in the scientific, development, medical and commercial areas of the business, particularly ~~as we hire additional personnel~~ in connection with our ~~planned~~ **ongoing** commercial launch of FILSPARI in the United States. Our headquarters are based in San Diego, California. This region is home to many other biopharmaceutical companies and many academic and research institutions. Competition for qualified key talent in our market is intense and may limit our ability to hire and retain employees on acceptable terms, or at all. As a result, we may not be able to retain our existing employees or hire new employees quickly enough to meet our needs. To induce valuable employees to remain at our company, in addition to salary, cash incentives and other employee benefits, we have provided stock options and restricted stock unit (" RSU") awards that vest over time. The value to employees of stock options and RSU awards that vest over time may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Current market conditions and the potential for extreme stock price volatility exacerbates this risk. Despite our efforts to retain valuable employees, members of our management, scientific, development and commercial teams may terminate their employment with us on short notice. All of our employees have at- will employment, which means that they could leave our employment at any time, with or without notice. We do not maintain " key person " insurance policies on the lives of any of our employees. If we fail to effectively manage our hiring and retention needs, our ability to meet our strategic objectives and our business and operating results may be adversely impacted. Health epidemics or pandemics could materially adversely affect our business, results of operations and financial condition. A health epidemic or pandemic poses the risk that we or our clinical trial subjects, employees, contractors, collaborators, suppliers and vendors may be prevented from conducting certain clinical trials or other business activities for an indefinite period of time, including due to travel restrictions, quarantines, " stay- at- home " and" shelter- in- place" orders or shutdowns that have been or may be requested or mandated by governmental authorities, or that our or their ability to conduct operations will be negatively impacted by staffing shortages while employees quarantine as a result of exposure to or transmission of the virus. In addition, a health epidemic or pandemic could impact personnel at third- party manufacturing facilities in the United States and other countries, including China, or the availability or cost of materials, which could potentially disrupt the supply chain for our commercial products, our product candidates or the comparator products in our ongoing clinical trials. The timelines and conduct of our ongoing clinical trials previously have been affected by COVID- 19 and we may experience similar delays or interruptions due to ~~COVID- 19 or~~ other health epidemics or pandemics in the future. For example, in 2020 we experienced a reduction in the rates of patient enrollment in our ongoing clinical trials as a result of the COVID- 19 pandemic. **New health epidemics** ~~While we remain in close contact with our~~ **or pandemics may emerge** ~~CROs, clinical sites and suppliers in an attempt to manage and mitigate the impacts~~ that ~~COVID- 19 may have on our clinical trials and projected timelines and we have implemented certain mitigating measures in accordance with COVID- 19 related FDA guidance in an effort to ensure the ongoing safety of the patients in our clinical trials and the continued collection of high quality data, there is no guarantee that such efforts will be successful. As challenging as conducting clinical trials is during normal times, the risks, operational challenges and costs of conducting clinical trials increased substantially during the COVID- 19 pandemic. In addition, restrictions caused by the COVID- 19 or other health epidemic or pandemic may~~ result in ~~impediments~~ **similar or more severe disruptions** to ~~obtaining biopsies~~ **our business** , which ~~could impact the ability to timely obtain diagnoses of IgAN or FSGS. Beginning in March 2020, substantially all of our workforce began working remotely either all or substantially all of the time as a result of applicable stay- at- home and shelter- in- place orders. As of the date of this report, the majority of our workforce is still working remotely, at least part of the time. The effects of any similar orders in the future or our related remote- work policies may negatively impact productivity, disrupt our business and delay our development programs, regulatory and commercialization timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. Remote work operations also heighten the risk of cyber- attacks and make it more difficult for us to protect our confidential information. In addition, as many of our employees have returned to the office at least part of the time, we cannot guarantee that our workforce will not face an outbreak that~~ could adversely impact our **business and operating results. Our strategic reorganization and the associated workforce reduction may not result in the level of savings that we currently anticipate, could result in costs and expenses that are greater than expected, and could disrupt our business. In December 2023, we announced a strategic reorganization including an approximate 20 % workforce reduction focused on non- field- based employees in an effort to align our resources on the ongoing FILSPARI launch and the pivotal Phase 3 HARMONY Study to support the potential approval of pegtibatinase as the first potential disease- modifying treatment for HCU. There is a chance that we will not realize the level of savings and improvements in our cost structure that we currently anticipate, and there may be unforeseen difficulties, delays or unexpected costs. If we are unable to realize the expected operational efficiencies and cost savings, our operating results and financial condition would be adversely affected. Furthermore,**

our strategic reorganization may be disruptive to our operations. ~~Moreover~~ **For example** , ~~COVID- 19 continues to evolve, and the extent to which COVID- 19 may impact~~ our **workforce reductions could yield unanticipated consequences** ~~business, results of operations and financial position will depend on future developments, which are highly uncertain and cannot be predicted with confidence~~ , such as **increased difficulties** ~~the emergence, infectiousness and severity of new variants, travel restrictions and social distancing~~ in **implementing our** ~~the United States and other countries,~~ business ~~closures~~ **strategy, including retention of** ~~or~~ **our remaining employees. Employee litigation related to** ~~business disruptions, global supply challenges, and the effectiveness of actions taken in the United States and other~~ -- **the** ~~countries to contain~~ **headcount reduction could be costly** and ~~treat~~ **prevent management from fully concentrating on** the ~~disease. New health epidemics or pandemics may emerge that result in similar or more severe disruptions to our~~ business. We will likely experience fluctuations in operating results and could incur substantial losses. We expect that our operating results will vary significantly from quarter- to- quarter and year- to- year as a result of investments in research and development, specifically our clinical and nonclinical development activities. We anticipate that **certain of** our expenses will continue to increase ~~as we~~ **, depending on factors including but not limited to** : ~~• continue~~ the ~~ongoing portion~~ **continuation and cost** of **our clinical** ~~the Phase 3 trial~~ **trials** ~~of FILSPARI for the treatment of IgAN to the confirmatory endpoint~~ and ~~through the open- label extension period; • continue the open- label portion of DUET and the Phase 3 trial of sparsentan for the treatment of FSGS; • continue~~ the research and development of additional product candidates **; the costs involved in seeking and obtaining marketing approvals for our products, and in maintaining quality systems standards for our products; the timing of, and costs involved in, commercial activities** , including **product marketing,** ~~pegtibatinase (TVT- 058); • expand our~~ sales and **distribution** ~~marketing infrastructure to commercialize our current approved products~~ , **costs related to our** ~~and any other products for which we may obtain regulatory approval; and • expand~~ operational, financial, and management information systems and personnel, including personnel to support product development efforts and our obligations as a public company. To attain and sustain profitability, we must succeed in developing and commercializing ~~drugs~~ **therapies** with significant market potential. This will require us to be successful in a range of challenging activities, including the discovery of product candidates, successful completion of nonclinical testing and clinical trials of our product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling those products for which we may obtain regulatory approval. We may not be successful enough in these activities to generate revenues that are substantial enough to recoup the expenses we have expended in conducting these activities to achieve profitability. Pursuant to the Ligand License Agreement, we are obligated to pay to Ligand an escalating annual royalty between 15 % and 17 % of net sales of FILSPARI and any other products containing sparsentan or related compounds, which will impact our potential future profit from the commercialization of FILSPARI in the United States and sparsentan for the treatment of IgAN in ~~Europe~~ **the EU** , if approved, as well as sparsentan for the treatment of FSGS, if approved. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become or remain profitable could depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. A decline in the market price of our common stock may also cause a loss of a part or all of your investment. Negative publicity regarding any of our products could impair our ability to market any such product and may require us to spend time and money to address these issues. If any of our products or any similar products distributed by other companies prove to be, or are asserted to be, harmful to consumers and / or subject to FDA **or comparable foreign regulatory authority** enforcement action, our ability to successfully market and sell our products could be impaired. Because of our dependence on patient and physician perceptions, any adverse publicity associated with illness or other adverse effects resulting from the use or misuse of our products or any similar products distributed by other companies could limit the commercial potential of our products and expose us to potential liabilities. We may not have sufficient insurance to cover our liability in any current or future litigation claims either due to coverage limits or as a result of insurance carriers seeking to deny coverage of such claims. We face a variety of litigation- related liability risks. Our certificate of incorporation, bylaws, other applicable agreements, and / or Delaware law require us to indemnify (and advance expenses to) our current and past directors and officers and employees from reasonable expenses related to the defense of any action arising from their service to us, including circumstances under which indemnification is otherwise discretionary. While our directors and officers are included in a director and officer liability insurance policy, which covers all our directors and officers in some circumstances, our insurance coverage does not cover all of our indemnification obligations and may not be adequate to cover any indemnification or other claims against us. In addition, the underwriters of our present coverage may seek to avoid coverage in certain circumstances based upon the terms of the respective policies. If we incur liabilities that exceed our coverage under our directors and officers insurance policy or incur liabilities not covered by our insurance, we would have to self- fund any indemnification amounts owed to our directors and officers and employees in which case our results of operations and financial condition could be materially adversely affected. Further, if D & O insurance becomes prohibitively expensive to maintain in the future, we may be unable to renew such insurance on economic terms or unable to renew such insurance at all. The **potential** lack of D & O insurance may make it difficult for us to retain and attract talented and skilled directors and officers to serve our company, which could adversely affect our business. We may need substantial funding and may be unable to raise capital when needed. We expect our general and research and development expenses to increase in connection with our ongoing and planned activities, particularly as we conduct later- stage clinical trials of our product candidates. In addition, in ~~anticipation of~~ **connection with** the ~~planned~~ commercial launch of FILSPARI in the United States, we have begun to incur significant commercialization expenses and expect to continue to incur significant commercialization expenses for FILSPARI and any other future approved products, including for product sales and marketing, securing commercial quantities of product from our manufacturers, and product distribution. Our expenses have and may continue to increase as a result of increasing inflation in the United States and abroad. We currently have no additional commitments or arrangements for any additional financing to fund the research and development and commercial launch of our product candidates. General market conditions,

