Risk Factors Comparison 2025-02-27 to 2024-03-01 Form: 10-K

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

An investment in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below before deciding whether to make an investment decision with respect to shares of our common stock. You should also refer to the other information contained in this Annual Report on Form 10- K, including " Management' s Discussion and Analysis of Financial Condition and Results of Operations " and our audited consolidated financial statements and related notes. Our business, financial condition, results of operations and prospects could be materially and adversely affected by any of these risks or uncertainties. In any such case, the trading price of our common stock could decline, and you could lose all or part of your investment. We caution you that the risks, uncertainties and other factors referred to below and elsewhere in this Annual Report on Form 10- K may not contain all of the risks, uncertainties and other factors that may affect our future results and operations ~~. Moreover~~ , **and** new risks will emerge from time to time. It is not possible for our management to predict all risks. **Moreover, some of the factors, events and contingencies discussed below may have occurred in the past, but the disclosures below are not representations as to whether or not the factors, events or contingencies have occurred in the past, and instead reflect our beliefs and opinions as to the factors, events or contingencies that could materially and adversely affect us in the future.** Risk Factor Summary ~~Investing in our common stock involves significant risks. You should carefully consider the risks described below before making a decision to invest in our common stock. If we are unable to successfully address these risks and challenges, our business, financial condition, results of operations, or prospects could be materially adversely affected. In such case, the trading price of our common stock would likely decline, and you may lose all or part of your investment. Below is a summary of some of the risks we face.~~ • We are a clinical- stage biopharmaceutical company with a limited operating history and no products approved for commercial sale. We have incurred net losses since our inception, we expect to incur significant and increasing operating losses and we may never be profitable. Our stock is a highly speculative investment. • Our business depends on the success of pegozafermin, our only product candidate under clinical development, which has not completed a pivotal trial. If we are unable to obtain regulatory approval for and successfully commercialize pegozafermin or other future product candidates, or we experience significant delays in doing so, our business will be materially harmed. • Clinical drug development involves a lengthy and expensive process with uncertain timelines and uncertain outcomes, and the results of prior preclinical or clinical trials are not necessarily predictive of our future results. • We will require substantial additional capital to finance our operations, which may not be available to us on acceptable terms, or at all. As a result, we may not complete the development and commercialization of pegozafermin or develop new product candidates. • If we experience delays in clinical testing, our commercial prospects will be adversely affected, our costs may increase and our business may be harmed. • If we encounter difficulties in enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected. • We have relied on, and expect to continue to rely on, third- party manufacturers and vendors to produce and release pegozafermin or any future product candidates. Any failure by a third- party to produce and release acceptable product candidates for us pursuant to our specifications and regulatory standards may delay or impair our ability to initiate or complete our clinical trials, obtain and maintain regulatory approvals or commercialize approved products. • Pegozafermin and any future product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval or limit the commercial profile of an approved label. • We are developing pegozafermin for the treatment of ~~NASH~~ **MASH** ~~, an~~ **and** ~~indication for which there are no approved products, and the treatment of~~ SHTG. The requirements for approval of pegozafermin by the FDA and comparable foreign regulatory authorities may be difficult to predict and may change over time, which makes it difficult to predict the timing and costs of the clinical development. • Lack of efficacy, adverse events or undesirable side effects may emerge in clinical trials conducted by third parties developing FGF product candidates, which could adversely affect our stock price, our ability to attract additional capital and our development program. • Interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data. • The manufacture of biologic products is complex and we are subject to many manufacturing risks, any of which could substantially increase our costs and limit supply of our products. • We face substantial competition, which may result in others discovering, developing or commercializing competing products before or more successfully than ~~us~~ **we do** . • Unstable market and economic conditions, inflation, ~~increases~~ **fluctuations** in interest rates, natural disasters, public health crises ~~such as the COVID- 19 pandemic~~ , political crises, geopolitical events, such as the crisis in Ukraine and Israel, or other macroeconomic conditions, may have serious adverse consequences on our business and financial condition. • Our ~~2023~~ Loan Agreement contains certain covenants that could adversely affect our operations and, if an event of default were to occur, we could be forced to repay any outstanding indebtedness sooner than planned and possibly at a time when we do not have sufficient capital to meet this obligation. • Pegozafermin has not received regulatory approval. If we are unable to obtain regulatory approvals to market pegozafermin or any future product candidates, our business will be adversely affected. • Our success depends upon our ability to obtain and maintain intellectual property protection for our products and technologies. • We rely on a license from Teva and a sublicense from ratiopharm to patents and know- how related to glycoPEGylation technology that are used in the development, manufacture and commercialization of pegozafermin. Any termination or loss of significant rights, including the right to glycoPEGylation technology, or breach, under these agreements or any future license agreement related to our product candidates, would materially and adversely affect our ability to continue the development and commercialization of the related