including **high** ~~increases in~~ interest rates and stock price volatility, **actual or anticipated bank failures,** and ongoing issues arising ~~from COVID- 19, Russia' s invasion of Ukraine and~~ global geopolitical tensions **, including the wars and other armed conflicts** , as well as market conditions affecting companies in the life sciences industry in general, may make it difficult for us to seek financing from the capital markets on attractive terms, or at all. Management believes our ability to continue our operations depends on our ability to sustain and grow revenue, results of operations and our ability to access capital markets when necessary to accomplish our strategic objectives. Management believes that we may incur losses in the immediate future. We expect that our operating results will vary significantly from quarter- to- quarter and year- to- year as a result of investments in research and development, specifically our clinical and nonclinical development activities. We expect to finance our cash needs from cash on hand and results of operations, and depending on results of operations we may either need additional equity or debt financing, or need to enter into strategic alliances on products in development to continue our operations until we can achieve sustained profitability and positive cash flows from operating activities. Additional funds may not be available to us when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to reduce or eliminate research development programs or commercial efforts. Our future capital requirements will depend on many factors, including: • the timing, progress, cost and results of our clinical trials, preclinical studies and other discovery and research and development activities; • the timing of, and costs involved in, seeking and obtaining marketing approvals for our products, and in maintaining quality systems standards for our products; • the timing of, and costs involved in, commercial activities, including product marketing, sales and distribution; • our ability to successfully commercialize FILSPARI in adult patients with IgAN, and to obtain regulatory approval for and successfully commercialize ~~sparsentan for FSGS and~~ our other or future product candidates; • increases or decreases in revenue from our marketed products, including decreases resulting from generic entrants or health epidemics or pandemics ~~such as COVID- 19~~ ; • debt service obligations on the 2025 Notes and 2029 Notes; • the number and development requirements of other product candidates that we pursue; • our ability to manufacture sufficient quantities of our products to meet expected demand; • the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property related claims; • our ability to enter into collaboration, licensing or distribution arrangements and the terms and timing of these arrangements; • the potential need to expand our business, resulting in additional payroll and other overhead expenses; • the potential in- licensing of other products or technologies; • the emergence of competing products and technologies and other adverse market developments; • the extent to which we acquire or invest in businesses, products and technologies; and • the potential impacts of inflation and resulting cost increases. The market price for shares of our common stock may be volatile and purchasers of our common stock could incur substantial losses. The price of our stock is likely to be volatile. The stock market in general, and the market for biotechnology companies in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock **has been in the past, and** may be **in the future,** influenced by many factors, including: • results of clinical trials of our product candidates or those of our competitors; • our entry into or the loss of a significant collaboration; • regulatory or legal developments in the United States and other countries, including changes in the health care payment systems; • our ability to obtain and maintain marketing approvals from the FDA or similar regulatory authorities outside the United States; • variations in our financial results or those of companies that are perceived to be similar to us; • changes in the structure of healthcare payment systems; • market conditions in the pharmaceutical and biotechnology sectors and issuance of new or changed securities analysts' reports or recommendations; • general economic, industry and market conditions, including the impacts thereon of inflation and ~~rising~~ **high** interest rates, ~~COVID- 19~~ **actual or anticipated bank failures** , **wars, armed conflicts** ~~Russia' s invasion of Ukraine~~ and global geopolitical tensions; • results of clinical trials conducted by others on ~~drugs~~ **therapies** that would compete with our product candidates; • developments or disputes concerning patents or other proprietary rights; • public concern over our product candidates or any products approved in the future; • litigation; • communications from government officials regarding health care costs or pharmaceutical pricing; • future sales or anticipated sales of our common stock by us or our stockholders; and • the other factors described in this " Risk Factors " section. In addition, the stock markets, and in particular, the Nasdaq Stock Market, have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many pharmaceutical companies. The realization of any of the above risks or any of a broad range of other risks, including those described in these " Risk Factors " could have a dramatic and material adverse impact on the market price of our common stock. We **might not receive some or all of the potential milestone payments from the sale of our bile acid product portfolio for the treatment of rare liver diseases. On July 16, 2023, we entered into a definitive asset purchase agreement (the " Purchase Agreement ") with Mirum Pharmaceuticals, Inc. (" Mirum "), pursuant to which we agreed to sell to Mirum, subject to the terms of the Purchase Agreement, our bile acid product portfolio including Chenodal and Cholbam (also known as Kolbam) (the " Products "). The closing of the transaction occurred on August 31, 2023. A portion of the consideration for the sale is in the form of milestone payments that will only be payable upon the achievement of certain milestones based on specified amounts of annual net sales of the Products (the " Milestone Events "). There is a risk that any or all of the Milestone Events might not be achieved and that any or all of the consideration tied to the achievement of the Milestone Events might not be received. We** may be unable to successfully integrate new products or businesses we may acquire. We ~~intend to~~ **may in the future** expand our product pipeline by pursuing acquisition of pharmaceutical products. If an acquisition is consummated, the integration of the acquired business, product or other assets into our company may also be complex and time-consuming and, if such businesses, products and assets are not successfully integrated, we may not achieve the anticipated benefits, cost- savings or growth opportunities. Potential difficulties that may be encountered in the integration process include the following: • integrating personnel, operations and systems, while maintaining focus on producing and delivering consistent, high quality products; • coordinating geographically dispersed organizations; • distracting employees from operations; • retaining existing customers and attracting new customers; and • managing inefficiencies associated with integrating the

operations of the acquired company or product into our own operations. Furthermore, these acquisitions and other arrangements, even if successfully integrated, may fail to further our business strategy as anticipated, expose us to increased competition or challenges with respect to our products or geographic markets, and expose us to additional liabilities associated with an acquired business, product, technology or other asset or arrangement. Any one of these challenges or risks could impair our ability to realize any benefit from our acquisitions or arrangements after we have expended resources on them. Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop. Our business exposes us to potential liability risks inherent in the research, development, manufacturing and marketing of pharmaceutical products. If any of our product candidates in clinical trials or commercialized products harm people **,** we may be subject to costly and damaging product liability claims. We have clinical trial insurance and commercial product liability coverage. However, this insurance may not be adequate to cover all claims. We may be exposed to product liability claims and product recalls, including those which may arise from misuse or malfunction of, or design flaws in, such products, whether or not such problems directly relate to the products ~~and services~~ we have provided. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in: • decreased demand for any product candidates or products that we may develop; • damage to our reputation; • regulatory investigations that could require costly recalls or product modifications; • withdrawal of clinical trial participants; • costs to defend the related litigation; • substantial monetary awards to trial participants or patients, including awards that substantially exceed our product liability insurance, which we would then be required to pay from other sources, if available, and would damage our ability to obtain liability insurance at reasonable costs, or at all, in the future; • loss of revenue; • the diversion of management' s attention from managing our business; and • the inability to commercialize any products that we may develop. A successful product liability claim or a series of claims brought against us could cause our stock price to fall and, if judgments exceed our insurance coverage, could decrease our available cash and adversely affect our business. We may become involved in litigation matters, which could result in substantial costs, divert management' s attention and otherwise have a material adverse effect on our business, operating results or financial condition. From time to time we may become involved in certain litigation matters, including those described in Note 11 of the Consolidated Financial Statements included in this report. Although we intend to vigorously defend our interests in each matter, there is no guarantee that we will be successful and we may have to pay damages awards or otherwise may enter into settlement arrangements in connection with such matters. Any such payments or settlement arrangements could have material adverse effects on our business, operating results or financial condition. Even if we are successful in defending our interests in each matter, litigation with respect to such matters could result in substantial costs and significant adverse impact on our reputation and divert management' s attention and resources, which could have a material adverse effect on our business, operating results or financial condition. We are subject to significant ongoing regulatory obligations and oversight, which may result in significant additional expense and may limit our commercial success. We are subject to significant ongoing regulatory obligations, such as safety reporting requirements and additional post- marketing obligations, including regulatory oversight of the promotion and marketing of our products. In addition, the manufacture, quality control, labeling, packaging, safety surveillance, adverse event reporting, storage and recordkeeping for our products are subject to extensive and ongoing regulatory requirements. If we become aware of previously unknown problems with any of our products, a regulatory ~~agency~~ **authority** may impose restrictions on our products, our contract manufacturers or us. If we, our products and product candidates, or the manufacturing facilities for our products and product candidates fail to comply with applicable regulatory requirements, a regulatory ~~agency~~ **authority** , including the FDA, may send enforcement letters, mandate labeling changes, suspend **, vary** or withdraw regulatory approval, suspend **, vary or terminate** any ongoing clinical trials, refuse to approve pending applications or supplements filed by us, suspend or impose restrictions on manufacturing operations, request a recall of, seize or detain a product, seek criminal prosecution or an injunction, or impose civil or criminal penalties or monetary fines. In such instances, we could experience a significant drop in the sales of the affected products, our product revenues and reputation in the marketplace may suffer, and we could become the target of lawsuits. We are also subject to regulation by **supranational,** national, regional, state and local agencies **and regulatory authorities** , including but not limited to the FDA, **the Centers for Medicare & Medicaid Services ("** CMS **")** , Department of Justice, the Federal Trade Commission, the HHS Office of Inspector General and other regulatory bodies. The FDC Act, Social Security Act, Public Health Service Act and other federal and state statutes and regulations **, and comparable foreign regulatory acts,** govern to varying degrees the research, development, manufacturing and commercial activities relating to prescription pharmaceutical products, including nonclinical testing, clinical research, approval, production, labeling, sale, distribution, post- market surveillance, advertising, dissemination of information, promotion, marketing, and pricing to government purchasers and government health care programs. Our manufacturing partners are subject to many of the same requirements. Companies may not promote drugs for " off- label " uses ~~–~~ — that is, uses that are not described in the product' s labeling and that differ from those approved by the FDA or other applicable regulatory ~~agencies~~ **authorities** . However, a company may share truthful and not misleading information that is otherwise consistent with the product' s labeling. A company that is found to have improperly promoted off- label uses may be subject to significant liability, including civil and administrative remedies as well as criminal sanctions. In addition, management' s attention could be diverted from our business operations and our reputation could be damaged. The federal health care program Anti- Kickback ~~statute~~ **Statute** prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any health care item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted broadly to apply to arrangements that pharmaceutical companies have with prescribers, purchasers and formulary managers, among others. Further, the PPACA, among other things, amends the intent requirement of the federal ~~anti~~ **Anti** - ~~kickback~~ **Kickback** ~~statute~~ **Statute** so that a person or entity no longer needs to have actual knowledge of this statute or specific intent to

violate it. In addition, the PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal ~~anti~~ **Anti** - ~~kickback~~ **Kickback** ~~statute~~ **Statute** constitutes a false or fraudulent claim for purposes of the civil False Claims Act. Although there are a number of statutory exceptions and regulatory safe harbors under the federal ~~anti~~ **Anti** - ~~kickback~~ **Kickback** ~~statute~~ **Statute** protecting certain common manufacturer business arrangements and activities from prosecution, the exceptions and safe harbors are drawn narrowly and an arrangement must meet all of the conditions specified in order to be fully protected from scrutiny under the federal ~~anti~~ **Anti** - ~~kickback~~ **Kickback** ~~statute~~ **Statute** . We seek to comply with the exceptions and safe harbors whenever possible, but our practices, such as our patient assistance programs and prompt pay discounts with certain customers, may not in all cases meet all of the criteria for protection from ~~anti~~ **Anti** - ~~kickback~~ **Kickback** liability and may be subject to scrutiny. The federal false claims laws, including the federal False Claims Act, prohibit any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to get a false claim paid. Additionally, the civil monetary penalties statute imposes penalties against any person or entity that, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Many pharmaceutical and other health care companies have been investigated and have reached substantial financial settlements with the federal government under the federal False Claims Act for a variety of alleged marketing activities, including providing free product to customers with the expectation that the customers would bill federal programs for the product; providing consulting fees, grants, free travel, and other benefits to physicians to induce them to prescribe the company' s products; and inflating prices reported to private price publication services, which may be used by states to set drug payment rates under government health care programs. Companies have been prosecuted for causing false claims to be submitted because of the marketing of their products for unapproved uses. Pharmaceutical and other health care companies have also been prosecuted on other legal theories of Medicare and Medicaid fraud. Legislative and regulatory proposals have been made to expand post- approval requirements and restrict sales and promotional activities for pharmaceutical products. It is not clear whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of any Travere products, if any, may be. In addition, increased scrutiny by the U. S. Congress of the FDA' s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements. We also could become subject to government investigations and related subpoenas. Such subpoenas are often associated with previously filed qui tam actions, or lawsuits filed under seal under the federal False Claims Act. Qui tam actions are brought by private plaintiffs suing on behalf of the federal government for alleged violations of the federal False Claims Act. The time and expense associated with responding to such subpoenas, and any related qui tam or other actions, may be extensive, and we cannot predict the results of our review of the responsive documents and underlying facts or the results of such actions. Responding to government investigations, defending any claims raised, and any resulting fines, restitution, damages and penalties, settlement payments or administrative actions, as well as any related actions brought by stockholders or other third parties, could have a material impact on our reputation, business and financial condition and divert the attention of our management from operating our business. The number and complexity of both federal and state laws continues to increase, and additional governmental resources are being added to enforce these laws and to prosecute companies and individuals who are believed to be violating them. In particular, the PPACA includes a number of provisions aimed at strengthening the government' s ability to pursue ~~anti~~ **Anti** - ~~kickback~~ **Kickback** and ~~false~~ **False** ~~claims~~ **Claims Act** cases against pharmaceutical manufacturers and other healthcare entities, including substantially increased funding for healthcare fraud enforcement activities, enhanced investigative powers, amendments to the federal False Claims Act that make it easier for the government and whistleblowers to pursue cases for alleged kickback and false claim violations and public reporting of certain payments and transfers of value by certain pharmaceutical manufacturers to physicians and teaching hospitals nationwide. We anticipate that government scrutiny of pharmaceutical sales and marketing practices will continue for the foreseeable future and subject us to the risk of further government investigations and enforcement actions. Responding to a government investigation or enforcement action would be expensive and time- consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects. The U. S. Foreign Corrupt Practices Act, and similar worldwide anti- bribery laws generally prohibit companies and their intermediaries from making improper payments to government officials for the purpose of obtaining or retaining business. Our policies mandate compliance with these anti-bribery laws. We operate in parts of the world that have experienced governmental corruption to some degree and in certain circumstances, strict compliance with anti- bribery laws may conflict with local customs and practices or may require us to interact with doctors and hospitals, some of which may be state controlled, in a manner that is different than in the United States. We cannot assure that our internal control policies and procedures will protect us from reckless or criminal acts committed by our employees or agents. Violations of these laws, or allegations of such violations, could disrupt our business and result in criminal or civil penalties or remedial measures, any of which could have a material adverse effect on our business, financial condition and results of operations and could cause the market value of our common stock to decline. The federal Health Insurance Portability and Accountability Act of 1996 (" HIPAA"), created new federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third- party payers, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the federal ~~anti~~ **Anti** - ~~kickback~~ **Kickback** ~~statute~~ **Statute** , the PPACA amended the intent standard for certain healthcare fraud provisions under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Additionally, the federal Physician Payments Sunshine Act within the PPACA, and its implementing regulations, require that certain manufacturers of drugs,