product candidates. Risks Related to Our Business and Industry We are a clinical- stage biopharmaceutical company with a limited operating history that may make it difficult to evaluate the success of our business to date and to assess our future viability. We commenced operations in 2018, and to date, our operations have been focused on organizing and staffing our company, raising capital, acquiring our initial product candidate, pegozafermin **,** and licensing certain related technology, conducting research and development activities, including preclinical studies and clinical trials, and providing general and administrative support for these operations. Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect and / or an acceptable safety profile, gain regulatory approval and become commercially viable. We have no products approved for commercial sale, we have not generated any revenue from product sales to date and we continue to incur significant research and development and other expenses related to our ongoing operations. We have limited experience as a company conducting clinical trials and no experience as a company commercializing any products. Pegozafermin is in development and, to date, we have not generated any revenue from the licensing or commercialization of pegozafermin. We will not be able to generate product revenue unless and until pegozafermin or any future product candidate, alone or with future partners, successfully completes clinical trials, receives regulatory approval and is successfully commercialized. As pegozafermin is in development, we do not expect to receive revenue from it for a number of years, if ever. Although we may seek to obtain revenue from collaboration or licensing agreements with third parties, we currently have no such agreements that could provide us with material, ongoing future revenue and we may never enter into any such agreements. We are not profitable and have incurred net losses since our inception. Consequently, predictions about our future success or viability may not be as accurate as they would be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products. We have spent, and expect to continue to spend, significant resources to fund research and development of, and seek regulatory approvals for, pegozafermin and any future product candidates. We expect to incur substantial and increasing operating losses over the next several years as our research and development, clinical trials and manufacturing activities increase. In addition, because of the numerous risks and uncertainties associated with pharmaceutical product development, including that our product candidates may not advance or may take longer than expected to advance through development or may not achieve the endpoints of applicable clinical trials, we are unable to predict the timing or amount of increased expenses, or if or when we will achieve or maintain profitability. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. The net losses we incur may fluctuate significantly from quarter- to- quarter such that a period- to- period comparison of our results of operations may not be a good indication of our future performance. Even if we eventually generate product revenue, we may never be profitable and, if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. The primary focus of our product development is pegozafermin for the treatment of patients with ~~NASH~~ **MASH** and the treatment of patients with SHTG. Currently, pegozafermin is our only product candidate under clinical development. This may make an investment in our company riskier than similar companies that have multiple product candidates in active development and that therefore may be able to better sustain a failure of a lead candidate. Successful continued development and ultimate regulatory approval of pegozafermin for the treatment of ~~NASH~~ **MASH** or SHTG is critical to the future success of our business. We have invested, and will continue to invest, a significant portion of our time and financial resources in the clinical development of pegozafermin. If we cannot successfully develop, obtain regulatory approval for and commercialize pegozafermin, we may not be able to continue our operations. The future regulatory and commercial success of pegozafermin is subject to a number of risks, including that, if approved for ~~NASH~~ **MASH** or SHTG, pegozafermin will likely compete with products that may reach approval for the treatment of ~~NASH~~ **MASH** prior to pegozafermin, products that are currently approved for the treatment of SHTG and the off- label use of currently marketed products for ~~NASH~~ **MASH** and SHTG. Pegozafermin and any future product candidates will be subject to rigorous and extensive clinical trials and extensive regulatory approval processes implemented by the FDA and comparable foreign regulatory authorities before obtaining marketing approval from these regulatory authorities. The drug development and approval process is lengthy and expensive, and approval is never certain. Investigational new drugs, such as pegozafermin, may not prove to be safe and effective in clinical trials. We have limited direct experience as a company in conducting pivotal trials required to obtain regulatory approval and we expect that the Phase 3 trials we are conducting will be more expansive and complex than the trials we have conducted to date. We may be unable to conduct clinical trials at preferred sites, enlist clinical investigators, enroll sufficient numbers of participants, procure sufficient drug supply or begin or successfully complete clinical trials in a timely fashion, if at all. In addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We may be unable to design and execute a clinical trial to support regulatory approval. Even if an ongoing clinical trial is successful, it may be insufficient to demonstrate that pegozafermin is safe or effective for registration purposes. There is a high failure rate for drugs and biologic products proceeding through clinical trials. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of pegozafermin or any future product candidate may not be predictive of the results of later- stage clinical studies or trials and the results of studies or trials in one set of patients or line of treatment may not be predictive of those obtained in another. In fact, many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late- stage clinical trials even after achieving promising results in preclinical studies and earlier stage clinical trials. In addition, data obtained from preclinical and clinical activities is subject to varying interpretations, which may delay, limit or prevent regulatory approval. It is impossible to predict when or if pegozafermin or any future product candidate will prove effective or safe in humans or will receive regulatory approval. Owing in part to the complexity of biological pathways, pegozafermin or any future product candidate may not demonstrate in patients the biochemical and pharmacological properties we anticipate based on laboratory studies or earlier stage clinical trials, and they may interact with human biological systems or other drugs in unforeseen, ineffective or harmful