devices, biologicals and medical supplies to report annually information related to certain payments or other transfers of value made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members. Moreover, the Drug Supply Chain Security Act imposes obligations on manufacturers of pharmaceutical products related to product tracking and tracing. We are not sure whether additional legislative changes will be enacted, or whether the current regulations, guidance or interpretations will be changed, or what the impact of such changes on our business, if any, may be. Also, many states have similar fraud and abuse statutes or regulations, including state anti- kickback and false claims laws, that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer. Further, certain states require implementation of commercial compliance programs and marketing codes, compliance with the pharmaceutical industry' s voluntary compliance guidelines, and compliance with the applicable compliance guidance promulgated by the federal government. Other various state level requirements include restricting payments or the provision of other items of value that may be made to healthcare providers and other potential referral sources; restricting various marketing practices; requiring prescription drug companies to report expenses relating to the marketing and promotion of drug products; requiring the posting of information relating to clinical studies and their outcomes; requiring the registration of sales representatives; requiring the reporting of certain information related to drug pricing; and requiring drug manufacturers to track and report information related to payments, gifts, compensation, and other items of value to physicians and other healthcare providers. ~~In February 2021~~ **If our operations are found to be in violation of any of the health regulatory laws described above or any other laws that apply to us** , we ~~entered into~~ **may be subject to significant penalties, including imprisonment, criminal fines, civil monetary penalties, administrative penalties, disgorgement, exclusion from participation in federal healthcare programs, contractual damages, injunctions, recall or seizure of products, total or partial suspension of production, reputational harm, administrative burdens, additional oversight and reporting obligations if we become subject to** a ~~limited co~~ **corporate integrity agreement or similar agreement to resolve allegation of non** - **compliance** ~~promotion arrangement~~ with ~~Albireo Pharma~~ **these laws** , **diminished profits and future earnings** ~~Inc. (" Albireo")~~ , ~~providing~~ **and the curtailment** ~~for~~ - **or restructuring** ~~our Cholbam dedicated sales representatives to dedicate a portion~~ of **our operations** ~~their efforts to promoting Albireo' s product~~ , ~~Bylvay (odevixibat), in~~ **any of which could adversely affect our ability to operate our business and our results of operations. We are also subject to foreign requirements comparable to those established above. Outside** the United States ~~following approval. In July 2021~~ , **interactions between pharmaceutical companies and health care professionals are also governed by strict laws, such** ~~Albireo announced that the U. S. Food & Drug Administration (" FDA") has~~ - **as national anti- bribery laws** ~~approved Bylvay (odevixibat) for the treatment~~ of ~~pruritis in patients~~ **European countries, national sunshine rules, regulations, industry self- regulation codes of conduct and physicians' codes of professional conduct. Failure to comply** with **these** ~~Progressive Familial Intrahepatic Cholestasis (" PFIC"). In addition to our activities in connection with promoting our own products, if our or Albireo' s sales representatives violate or are perceived to have violated any applicable regulatory requirement~~ **requirements** ~~in promoting Bylvay (odevixibat), we~~ could ~~become subject to investigations~~ **result in reputational risk** , ~~litigation~~ **public reprimands** , **administrative** ~~and / or~~ penalties ~~as described above~~ , **fines** ~~reputational harm, as well as contractual liabilities associated with the Albireo co- promotion agreement, any of which could have a material adverse effect on our~~ - **or imprisonment** ~~business. The limited co- promotion agreement terminated in July 2022, in accordance with our mutual agreement with Albireo to terminate the agreement upon the one- year anniversary of the July 2021 launch~~ . If we are not able to obtain and maintain required regulatory approvals, we will not be able to commercialize our products, and our ability to generate revenue will be materially impaired. Our product candidates, once approved, and the activities associated with their manufacture, marketing, distribution, and sales are subject to extensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to adhere to regulations set out by these bodies for one or more of our commercial products could prevent us from commercializing the product candidate in the jurisdiction of the regulatory authority. We have only limited experience in meeting the regulatory requirements incumbent on the sale of drugs in the United States and elsewhere, and expect to rely on third ~~-~~ parties to assist us in these processes. If these third parties fail to adequately adhere to the regulations governing drug distribution and promotion **,** we may be unable to sell our products, which could have a material effect on our ability to generate revenue. Our product candidates and the activities associated with their development and commercialization, including testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain regulatory approval for a product candidate will prevent us from commercializing the product candidate in the jurisdiction of the regulatory authority. We have only limited experience in filing and prosecuting the applications necessary to obtain regulatory approvals and expect to rely on third- party contract research organizations to assist us in this process. Securing FDA approval requires the submission of extensive nonclinical and clinical data and supporting information to the FDA for each therapeutic indication to establish the product candidate' s safety and efficacy. Securing FDA approval also requires the submission of information about the product manufacturing process to, and successful inspection of manufacturing facilities by, the FDA. Our future products may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining regulatory approval or prevent or limit commercial use **. Comparable requirements are applicable outside the United States** . Our product candidates may fail to obtain regulatory approval for many reasons, including: • our failure to demonstrate to the satisfaction of the FDA or comparable regulatory authorities that a product candidate is safe and effective for a particular indication; • the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable

regulatory authorities for approval; • our inability to demonstrate that a product candidate' s benefits outweigh its risks; • our inability to demonstrate that the product candidate presents an advantage over existing therapies; • the FDA' s or comparable regulatory authorities' disagreement with the manner in which we interpret the data from nonclinical studies or clinical trials; • failure of the third- party manufacturers with which we contract for clinical or commercial supplies to satisfactorily complete an FDA **or comparable foreign regulatory authority** pre- approval inspection of the facility or facilities at which the product is manufactured to assess compliance with the FDA' s cGMP regulations **or comparable foreign regulatory authority requirements** to assure that the facilities, methods and controls are adequate to preserve the drug' s identity, strength, quality and purity; and • a change in the approval policies or regulations of the FDA or comparable regulatory authorities or a change in the laws governing the approval process. The process of obtaining regulatory approvals is expensive, often takes many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in regulatory approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application. The FDA and non- United States regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional nonclinical, clinical or other studies. In addition, varying interpretations of the data obtained from nonclinical and clinical testing could delay, limit or prevent regulatory approval of a product candidate. Any regulatory approval we ultimately obtain may be limited or subject to restrictions or post approval commitments that render the approved product not commercially viable. Any FDA or other regulatory approval of our product candidates, once obtained, may be **suspended, varied or** withdrawn, including for failure to comply with regulatory requirements or if clinical or manufacturing problems follow initial marketing. We are subject to stringent and changing U. S. and foreign laws, regulations, **and** rules, contractual obligations **, industry standards** , policies and other obligations related to data privacy and security. Our 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; loss of customers or sales; 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, and sensitive third- party 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, contracts, and other obligations that govern the processing of personal data by us and on our behalf. 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 the Health Information Technology for Economic and Clinical Health Act (" HITECH"), and their respective implementing regulations, imposes specific requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH, through its implementing regulations, makes certain of HIPAA' s privacy and security standards directly applicable to business associates, defined as a person or organization, other than a member of a covered entity' s workforce, that creates, receives, maintains or transmits protected health information for or on behalf of a covered entity for a function or activity regulated by HIPAA as well as their covered subcontractors. ~~In addition~~ **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 ") ~~imposes obligations on~~ **, applies to personal data of consumers, business representatives, and employees who are California residents, and requires** businesses to ~~which it applies. These obligations include, without limitation, providing~~ **provide** specific disclosures in privacy notices, **and** ~~affording~~ --- **afford** California residents certain **privacy** rights related to their personal data, **such as** ~~and requiring businesses subject to the~~ **those noted below** ~~CCPA to implement certain measures to effectuate California residents' personal data rights~~ . The CCPA allows for ~~statutory~~ fines for noncompliance (up to $ 7, 500 per **intentional** violation) **and allows private litigants affected by certain data breaches to recover significant statutory damages** . Although the CCPA **(like other U. S. comprehensive privacy laws)** exempts some data processed in the context of clinical trials, the CCPA increases compliance costs and potential liability with respect to other personal data we maintain about California residents. ~~In addition,~~ **Similar laws are being considered in several** ~~the~~ **other** ~~California~~ **states, as well as at the state and local levels, and we expect more jurisdictions to pass similar laws in the future. We may also be subject to new laws governing the** ~~Privacy~~ **privacy of consumer health data, including reproductive, sexual orientation, and gender identity privacy** ~~Rights~~ **rights . For example, Washington' s My Health My Data** Act ~~of 2020~~ (" ~~CPRA~~ **MHMD** ") **broadly defines consumer health data** , ~~operative~~ **places restrictions** on **processing consumer health data** ~~January 1, 2023, expands the CCPA, by applying it to personal information of business representatives and employees, establishing a new California Privacy Protection Agency to implement and enforce the CCPA~~ (~~as amended~~ **including imposing stringent requirements for consents**) **, provides consumers certain rights with respect to their health**