ways. The number of patients exposed to product candidates and the average exposure time in the clinical development programs may be inadequate to detect rare adverse events or findings that may only be detected once a product candidate is administered to more patients and for greater periods of time. To date, our Phase 1a, Phase 1b / 2a and Phase 2 clinical trials have involved small patient populations and, because of the small sample size in such trials, the results of those clinical trials may be subject to substantial variability, including the inherent variability associated with biopsies in ~~NASH~~ **MASH** patients, and may not be indicative of either future interim results or final results in future trials of patients with liver or cardio- metabolic diseases. If we are unable to successfully demonstrate the safety and efficacy of pegozafermin or other future product candidates and receive the necessary regulatory approvals, our business will be materially harmed. As a clinical- stage biopharmaceutical company, our operations have consumed significant amounts of cash since our inception. We expect our research and development expenses to increase in connection with our ongoing activities, particularly as we conduct **Phase 3** clinical trials of ~~and~~ **,** seek regulatory approval for **and prepare for commercialization of** pegozafermin. We believe our existing cash, cash equivalents and marketable securities **, supplemented by $ 269. 9 million in net proceeds from our February 2025 equity offering,** will be sufficient to fund our projected operating requirements for a period of at least one year ~~from~~ **following** the ~~date~~ **filing of** this ~~Annual Report on~~ Form 10- K ~~is filed with the SEC~~ . We will require additional capital to discover, develop, obtain regulatory approval for and commercialize pegozafermin and any future product candidates. Our ability to complete new and ongoing clinical trials for pegozafermin may be subject to our ability to raise additional capital. We do not have any committed external source of funds other than as a result of any sales that we may make **under** ~~pursuant to~~ the **2023** ~~Sales Agreement for our~~ ATM Facility (**as** defined ~~above~~ **below**) and proceeds from our ~~2023~~ Loan Agreement, which are subject to the achievement of certain milestones and / or consent of the lenders ~~. We may also receive additional funds from the exercise of outstanding warrants~~ . We expect to finance future cash needs through public or private equity or debt offerings or product collaborations. Additional capital may not be available in sufficient amounts or on reasonable terms, if at all. The current market environment for small biotechnology companies, like 89bio, and broader macroeconomic factors may preclude us from successfully raising additional capital. If we do not raise additional capital, we may not be able to expand our operations or otherwise capitalize on our business opportunities, our business and financial condition will be negatively impacted and we may need to: significantly delay, scale back or discontinue research and discovery efforts and the development or commercialization of any product candidates or cease operations altogether; seek strategic alliances for research and development programs when we otherwise would not, or at an earlier stage than we would otherwise desire or on terms less favorable than might otherwise be available; or relinquish, or license on unfavorable terms, our rights to technologies or any product candidates that we otherwise would seek to develop or commercialize ourselves. In addition, if pegozafermin receives approval and is commercialized, we will be required to make milestone and royalty payments to Teva, from whom we acquired certain patents and intellectual property rights relating to pegozafermin, and from whom we licensed patents and know- how related to glycoPEGylation technology that is used in the manufacture of pegozafermin. For additional information regarding this license agreement, please see Note 5 to our consolidated financial statements appearing under Part II, Item 8 of this Annual Report. We cannot guarantee that we will be able to initiate and complete clinical trials and successfully accomplish all required regulatory activities or other activities necessary to gain approval and commercialize pegozafermin or any future product candidates. We currently have two active ~~investigational new drug (“~~ IND ~~”)~~ applications with the FDA in the United States for pegozafermin. In the future, we may file an additional IND with another division for any future indications or future product candidates. If any such future IND is not approved by the FDA, our clinical development timeline may be negatively impacted and any future clinical programs may be delayed or terminated. As a result, we may be unable to obtain regulatory approvals or successfully commercialize our products. We do not know whether any other clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Our product development costs will increase if we experience delays in clinical testing. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize pegozafermin and any future product candidates or allow our competitors to bring products to market before we do, which would impair our ability to successfully commercialize pegozafermin or any future product candidates and may harm our business, results of operations and prospects. Our or our future collaborators’ inability to timely complete clinical development could result in additional costs to us as well as impair our ability to generate product revenue, continue development, commercialize pegozafermin and any future product candidates, reach sales milestone payments and receive royalties on product sales. In addition, if we make changes to a product candidate including, for example, a new formulation, we may need to conduct additional nonclinical studies or clinical trials to bridge or demonstrate the comparability of our modified product candidate to earlier versions, which could delay our clinical development plan or marketing approval for pegozafermin and any future product candidates. The timely completion of clinical trials largely depends on patient enrollment. We may encounter delays in enrolling, or be unable to enroll, a sufficient number of patients to complete any of our future clinical trials, and even once enrolled, we may be unable to retain a sufficient number of patients to complete any of our trials. Furthermore, there are inherent difficulties in diagnosing ~~NASH~~ **MASH** , which can currently only be definitively diagnosed through a liver biopsy, and identifying SHTG patients. Specifically, identifying patients most likely to meet ~~NASH~~ **MASH** enrollment criteria on biopsy is an ongoing challenge, with existing clinical indicators lacking both sensitivity and specificity. As a result, ~~NASH~~ **MASH** trials often suffer from high levels of screen failure following central review of the baseline liver biopsy, which can lead to lower enrollment. In addition, we do not have experience enrolling patients with cirrhosis and such enrollment make take longer than we expect. As a result of such difficulties and the significant competition for recruiting ~~NASH~~ **MASH** and SHTG patients in clinical trials, we or our future collaborators may be unable to enroll the patients we need to complete clinical trials on a timely basis, or at all. In addition, our competitors, some of whom have significantly greater resources than we do, are conducting clinical trials for the same indications and seek to enroll patients in their studies that may otherwise be eligible for our clinical studies or trials. Since the number of qualified clinical investigators is limited, we expect to conduct some of our

clinical trials at the same clinical trial sites that some of our competitors use, which could further reduce the number of patients who are available for our clinical trials in these sites. Further, **enrollment** in **Phase 3 clinical trials may be adversely affected by** the **marketing** ~~event one of our competitors receives regulatory~~ approval for **Rezdiffra ™ or** ~~their~~ -- **the** ~~product candidate before we do, we may have difficulty enrolling~~ **potential marketing approvals for one or more investigational MASH drugs if** patients ~~if they~~ choose to take an approved drug ~~,~~ rather than enroll in a clinical trial **. In addition, our ability to receive accelerated approval of pegozafermin using data from the histology cohorts for non- cirrhotic (F2- F3) and cirrhotic (F4) MASH may be adversely affected if another company' s product candidate receives full approval before we receive accelerated approval** . Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Even if we are able to enroll a sufficient number of patients in our clinical studies or trials, delays in patient enrollment may result in increased costs or may affect the timing or outcome of our clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of pegozafermin and any future product candidates. We plan to leverage the safety database from the SHTG Phase 3 program across both the SHTG and ~~NASH~~ **MASH** indications. If we are not able enroll enough patients in our trials sufficient to support the safety database, our ability to advance the development of pegozafermin may be adversely affected. We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates, and we lack the resources and the capabilities to do so. As a result, we currently rely, and expect to rely for the foreseeable future, on third- party manufacturers to supply us with pegozafermin and any future product candidates. We currently have **contractual** ~~a sole- source relationship~~ **relationships** with BTPH **and BiBo** pursuant to which they supply us with pegozafermin **for our clinical trials** . If there should be any disruption in our supply arrangement with BTPH **or BiBo** , including any adverse events affecting ~~BTPH~~ **either party** , it could have a negative effect on the clinical development of pegozafermin ~~and~~ **if our** other ~~operations while we work~~ **manufacturer is not able** to ~~identify~~ **produce sufficient quantities of pegozafermin** and **we need to** qualify an alternate supply source. ~~In addition~~ **We expect to continue to rely on third- party manufacturers and suppliers** , **including BiBo, if** we ~~will require large quantities of~~ **receive regulatory approval for pegozafermin or any other product candidates. BiBo is constructing a production facility in China specifically designed to produce** pegozafermin for ~~large clinical trials and to commercialize~~ --- **commercial supply** ~~pegozafermin. Our current manufacturer may not be able to produce the larger quantities required for Phase 3 studies~~ . We ~~have identified a manufacturing partner for commercial- scale manufacturing, however, we~~ cannot guarantee that **BiBo** ~~such partner~~ will **be able to complete or make operational the production facility in a timely manner or at all, or** be able to scale up and produce the quantities we would require to commercialize pegozafermin. **Under our Collaboration Agreement with BiBo, we are required to pay BiBo an aggregate of $ 135. 0 million (exclusive of applicable value- added tax) toward the construction of the production facility, however, if the actual costs of the production facility are substantially greater than the estimated budget, we and Bibo will negotiate a means of allocating such cost overruns.** We ~~do~~ **may be ultimately responsible for a substantial portion of such overruns and it could negatively impact our financial condition and results of operations. For additional information regarding the production facility, please see Part I, Item 7 " Management' s Discussion and Analysis of Financial Condition and Results of Operations — Contractual Obligations and Commitments " and Note 5 to our consolidated financial statements appearing under Part II, Item 8 of this Annual Report. The terms of our commercial supply of pegozafermin may** not **be favorable to us and could** have a **material impact on our results of operations.** ~~long- term supply agreement with any third- party manufacturer and there~~ **There** is no guarantee that our third- party manufacturers will be able to fulfill our supply needs. Reliance on third- party manufacturers entails risks to which we would not be subject if we manufacture product candidates or products ourselves. For example, if any of our third- party manufacturers or vendors, including our fill- finish vendor, are not able to fulfill their supply or manufacturing obligations in a timely manner, our clinical trials may be delayed. In addition, if we do not maintain our key manufacturing relationships, we may fail to find replacement manufacturers or develop our own manufacturing capabilities in a timely manner or at all, which could delay or impair our ability to obtain regulatory approval for our products and substantially increase our costs or deplete profit margins, if any. If we do find replacement manufacturers, we may not be able to enter into agreements with them on terms and conditions favorable to us, and there could be a substantial delay before new facilities could be qualified