data, and ~~adding~~ **creates** a ~~new~~ **private** right ~~for~~ **of action to allow** individuals to ~~correct~~ **sue for violations of** ~~their~~ -- **the law** ~~personal information~~. Other states ~~have enacted data~~ **are considering and may adopt similar laws. California also recently passed a law protecting privacy of abortion- related records and other reproductive healthcare services. 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, since we obtain consumer information from third parties through various methods. 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 ~~Virginia~~ **class action litigation** and **mass arbitration demands** ~~Colorado, both of which differ from the CPRA and become effective in 2023. Additional data privacy and security legislation has been proposed at the federal, state, and local levels in recent years. While these states, like the CCPA, also exempt some data processed in the context of clinical trials, such laws could increase our potential liability, increase compliance costs, or adversely affect our business~~. Outside the United States, an increasing number of laws, regulations, and industry standards apply to data privacy and security. For example, the European Union' s General Data Protection Regulation (" EU GDPR "), the United Kingdom' s GDPR (" UK GDPR " **) (EU GDPR and UK GDPR, collectively" 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, the ~~EU~~ GDPR imposes significant and complex burdens on processing personal data, particularly for processing " special category personal data " (such as personal data related to health and genetic information), which could be relevant to our operations in the context of our conduct of clinical trials and is of interest to relevant regulators. Under the ~~EU~~ GDPR, government regulators may impose temporary or definitive bans on data processing, as well as fines of up to 20 million euros **under the EU GDPR, 17. 5 million pounds sterling under the UK GDPR or, in each case,** or 4 % of annual global revenue, whichever is greater. Further, under the ~~EU~~ GDPR, individuals may initiate litigation related to processing of their personal data, as well as consumer protection organizations authorized at law to represent data subjects' interests. In addition, privacy advocates and industry groups around the world have proposed, and may propose, standards with which we are legally or contractually bound to comply **, or may become subject to in the future** . We ~~may~~ **are** also ~~be~~ bound by contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. Additionally, we ~~may~~ publish privacy policies, marketing materials and other statements, such as compliance with certain certifications, regarding data privacy and security. If these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators or other adverse consequences. In the ordinary course of business, we may transfer personal data from Europe and other jurisdictions to the United States or other countries. 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 United Kingdom (**"** UK **"**) have significantly restricted the transfer of personal data to the United States and other countries whose privacy laws it **generally** believes are inadequate. Other jurisdictions may adopt similarly stringent interpretations of their data localization and cross- border transfer laws, which could make it more difficult to transfer information across jurisdictions or prevent us from conducting business in certain countries. 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 and~~ **EU Standard Contractual Clauses (" EU SCCs"), the** UK' s ~~standard contractual clauses~~ **International Data Transfer Agreement / International Data Transfer Addendum to the EU SCCs, 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 applicable frameworks)** , these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on ~~these~~ -- **the** ~~measures~~ **Data Privacy Framework** to lawfully transfer personal data to the United States. If we are unable to implement a valid compliance mechanism for cross- border personal data transfers, or if the requirements for a legally- compliant transfer are too onerous, we may face significant adverse consequences, including increased exposure to regulatory actions, substantial fines and injunctions against processing or transferring personal data from Europe. Inability to import personal data from Europe to the United States may significantly and negatively impact our business operations, including by limiting our ability to conduct clinical trial activities in Europe and elsewhere; limiting our ability to collaborate with CROs, service providers, contractors and other companies that are subject to such cross- border data transfer or localization laws; the need to relocate part of or all of our business or data processing activities to other jurisdictions **(such as Europe)** at significant expense; or requiring us to increase our personal data processing capabilities and infrastructure in foreign jurisdictions at significant expense. Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activities groups. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers out of Europe for allegedly violating the GDPR' s cross- border data transfer limitations. Our obligations related to data privacy and security **(and consumers' data privacy expectations)** are quickly changing in an increasingly stringent fashion, creating ~~regulatory~~ uncertainty. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent or conflict among jurisdictions. Preparing for and complying with these obligations requires significant resources and may necessitate changes to our information technologies, systems, and practices and to those of any third parties that process personal data on our behalf. Although we endeavor to comply with all applicable data privacy and security obligations, we may at times fail (or be perceived to have failed) to do so. Moreover, despite our efforts, our personnel or third parties upon whom we rely may fail to comply with such obligations, which could negatively impact our business operations and compliance posture. For example, any failure by a third- party service provider to comply with applicable law, regulations, or contractual obligations could result in adverse effects, including proceedings against us by governmental entities or others. If we or any of our partners fail to comply or are perceived to have failed to comply with

applicable obligations, we or they could be subject to a range of regulatory actions ~~or ,~~ litigation **(including class actions), or mass arbitration demands** that could affect our or our partners' ability to commercialize our products and conduct necessary research and development, and could harm or prevent sales of the affected products, or could substantially increase the costs and expenses of commercializing and marketing our products **. In particular, plaintiffs have become increasingly more active in bringing privacy- related claims against companies, including class claims and mass arbitration demands. 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 threatened or actual government enforcement action or litigation could also generate adverse publicity and require that we devote substantial resources that could otherwise be used in other aspects of our business. Compliance with applicable federal, state, and foreign laws is difficult and time consuming, and companies that violate them may face substantial penalties. The potential sanctions include significant criminal fines, civil monetary penalties, administrative penalties, disgorgement, exclusion from participation in federal health care programs, individual imprisonment, injunctions, recall or seizure of products, total or partial suspension of production, reputational harm, administrative burdens, interruption or cessation of clinical trials, additional oversight and reporting obligations if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, diminished profits and future earnings, and the curtailment or restructuring of our operations, and other sanctions. Because of the breadth of these laws, it is possible that some of our business activities could be subject to challenge under one or more of these laws. Such a challenge, irrespective of the underlying merits of the challenge or the ultimate outcome of the matter, could have a material adverse effect on our business, financial condition, results of operations and growth prospects. **Moreover, clinical trial subjects and other individuals about whom we or our potential collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect, use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time- consuming to defend and could result in adverse publicity that could harm our business.** If our information technology systems or data, or those of third parties upon which we rely, are or were compromised, we could experience adverse impacts resulting from such compromise, including, but not limited to, regulatory investigations or actions; litigation; fines and penalties; interruptions to our **commercial** operations **,** ~~such as~~ clinical trials **or other operations** ; harm to our reputation; loss of revenue or profits; loss of sales and other adverse consequences. In the ordinary course of our business, we and our third- party service providers may process proprietary, confidential, and sensitive data, including personal data (such as health- related data and data related to our clinical trials), intellectual property, and trade secrets (collectively, sensitive information). Cyberattacks,malicious internet- based activity,and online and offline fraud are prevalent and continue to increase.These threats are becoming increasingly difficult to detect.These threats come from a variety of sources,including traditional computer " hackers," threat actors,personnel (such as through theft or misuse)," hacktivists",organized criminal threat actors,sophisticated nation- states,and nation- state- supported actors.Some actors now engage and are expected to continue to engage in cyberattacks,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, ~~including the war in Ukraine,~~ we and the third parties upon which we rely may be vulnerable to a heightened risk of these attacks,including retaliatory cyberattacks that could materially disrupt our systems and operations,supply chain,and ability to produce,sell and distribute our **products** ~~goods and services~~ . ~~We and the~~ **For example,we have** third parties upon which we rely ~~may be subject~~ to ~~a variety of~~ **support our business located in unstable regions and regions experiencing (or expected to experience) geopolitical or** other **conflicts** ~~evolving threats~~ ,including **in Israel** , **where businesses have experienced** ~~but not limited to,social- engineering attacks (including through phishing attacks),malicious code (such as viruses and~~ **an** ~~worms~~ **increase in cyberattacks in relation to the Israel / Hamas conflict.** We **and the third parties upon which we rely** may ~~,supply chain,and ability to produce,sell and distribute our goods and services.We and the third parties upon which we rely may~~ be subject to a variety of other 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 **,** ~~(such as~~ credential stuffing ~~)~~ ,credential harvesting,personnel misconduct or error,ransomware attacks,supply- chain attacks,software bugs,server malfunctions,software or hardware failures,loss of data or other information technology assets,adware,telecommunications failures **,attacks enhanced or facilitated by artificial intelligence** ,and other similar threats.In particular,ransomware attacks,including those from 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, **ability to provide our products,** disruption of clinical trials,loss of data (including data related to clinical trials),loss of income,significant extra expenses to restore data or systems,reputational loss and the diversion of funds.To alleviate the financial,operational and reputational impact of a ransomware attack,it may be preferable to make extortion payments,but we may be unwilling or unable to do so (including,for example,if applicable laws prohibit such payments).Additionally, **hybrid and** remote work has become more common and has increased risks to our information technology systems and data,as more of our employees utilize network connections,computers,and devices outside our premises or network,including working at home,while in transit,and in public locations.Future or past business transactions (such as acquisitions or integrations) could also 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** ~~Any of~~ rely upon third **parties** ~~- party service providers~~ and technologies to operate critical business systems to process sensitive information in a variety of contexts, including, without limitation, third- party