and registered with the FDA and other comparable foreign regulatory authorities. We have begun producing certain of the reagents required for the glycoPEGylation at BTPH **and Merck & Cie** using the know- how transferred to us from Teva under our Reagent Supply and Technology Transfer Agreement. We have not completed the manufacturing process for all these reagents and cannot guarantee that we will be able to produce them successfully, or scale up our production for the quantities needed for commercialization. Any significant delay in the acquisition or decrease in the availability of these raw materials from suppliers could considerably delay the manufacture of pegozafermin, which could adversely impact the timing of any planned trials or the regulatory approvals of pegozafermin. We rely on third- party vendors for our assay development and testing. If such third- party vendors are unable to successfully produce or test such assays, it may substantially increase our cost or could adversely impact the timing of any planned trials or the regulatory approvals of pegozafermin. The FDA and other comparable foreign regulatory authorities require manufacturers to register manufacturing facilities. The FDA and other comparable foreign regulatory authorities also inspect these facilities to confirm compliance with ~~current good manufacturing practices (" cGMP ")~~ . We have little to no control regarding the occurrence of third- party manufacturer incidents. Any failure to comply with cGMP requirements or other FDA or comparable foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop pegozafermin or any future product candidates and market our products following approval. Our ~~sole~~ **primary** source ~~supplier~~ **suppliers** , BTPH **and BiBo** , ~~has~~ **have** not yet manufactured a commercial product, and as a result, ~~has~~ **have** not been subject to inspection by the FDA and other comparable foreign regulatory authorities. Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to develop our product

candidates and commercialize any products that receive regulatory approval on a timely basis. Supply chain issues, including those resulting from the ongoing war in Ukraine and the acts of piracy and military unrest in the Red Sea, may affect our third-party vendors and cause delays. Furthermore, since we have engaged a manufacturer located in China, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the legislation or policies of the United States ~~, including the proposed BIOSECURE bill,~~ or Chinese governments, political unrest or unstable economic conditions in China **. For example, WuXi Biologics, which we have engaged as a potential commercial supply chain vendor, is identified in the U. S. legislation known as the BIOSECURE Act, which was proposed in the 118th Congress, as a " biotechnology company of concern. " The version of the BIOSECURE Act introduced in the U. S. House of Representatives during the 118th Congress would prohibit federal agencies from entering into procurement contracts with, as well as providing grants and loans to, an entity that uses biotechnology equipment or services from a biotechnology company of concern, and includes a grandfathering provision allowing biotechnology equipment and services provided or produced by named " biotechnology companies of concern " under a contract or agreement entered into before the effective date until January 1, 2032. The pathway and timing for the BIOSECURE Act or its provisions to become law are uncertain. Foreign CMOs may be subject to U. S. legislation, including the proposed BIOSECURE Act, trade restrictions, and other foreign regulatory requirements that could increase the cost or reduce the supply of material available to us, delay the procurement or supply of such material or have an adverse effect on our ability to secure significant commitments from governments to purchase our potential therapies. These and other risks associated with our collaboration with BiBo, based in China, may materially adversely affect our ability to attain or maintain quantities of pegozafermin needed for commercialization, if approved. In addition, we have agreed to arbitrate claims related to the Collaboration Agreement with BiBo in Shanghai under the laws of the People' s Republic of China, which may limit our ability to enforce our contractual rights against BiBo. Changes to Chinese regulations or government policies affecting biopharmaceutical companies are unpredictable and may have a material adverse effect on our collaborators in China, which could have an adverse effect on our business, financial condition, results of operations and prospects. Developments in China' s public health, economic, political, and social conditions and the uncertainty around China' s relationship with other governments, such as the United States and the United Kingdom, could also negatively impact our ability to manufacture our product candidates for our planned clinical trials or have an adverse effect on our ability to secure government funding, which could adversely affect our financial condition and cause delay to our clinical development programs. Furthermore, if the BIOSECURE Act is passed and one or more of our collaborators in China is deemed to be a biotechnology company of concern, our operations and financial condition may be negatively impacted as a result of any delays or increased costs arising from the trade restrictions and other foreign regulatory requirements affecting such collaborators** . If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. For example, in the event that we need to switch our third- party manufacturer of pegozafermin from BTPH **or BiBo** , which ~~is~~ **are** our ~~sole~~ **primary** manufacturing ~~source~~ **sources** for pegozafermin, we anticipate that the complexity of the glycoPEGylation manufacturing process may materially impact the amount of time it may take to secure a replacement manufacturer. The delays associated with the verification of a new manufacturer, if we are able to identify an alternative source, could negatively affect our ability to develop product candidates in a timely manner or within budget **. While we believe that pegozafermin has been generally well tolerated with a favorable safety profile in our clinical trials, patients have experienced adverse events that have been considered treatment- related. Some of the more common adverse events included diarrhea, nausea, injection site erythema, injection site rash and increase appetite** . Undesirable side effects caused by pegozafermin or any future **product candidates or by other companies' similar approved drugs or** product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. Additional clinical studies may be required to evaluate the safety profile of pegozafermin or any future product candidates. As with other drugs, we have seen evidence of adverse effects in animal and human studies and it is possible that other adverse effects will become apparent in ongoing or future animal or human studies. It may be difficult to discern whether certain events or symptoms observed during our clinical trials or by patients using our approved products are related to pegozafermin or any future product candidates or approved products or some other factor. As a result, we and our development programs may be negatively affected even if such events or symptoms are ultimately determined to be unlikely related to pegozafermin or any future product candidates or approved products. **Our Phase 1 and Phase 2 clinical trials have involved a limited number of patients and limited duration of exposure to pegozafermin. As a result, we cannot be assured that adverse effects of pegozafermin will not be uncovered when a larger number of patients are exposed to the product candidate in our Phase 3 clinical trials.** Further, we expect that pegozafermin will require multiple administrations via subcutaneous injection in the course of a clinical trial. This chronic administration increases the risk that rare adverse events or chance findings are discovered in the commercial setting, where pegozafermin would be administered to more patients or for greater periods of time, that were not uncovered by our clinical drug development programs. We are developing pegozafermin for the treatment of ~~NASH~~ **MASH** ~~, an indication for which there are no approved products~~ . Although there are guidelines issued by the FDA **and comparable foreign regulatory authorities** for the development of drugs for the treatment of ~~NASH~~ **MASH** , the development of a novel product candidates such as pegozafermin may be more expensive and take longer than for other, better known or extensively studied product candidates. As other companies are in later stages of clinical trials for their potential ~~NASH~~ **MASH** therapies, we expect that the path for regulatory approval for ~~NASH~~ **MASH** therapies may continue to evolve in the near term as these other companies refine their regulatory approval strategies and interact with regulatory authorities. Such evolution may impact our future clinical trial designs, including trial size and endpoints, in ways that we cannot predict today. In particular, regulatory

authority expectations about liver biopsy data may evolve especially as more information is published about the inherent variability in liver biopsy data. Certain of our competitors have experienced regulatory setbacks for ~~NASH~~ **MASH** therapies following communications from the FDA **and comparable foreign regulatory authorities** . We currently do not know the impact, if any, that these setbacks could have on the path for regulatory approval for ~~NASH~~ **MASH** therapies generally or for pegozafermin. In addition, ~~if one of the other~~ **another** ~~companies~~ **company has** ~~receives~~ **received** regulatory approval for its ~~NASH~~ **MASH** therapy ~~before we do~~ , **and** such approval could impact our development of pegozafermin. We may have difficulty enrolling patients in our Phase 3 program for patients with ~~NASH~~ **MASH** if patients choose to take ~~an~~ **such** approved drug, rather than enroll in a clinical trial. In addition, **such approved MASH** ~~we expect that the first~~ therapy ~~that is approved for the treatment of NASH~~ will establish initial pricing and labelling expectations, which could impact our pricing and labelling if pegozafermin receives marketing approval. We are also developing pegozafermin for the treatment of SHTG. Clinical trials for the treatment of SHTG may be relatively costly and time- consuming. In addition, the requirements for approval by the FDA and comparable foreign regulatory authorities may change over time. If the FDA **or comparable foreign regulatory authorities** ~~requires~~ **require** additional evidence in addition to our ongoing Phase 3 program in SHTG to support a successful submission for approval, we may be required to make changes to our program design that could impact timelines and cost. Our anticipated development costs would likely increase if development of pegozafermin or any future product candidate is delayed because we are required by the FDA **and comparable foreign regulatory authorities** to perform studies or trials in addition to, or different from, those that we currently anticipate, or make changes to ongoing or future clinical trial designs. In addition, if we are unable to leverage our safety database for both SHTG and ~~NASH~~ **MASH** indications, we may be required to perform additional trials, which would result in increased costs and may affect the timing or outcome of our clinical trials. Lack of efficacy, adverse events or undesirable side effects may emerge in clinical trials conducted by third parties developing FGF product candidates like ours. For example, Novo Nordisk, Akero Therapeutics, Inc. and Boston Pharmaceuticals are also developing FGF21 product candidates for the treatment of ~~NASH~~ **MASH** . We have no control over their clinical trials or development program, and lack of efficacy, adverse events or undesirable side effects experienced by subjects in their clinical trials could adversely affect our stock price, our ability to attract additional capital and our clinical development plans for pegozafermin or even the viability or prospects of pegozafermin as a product candidate, including by creating a negative perception of FGF therapeutics by healthcare providers or patients. From time to time, we may publicly disclose preliminary or topline data from our clinical trials, which are 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 or trial. 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 until the final data are available. From time to time, we may also disclose interim data from our clinical trials. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. 