providers of cloud- based infrastructure, encryption and authentication technology, employee email, and other functions. We also rely on third **parties** ~~- party service providers~~ to provide certain products, including active pharmaceutical ingredients, to operate our business, including in China. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. While we may be entitled to damages if ~~our~~ **the** third ~~- party service providers~~ **parties upon which we rely** fail to satisfy their privacy or security- related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. In addition, supply- chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third- party partners' supply chains have not been compromised. We may share or receive sensitive information with or from third parties. Cyberattacks, malicious internet- based activity..... information technology systems and sensitive information. 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 we rely)** , but we may not be able to detect **, mitigate,** and remediate all ~~vulnerabilities because the threats and techniques used to exploit the vulnerability change frequently and are often sophisticated in nature. Therefore,~~ such vulnerabilities **including on a timely basis. Further, we may experience delays in developing and deploying remedial measures and patches designed to address identified vulnerabilities. Vulnerabilities** could be exploited **and result in** ~~but may not be detected until after~~ a security incident ~~has occurred~~ . **Any of the previously identified** ~~These vulnerabilities pose material risks to our~~ **or** ~~business. Despite~~ **similar threats could cause a security incident** ~~our~~ **or other interruption that could result** ~~efforts to identify and remediate vulnerabilities, if any,~~ in **unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive information or** our information technology systems, ~~our~~ **or** ~~efforts may not be successful and~~ **those of the third parties upon whom we rely. A security incident or other interruption** could ~~result in a material disruption~~ --- **disrupt our ability (and that** of **third parties upon whom we rely) to provide our products. We may expend significant resources** ~~our~~ **or modify our business activities (including our** ~~programs and operations. For example, the loss of~~ clinical trial **activities) to try to protect against security incidents. Certain** data **privacy** ~~from completed or ongoing clinical trials for any of our product candidates could result in delays in our regulatory approval efforts~~ and ~~significantly increase our costs~~ **security obligations require us** to **implement** ~~recover or reproduce the data. Further, we may experience delays in developing~~ and ~~deploying remedial~~ **maintain specific security** measures ~~designed~~ **, industry- standard or reasonable security measures** to ~~address any such identified vulnerabilities~~ **protect our information technology systems and sensitive information.** Applicable data security **and public company disclosure** obligations may require us to notify relevant stakeholders of ~~any~~ **certain** security incidents, including affected individuals, customers, ~~and~~ regulators **and investors** . Such disclosures are costly, and the disclosures or the failure to comply with such requirements, could lead to adverse consequences. If we (or a third party upon whom we rely) 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 information (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 cause customers to stop using our products or~~ **For** ~~services~~ **example** , ~~deter new customers~~ **the loss of clinical trial data** from ~~using~~ **completed** ~~our~~ **or ongoing clinical trials for any of our** ~~products~~ **product candidates could result in delays in** ~~or~~ **our** ~~services,~~ **regulatory approval efforts** and **significantly increase our costs to recover or reproduce the data. Whether a cybersecurity incident is reportable to our investors may not be straightforward, may take considerable time to determine, and may be subject to change as the investigation of the incident progresses, including changes that may significantly alter any initial disclosure that we provide. Moreover, experiencing a material cybersecurity incident and any mandatory disclosures could lead to** ~~negatively~~ -- **negative** ~~impact~~ **publicity, loss of customer, investor** ~~our~~ **or partner confidence in the effectiveness of our cybersecurity measures, diversion of management' s attention, governmental investigations, lawsuits, and the expenditure of significant capital and other resources. Our contracts may not contain limitations of** ~~ability~~ **liability ,** ~~to grow~~ and ~~operate~~ **even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages,** ~~our~~ **or** ~~business~~ **claims related to our data privacy and security obligations. In addition, our insurance coverage may not be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices or that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims** . In addition to experiencing a security incident, third parties may gather, collect, or infer sensitive information 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. **Sensitive information** ~~Our contracts may not contain limitations~~ of **us or our customers could also** ~~liability, and even where they do, there can~~ be **leaked, disclosed,** ~~no assurance that limitations of liability in our~~ **or revealed as a result of** ~~contracts are sufficient to protect us from liabilities, damages, or claims related to our~~ **or in connection with** ~~data privacy and security obligations. In addition, our insurance coverage may not be adequate or~~ **our employee' s, personnel' s,** ~~sufficient to protect us from or to mitigate liabilities arising out of our~~ **or vendor' s use of generative AI technologies** ~~privacy and security practices or that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims~~ . Uncertainties in the interpretation and application of existing, new and proposed tax laws and regulations could materially affect our tax obligations and effective tax rate. The tax regimes to which we are subject or under which we operate are unsettled and may be subject to significant change. The issuance of additional guidance related to existing or future tax laws, or changes to tax

laws or regulations proposed or implemented by the current or a future U. S. presidential administration, Congress, or taxing authorities in other jurisdictions, including jurisdictions outside of the United States, could materially affect our tax obligations and effective tax rate. To the extent that such changes have a negative impact on us, including as a result of related uncertainty, these changes may adversely impact our business, financial condition, results of operations, and cash flows. 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. 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. If such a challenge or disagreement were to occur, and our position was not sustained, 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. Effective January 1, 2022, the Tax Cuts and Jobs Act **of 2017** 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 of research activities conducted outside the United States. Unless the United States Department of the Treasury issues regulations that narrow the application of this provision to a smaller subset of our research and development expenses or the provision is deferred, modified, or repealed by Congress, in future years we may experience a material decrease in our cash flows from operations and an offsetting similarly sized increase in our net deferred tax assets over these amortization periods. The actual impact of this provision will depend on multiple factors, including the amount of research and development expenses we will incur and whether we conduct our research and development activities inside or outside the United States and our overall net operating loss position. Our ability to use net operating loss carryforwards and certain other tax attributes to offset future taxable income and taxes may be subject to limitations. Under current law, our federal net operating losses (" NOLs") generated in tax years beginning after December 31, 2017, may be carried forward indefinitely, but the deductibility of such federal NOLs is limited to 80 % of taxable income. As of December 31, ~~2022~~ **2023**, we had federal ~~net operating loss (" NOL~~ **NOLs** ~~")~~ of $ ~~90~~ **154**. ~~2~~ **3** million. 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, and corresponding provisions of state law, if a corporation undergoes an " ownership change, " which is generally defined as a greater than 50 % change, by value, in its equity ownership over a three- year period, the corporation' s ability to use its pre- change NOL carryforwards and other pre- change U. S. tax attributes (such as research tax credits) to offset its post- change income or taxes may be limited **. We completed a study to analyze whether any ownership changes occurred through March 31, 2023, and determined no ownership changes occurred. We are in the process of updating our analysis of owner shifts to determine whether an ownership change occurred since March 31, 2023**. It is possible that we have experienced an ownership change in the past. In addition, we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. As a result, our federal NOL carryforwards may be subject to a percentage limitation if used to offset income in tax years following an ownership change. In addition, it is possible that we have in the past undergone, and in the future may undergo, additional ownership changes that could limit our ability to use all of our pre- change NOL carryforwards and other pre- change tax attributes (such as research tax credits) to offset our post- change income or taxes. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. In addition, at the state level, there may be periods during which the use of NOL carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, we may be unable to use all or a material portion of our NOL carryforwards and other tax attributes, which would harm our future operating results by effectively increasing our future tax obligations. Changes in funding for the FDA, the SEC and other government agencies **or regulatory authorities** could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner **,** or otherwise prevent 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, 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 the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new ~~drugs~~ **therapies** to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U. S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, or if the FDA or EDA experience resource constraints, it could significantly impact the ability of the applicable regulatory agency to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations **. Comparable considerations may be applicable in relation to foreign regulatory authorities**. Our business could be negatively impacted by environmental, social and corporate governance (ESG) matters or our reporting of such matters. There is an increasing focus from certain investors,