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 continues and more patient data become available. To date, pegozafermin has been manufactured by ~~a single~~ third- party ~~manufacturer~~ **manufacturers** ~~, BTPH, solely~~ for preclinical studies and clinical trials. The process of manufacturing pegozafermin, and in particular, the glycoPEGylation process, is complex, highly regulated and subject to several risks and requires significant expertise and capital investment, including for the development of advanced manufacturing techniques and process controls. Manufacturers of biologic products often encounter difficulties in production, including difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, operator error and shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. We cannot assure you that any stability or other issues relating to the manufacture of pegozafermin will not occur in the future. We have limited process development capabilities and have access only to external manufacturing capabilities. We do not have and we do not currently plan to acquire or develop the facilities or capabilities to manufacture bulk drug substance or filled drug product for use in human clinical trials or commercialization. The biopharmaceutical industry is intensely competitive and subject to rapid innovation and significant technological advancements. Our competitors include multinational pharmaceutical companies, specialized biotechnology companies, universities and other research institutions. A number of biotechnology and pharmaceutical companies are pursuing the development or marketing of pharmaceuticals that target the same diseases that we are targeting. Certain of these companies have published positive data regarding their clinical trials, which may further increase the competition we face. Smaller or earlier- stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Given the high incidence of ~~NASH~~ **MASH** and SHTG, it is likely that the number of companies seeking to develop products and therapies for the treatment of liver and cardio- metabolic diseases, such as ~~NASH~~ **MASH** and SHTG, will increase. We may also face competition indirectly from companies developing therapies like the incretins to treat obesity and / or Type 2 diabetes. Some incretin- based therapies are also being developed for the treatment of ~~NASH~~ **MASH** . There are numerous currently approved therapies for treating diseases other than ~~NASH~~ **MASH** and some of these currently approved therapies may exert effects that could be similar to pegozafermin in ~~NASH~~ **MASH** . Many of these approved drugs are well- established therapies or products and are widely accepted by physicians, patients and third- party payors. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. This may make it difficult for us to differentiate our products from currently approved therapies, which may adversely impact our business strategy. We expect that if pegozafermin or any future product candidates are approved, they will be priced at a significant premium over competitive generic products, including branded generic products. Insurers and other

third- party payors may also encourage the use of generic products or specific branded products prior to utilization of pegozafermin. In addition, many companies are developing new therapeutics, and we cannot predict what the standard of care will be as pegozafermin or any future product candidates progress through clinical development. In addition, to the extent pegozafermin or any future product candidates are approved for liver or cardio- metabolic indications, such as SHTG, the commercial success of our products will also depend on our ability to demonstrate benefits over the then- prevailing standard of care, including diet, exercise and lifestyle modifications. Further, if pegozafermin or any future product candidates are approved for the treatment of SHTG, we will compete with currently approved therapies and therapies further along in development. Our competitors both in the United States and abroad include large, well- established pharmaceutical and generic companies with significantly greater name recognition. Our competitors may be able to charge lower prices than we can, which may adversely affect our market acceptance. Many of these competitors have greater resources than we do, including financial, product development, marketing, personnel and other resources. If our competitors market products that are more effective, safer or cheaper than our products or that reach the market sooner than our products, we may not achieve commercial success. Many of our competitors have substantially greater financial, technical, human and other resources than we do and may be better equipped to develop, manufacture and market technologically superior products. As a result, our competitors may obtain regulatory approval of their products more rapidly than we do or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidate or any future product candidates. Our competitors may also develop and succeed in obtaining approval for drugs that are more effective, more convenient, more widely used and less costly or have a better safety profile than our products and these competitors may also be more successful than we are in manufacturing and marketing their products. The global economy, including credit and financial markets, have experienced extreme volatility and disruptions at various points over the last few decades, including, among other things, diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, supply chain shortages, increases in inflation rates, ~~higher~~ **fluctuating** interest rates, and uncertainty about economic stability. **In addition, the effects of global economic conditions, including new or increased tariffs and other barriers to trade, trade and other international disputes, slower growth or recession, high unemployment, labor availability constraints, significant natural disasters, including as a result of climate change, changes to fiscal and monetary policy or government budget dynamics, particularly in the pharmaceutical and biotech areas, may have adverse effects on our business and financial condition.** For example, **public health crises have** ~~the COVID- 19 pandemic~~ resulted in widespread unemployment, economic slowdown and extreme volatility in the capital markets. ~~The~~ **In addition, the** Federal Reserve has **previously** raised interest rates multiple times in response to concerns about inflation and it may raise them again. ~~Higher~~ **Fluctuation in** interest rates, coupled with reduced government spending and volatility in financial markets, may increase economic uncertainty and affect consumer spending. Similarly, the ongoing military conflicts between Russia and Ukraine and between Israel and surrounding areas and the rising tensions between China and Taiwan have created extreme volatility in the global capital markets and may have further global economic consequences, including disruptions of the global supply chain. Any such volatility and disruptions may adversely affect our business or the third parties on whom we rely. If the equity and credit markets deteriorate, including as a result of political unrest or war, it may make any necessary debt or equity financing more difficult to complete, 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 growth strategy, financial performance and share price and could require us to delay or abandon development or commercialization plans. In addition, there is a risk that one or more of our service providers, manufacturers or other partners would not survive or