employees, partners, and other stakeholders concerning ESG matters. While we have internal efforts directed at ESG matters and preparations for increased future disclosures, we may be perceived by certain stakeholders as not acting responsibly in connection with these matters, which could negatively impact us. Moreover, the SEC has recently proposed, and may continue to propose, certain mandated ESG reporting requirements, such as the SEC' s proposed rules designed to enhance and standardize climate- related disclosures, which, if finally approved, would significantly increase our compliance and reporting costs and may also result in disclosures that certain investors or other stakeholders deem to negatively impact our reputation and / or that harm our stock price. In addition, given our business model, we currently do not report our environmental emissions and absent a legal requirement to do so we currently do not plan to report our environmental emissions, and lack of reporting could result in certain investors declining to invest in our common stock. The withdrawal of the United Kingdom from the European Union, commonly referred to as " Brexit, " may adversely impact our ability to obtain regulatory approvals of our product candidates in the United Kingdom, result in restrictions or imposition of taxes and duties for importing our product candidates into the United Kingdom, and may require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the United Kingdom. **The** ~~Following the result of a referendum in 2016, the~~ United Kingdom ~~left~~ **' s (" UK ") withdrawal from** the **EU** ~~European Union~~ on January 31, 2020, commonly referred to as ~~"~~ Brexit ~~." Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union~~ , **has changed** the **regulatory** ~~United Kingdom was subject to a transition period that ended December 31, 2020, or the Transition Period, during which EU rules continued to apply. A trade and cooperation agreement, or the Trade and Cooperation Agreement, that outlines the future trading~~ relationship between the **UK** ~~United Kingdom~~ and the **EU** ~~European Union was agreed in December 2020 and has been in effect since January 1, 2022~~ . ~~Since a significant proportion of~~ **The Medicines and Healthcare products Regulatory Agency, or MHRA, is now** the **UK' s standalone regulator for medicinal products and medical devices. Great Britain (England, Scotland and Wales) is now a third country to the EU. Northern Ireland will, with regard to EU regulations, continue to follow the EU regulatory rules for now. The UK** regulatory framework in **relation** ~~the United Kingdom applicable~~ to ~~our business and our product candidates~~ **clinical trials is governed by the Medicines for Human Use (Clinical Trials) Regulations 2004, as amended, which** is derived from **the CTD, as implemented into UK national law through secondary legislation. On January 17, 2022, the MHRA launched an eight- week consultation on reframing the UK legislation for clinical trials, and which aimed to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The UK Government published its response to the consultation on March 21, 2023 confirming that it would bring forward changes to the legislation. These resulting legislative amendments will determine how closely the UK regulations will align with the CTR. In October 2023, the MHRA announced a new Notification Scheme for clinical trials which enables a more streamlined and risk- proportionate approach to initial clinical trial applications for Phase 4 and low- risk Phase 3 clinical trial applications. Marketing authorizations in the UK are governed by the Human Medicines Regulations (SI 2012 / 1916), as amended. Since January 1, 2021, an applicant for the** EU ~~directives and regulations~~ **centralized procedure marketing authorization can no longer be established in the UK. As a result** , **since this date, companies established in the UK cannot use the EU centralized procedure and instead must follow one of the UK national authorization procedures or one of the remaining post-** Brexit **international cooperation procedures** ~~has had, and may continue~~ to **obtain** ~~have,~~ a **marketing authorization** ~~material impact on the regulatory regime with respect~~ to **market** ~~the development, manufacture, importation, approval and commercialization of our product~~ **products** ~~candidates~~ in the ~~United Kingdom~~ **UK. All existing EU marketing authorizations** ~~or~~ **for centrally authorized** ~~, to the extent any development of our product~~ **products were automatically converted** ~~candidates takes place in the United Kingdom, the European Union. For~~ ~~-~~ **or** ~~example~~ **grandfathered into UK marketing authorization** , **effective in** Great Britain **only, free of charge on January 1, 2021, unless the marketing authorization holder opted- out of this possibility. Northern Ireland currently remains within the scope of EU authorizations in relation to centrally authorized medicinal products. Accordingly, until the Windsor Framework is implemented in Northern Ireland on January 1, 2025, products falling within the scope of the EU centralized procedure can only be authorized through UK national authorization procedures in Great Britain. The MHRA has also introduced changes to national marketing authorization procedures. This includes introduction of procedures to prioritize access to new medicines that will benefit patients, including a 150- day assessment route, a rolling review procedure and the International Recognition Procedures which entered into application on January 1, 2024. Since January 1, 2024, the MHRA may rely on the International Recognition Procedure, or IRP, when reviewing certain types of marketing authorization applications. This procedure is available for applicants for marketing authorization who have already received an authorization for the same product from a reference regulator. These include the FDA, the EMA, and national competent authorities of individual EEA countries. A positive opinion from the EMA and CHMP, or a positive end of procedure outcome from the mutual recognition or decentralized procedures are considered to be authorizations for the purposes of the IRP. There** is no **pre** ~~longer covered by the centralized procedures for obtaining EU~~ ~~-~~ ~~wide~~ marketing authorization ~~from~~ **orphan designation for medicinal products in** the ~~EMA~~ **UK. Instead** , ~~and a separate~~ **the MHRA reviews applications for orphan designation in parallel to the corresponding** marketing authorization **application. The criteria are essentially the same as those in the EU, but have been tailored for the market. This includes the criterion that prevalence of the condition in Great Britain, rather than the EU, must not be more than five in 10, 000. Upon the grant of a marketing authorization with orphan status, the medicinal product will benefit from up to 10 years of market exclusivity from similar products in the approved orphan indication. The start of this market exclusivity period** will be ~~required to market our~~ **set from the date of first approval of the** product ~~candidates~~ in Great Britain ~~. Centralized marketing authorizations continue to allow marketing in Northern Ireland. While the Trade and Cooperation Agreement provides for the tariff- free trade of medicinal products between the United Kingdom and the European Union there~~

~~are additional non- tariff costs which did not exist prior to the end of the Transition Period. Further, should the United Kingdom further diverge from the European Union from a regulatory perspective in relation to medicinal products, tariffs could be put into place in the future. We could therefore, both now and in the future, face significant additional expenses (when compared to the position prior to the end of the Transition Period) to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import / export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non- tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the European Union and the United Kingdom~~ . Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses. Our operations, and those of our third- party manufacturers, CROs and other contractors and consultants, could be subject to disruptions resulting from earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, health epidemics or pandemics, wars and other geopolitical conflicts ~~(including related to Russia' s invasion of Ukraine)~~ , and other natural or man- made disasters or business interruptions, for which we are predominantly self- insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. Our corporate headquarters are located in San Diego, California, an area prone to wildfires and earthquakes. These and other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third- party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. Any disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, could have a material adverse effect on our business. In addition, we rely on third- party manufacturers, some of whom are located in China, to manufacture API for FILSPARI and certain of our product candidates. Any disruption in production or inability of our manufacturers in China to produce or ship adequate quantities to meet our needs, whether as a result of a natural disaster or other causes (such as staffing shortages, ~~COVID- 19~~ or ~~other~~ **a** health epidemic or pandemic), could impair our ability to meet commercial demand for FILSPARI, to operate our business on a day- to- day basis and to continue our research and development of our product candidates. In addition, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the policies of the United States or Chinese governments (such as tariffs on chemical intermediates we use that are manufactured in China), political unrest or unstable economic conditions in China. Any recall of the manufacturing lots or similar action regarding our API used in clinical trials could delay the trials or detract from the integrity of the trial data and its potential use in future regulatory filings. In addition, manufacturing interruptions or failure to comply with regulatory requirements by any of these manufacturers could significantly delay clinical development of potential products and reduce third- party or clinical researcher interest and support of proposed trials. These interruptions or failures could also impede commercialization of our product candidates and impair our competitive position. We have **previously** identified a material weakness in our internal control over financial reporting ~~, and~~ **. If additional material weaknesses in** our **internal control over** financial ~~controls and procedures may not~~ **reporting are discovered or occur** in the future ~~be sufficient to ensure timely and reliable reporting of financial information~~ , ~~which could, if not remediated, result in a material misstatement in~~ our **consolidated** financial statements **may contain material misstatements** and **we could be required to restate our financial results, which** could adversely affect our ~~future results of operations and our~~ stock price **and result in an inability to maintain compliance with applicable stock exchange listing requirements. We previously concluded that there was a matter that constituted a material weakness in our internal control over financial reporting that has since been remediated** . A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our annual or interim consolidated financial statements will not be prevented or detected on a timely basis. As disclosed under Item 9A of ~~this~~ **our** Annual Report **on Form 10- K for the fiscal year ended December 31, 2022** , there was a material weakness in our internal control over financial reporting as of December 31, 2022 because we did not design effective controls and procedures to evaluate the accounting for a certain pre- launch inventory contract affecting the timing of recognition of research and development expense. As a result of the material weakness, we **added** ~~are adding~~ controls ~~to ensure~~ **for the** timely accounting evaluation of research and development **contracts that were intended to ensure appropriate** expense recognition of certain pre- launch inventory. ~~However~~ **As of December 31** , **2023, the material weakness had been remediated. If additional material weaknesses in our internal control over financial reporting are discovered or occur in the future, or** if we are ~~unable to remediate this material weakness, or are otherwise~~ unable to maintain effective internal control over financial reporting or disclosure controls and procedures **for any reason** , our ability to record, process and report financial information accurately, and to prepare financial statements within required time periods, could be adversely affected, which could subject us to litigation or investigations requiring management resources and payment of legal and other expenses and negatively impact the price of our common stock. In addition, we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources. Furthermore, investor perceptions of our company may suffer as a result of the ~~current~~ **previous** material weakness or any future material weakness in our internal controls, and this could cause a decline in the market price of our stock. Any failure of our internal control over financial reporting could have a material adverse effect on our stated operating results, result in an adverse opinion on our internal control over financial reporting from our independent registered public accounting firm, and harm our reputation.

Adverse developments affecting the financial services industry could adversely affect our current and projected business operations and our financial condition and results of operations. Adverse developments that affect financial institutions,

such as events involving liquidity that are rumored or actual, have in the past and may in the future lead to bank failures and market- wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank (SVB) was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation (FDIC) as receiver. Similarly, on March 12, 2023, Signature Bank and Silvergate Capital Corp. were each swept into receivership. In addition, on May 1, 2023, the FDIC seized First Republic Bank and sold its assets to JPMorgan Chase & Co. It is uncertain whether the U. S. Department of Treasury, FDIC and Federal Reserve Board will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions, or that they would do so in a timely fashion. Although we assess our banking relationships as we believe necessary or appropriate, our access to cash in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect the financial institutions with which we have banking relationships. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. These factors could also include factors involving financial markets or the financial services industry generally. The results of events or concerns that involve one or more of these factors could include a variety of material and adverse impacts on our current and projected business operations and our financial condition and results of operations. These could include, but may not be limited to, delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets; or termination of cash management arrangements and / or delays in accessing or actual loss of funds subject to cash management arrangements. In addition, widespread investor concerns regarding the U. S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our financial and / or contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity and our current and / or projected business operations and financial condition and results of operations. We maintain our cash at financial institutions, often in balances that exceed federally insured limits. We maintain the majority of our cash and cash equivalents in accounts at banking institutions in the United States that we believe are of high quality. Cash held in these accounts often exceed the FDIC insurance limits. If such banking institutions were to fail, we could lose all or a portion of amounts held in excess of such insurance limitations. In the event of failure of any of the financial institutions where we maintain our cash and cash equivalents, there can be no assurance that we would be able to access uninsured funds in a timely manner or at all. Any inability to access or delay in accessing these funds could adversely affect our business and financial position. Risks Related to our Indebtedness and Investments Our indebtedness could adversely affect our financial condition. As of December 31, ~~2022~~ **2023** , we had approximately $ 385 million of total debt outstanding, classified as long term. As a result of our indebtedness, a portion of our cash flow will be required to pay interest and principal on the 2025 Notes and 2029 Notes if the notes are not converted to shares of common stock prior to maturity. We may not generate sufficient cash flow from operations or have future borrowings available to enable us to repay our indebtedness or to fund other liquidity needs. Our indebtedness pursuant to the 2025 Notes and 2029 Notes could have important consequences. For example, it could: • make it more difficult for us to satisfy our obligations with respect to any other debt we may incur in the future; • increase our vulnerability to general adverse economic and industry conditions; • require us to dedicate a substantial portion of our cash flow from operations to payments on our indebtedness and related interest, thereby reducing the availability of our cash flow to fund working capital, capital expenditures and other general corporate purposes; • limit our flexibility in planning for, or reacting to, changes in our business and the industry in which we operate; • increase our cost of borrowing; • place us at a competitive disadvantage compared to our competitors that may have less debt; and • limit our ability to obtain additional financing for working capital, capital expenditures, acquisitions, debt service requirements or general corporate purposes. We expect to use cash flow from operations and outside financings to meet our current and future financial obligations, including funding our operations, debt service and capital expenditures. Our ability to make these payments depends on our future performance, which will be affected by financial, business, economic and other factors, many of which we cannot control. Our business may not generate sufficient cash flow from operations in the future, which could result in our being unable to repay indebtedness, or to fund other liquidity needs. If we do not generate sufficient cash from operations, we may be forced to reduce or delay our business activities and capital expenditures, sell assets, obtain additional debt or equity capital or restructure or refinance all or a portion of our debt, including the 2025 Notes and 2029 Notes, on or before maturity. We cannot make any assurances that we will be able to accomplish any of these alternatives on terms acceptable to us, or at all. In addition, the terms of existing or future indebtedness may limit our ability to pursue any of these alternatives. In addition, we may from time to time seek to retire or purchase our outstanding debt, including the 2025 Notes or 2029 Notes, through cash purchases and / or exchanges for equity securities, in open market purchases, privately negotiated transactions or otherwise. Such repurchases or exchanges, if any, will depend on prevailing market conditions, our liquidity requirements, contractual restrictions, and other factors. The amounts involved in any such transactions, individually or in the aggregate, may be material. Further, any such purchases or exchanges may result in us acquiring and retiring a substantial amount of such indebtedness, which could impact the trading liquidity of such indebtedness. We may be unable to raise the funds necessary to repurchase the 2025 Notes and 2029 Notes for cash following a fundamental change, or to pay any cash amounts due upon conversion, and our

future indebtedness may limit our ability to repurchase the 2025 Notes and 2029 Notes or pay cash upon their conversion. Noteholders may require us to repurchase their 2025 Notes and 2029 Notes following a fundamental change at a cash repurchase price generally equal to the principal amount of the 2025 Notes and 2029 Notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date. In addition, upon conversion, we would satisfy part or all of our conversion obligation in cash unless we elected to settle conversions solely in shares of our common stock. We may not have enough available cash or be able to obtain financing at the time we are required to repurchase the 2025 Notes and 2029 Notes or pay the cash amounts due upon conversion of the 2025 Notes and 2029 Notes. In addition, applicable law, regulatory authorities and the agreements governing our future indebtedness may restrict our ability to repurchase the 2025 Notes and 2029 Notes or pay the cash amounts due upon conversion of the 2025 Notes and 2029 Notes. Our failure to repurchase the 2025 Notes and 2029 Notes or to pay the cash amounts due upon conversion of the 2025 Notes and 2029 Notes when required will constitute a default under the base and supplemental indentures that govern the 2025 Notes and 2029 Notes, which we refer to collectively as the " indenture. " We may not have sufficient funds to satisfy all amounts due under the other indebtedness and the 2025 Notes and 2029 Notes. A default under the 2025 Notes or 2029 Notes may have a material adverse effect on our financial condition. If an event of default under the 2025 Notes or 2029 Notes occurs, the principal amount of the 2025 Notes or the 2029 Notes, as applicable, plus accrued and unpaid interest (including additional interest, if any) may be declared immediately due and payable, subject to certain conditions set forth in the indenture governing such notes. Events of default include, but are not limited to: • failure to pay (for more than 30 days) interest when due; • failure to pay principal when due; • failure to deliver shares of common stock upon conversion of a 2025 Note or 2029 Note; • failure to provide notice of a fundamental change; • acceleration on our other indebtedness in excess of $ 10 million (other than indebtedness that is non- recourse to us); or • certain types of bankruptcy or insolvency involving us. Accordingly, the occurrence of a default under the 2025 Notes or 2029 Notes, unless cured or waived, may have a material adverse effect on our results of operations. Provisions of the 2025 Notes and 2029 Notes could discourage an acquisition of us by a third party. Certain provisions of the 2025 Notes and 2029 Notes could make it more difficult or more expensive for a third party to acquire us. Upon the occurrence of certain transactions constituting a fundamental change, holders of the 2025 Notes and 2029 Notes will have the right, at their option, to require us to repurchase all of their 2025 Notes and 2029 Notes or any portion of the principal amount of such Notes in integral multiples of $ 1, 000. We may also be required to increase the conversion rate for conversions in connection with certain fundamental changes. Conversion of the Notes may dilute the ownership interest of existing stockholders, including holders who had previously converted their 2025 Notes or 2029 Notes. To the extent we issue shares of common stock upon conversion of the 2025 Notes or 2029 Notes, the conversion of some or all of the 2025 Notes or 2029 Notes will dilute the ownership interests of existing stockholders. Any sales in the public market of shares of the common stock issuable upon such conversion could adversely affect prevailing market prices of shares of our common stock. In addition, the existence of the 2025 Notes and 2029 Notes may encourage short selling by market participants because the conversion of the 2025 Notes and 2029 Notes could depress the price of shares of our common stock. General Risk Factors Unstable market, economic and geopolitical conditions may have serious adverse consequences on our business, financial condition and stock price. The global credit and financial markets have experienced extreme volatility and disruptions, including as a result of inflation and ~~rising~~ **high** interest rates, **bank failures** ~~COVID- 19~~ , **wars, armed conflicts** ~~Russia' s invasion of Ukraine~~ and global geopolitical tension, and may experience disruptions in the future. These disruptions can result in severely diminished liquidity and credit availability, increase in inflation, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment, higher inflation, or ~~continued~~ unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our operations, growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans ~~. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive an economic downturn or rising inflation, which could directly affect our ability to attain our operating goals on schedule and on budget~~ . Other international and geopolitical events could also have a serious adverse impact on our business. For instance, in February 2022, Russia initiated military action against Ukraine. In response, the United States and certain other countries imposed significant sanctions and trade actions against Russia and could impose further sanctions, trade restrictions, and other retaliatory actions. While we cannot predict the broader consequences, the conflict and retaliatory and counter- retaliatory actions could materially adversely affect global trade, currency exchange rates, inflation, regional economies, and the global economy, which in turn may increase our costs, disrupt our supply chain, impair our ability to raise or access additional capital when needed on acceptable terms, if at all, or otherwise adversely affect our business, financial condition, and results of operations.