be able to meet their commitments to us under such circumstances, which could directly affect our ability to attain our operating goals on schedule and on budget. We have experienced and may in the future experience disruptions as a result of such macroeconomic conditions, including delays or difficulties in initiating or expanding clinical trials and manufacturing sufficient quantities of materials. Any one or a combination of these events could have a material and adverse effect on our results of operations and financial condition. The ~~2023~~ Loan Agreement contains certain covenants that could adversely affect our operations and, if an event of default were to occur, we could be forced to repay any outstanding indebtedness sooner than planned and possibly at a time when we do not have sufficient capital to meet this obligation. Pursuant to the ~~2023~~ Loan Agreement, we have pledged substantially all of our assets, other than our intellectual property rights, and have agreed that we may not sell or assign rights to our patents and other intellectual property without the prior consent of our lenders. Additionally, the ~~2023~~ Loan Agreement contains certain affirmative and negative covenants that could prevent us from taking certain actions without the consent of our lenders. These covenants may limit our flexibility in operating our business and our ability to take actions that might be advantageous to us and our stockholders. The ~~2023~~ Loan Agreement also includes customary events of default, including, among other things, an event of default upon a change of control. Upon the occurrence and continuation of an event of default, all amounts due under the ~~2023~~ Loan Agreement become automatically (in the case of a bankruptcy event of default) or may become (in the case of all other events of default and at the option of the administrative agent), immediately due and payable. If an event of default under the ~~2023~~ Loan Agreement should occur and be continuing, we could be required to immediately repay any outstanding indebtedness. If we are unable to repay such debt, the lenders would be able to foreclose on the secured collateral, including our cash accounts, and take other remedies permitted under the ~~2023~~ Loan Agreement. Even if we are able to repay such accelerated debt amount under the ~~2023~~ Loan Agreement upon an event of default, the repayment of these sums may significantly reduce our working capital and impair our ability to operate as planned. We may encounter difficulties in managing our growth, which could adversely affect our operations. We are in the early stages of building the full team that we anticipate we will need to complete the development pegozafermin and other future product candidates. As we advance our preclinical and clinical development programs for product candidates, seek regulatory approval in the United States and elsewhere and increase the number of ongoing product development programs, we anticipate that we will need to increase our product development, scientific and administrative headcount. We will also need to establish

commercial capabilities in order to commercialize any product candidates that may be approved. Such an evolution may impact our strategic focus and our deployment and allocation of resources. Our ability to manage our operations and growth effectively depends upon the continual improvement of our procedures, reporting systems and operational, financial and management controls. We may not be able to implement administrative and operational improvements in an efficient or timely manner and may discover deficiencies in existing systems and controls. In addition, in order to continue to meet our obligations as a public company and to support our anticipated long- term growth, we will need to increase our general and administrative capabilities. Our management, personnel and systems may experience difficulty in adjusting to our growth and strategic focus. We must attract and retain highly skilled employees in order to succeed. If we are not able to retain our current senior management team and our scientific advisors or continue to attract and retain qualified scientific, technical and business personnel, our business will suffer. We may not be able to attract or retain qualified personnel and consultants due to the intense competition for such individuals in the biotechnology and pharmaceutical industries. If we are not able to attract and retain necessary personnel and consultants to accomplish our business objectives, it may significantly impede the achievement of our development and commercial objectives and our ability to implement our business strategy. In addition, we are highly dependent on the development, regulatory, manufacturing, commercialization and financial expertise of the members of our executive team, as well as other key employees and consultants. If we lose one or more of our executive officers or other key employees or consultants, our ability to implement our business strategy successfully could be seriously harmed. We rely on third parties for certain aspects of our product candidate development process and we may not be able to obtain and maintain the third- party relationships that are necessary to develop, commercialize and manufacture some or all of our product candidates. If these third parties do not successfully perform and comply with regulatory requirements, we may not be able to successfully complete clinical development, obtain regulatory approval, or commercialize our product candidates and our business could be substantially harmed. We depend on collaborators, partners, licensees, clinical investigators, contract research organizations, manufacturers and other third parties to support our discovery efforts, to formulate product candidates, to conduct clinical trials for some or all of our product candidates and to manufacture clinical and commercial scale quantities of our drug substance and drug product and expect to depend on these third parties to market, sell and distribute any products we successfully develop. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities and such alternative arrangements may not be available on terms acceptable to us. We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development, marketing approval and / or commercialization of pegozafermin or any future product candidates, producing additional losses and depriving us of potential revenue. In addition, we have relied upon and plan to continue to rely upon third party contract research organizations (“ CROs ”) to conduct, monitor, and manage preclinical and clinical programs. We rely on these parties for execution of clinical trials, and we manage and control only some aspects of their activities. We remain responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs and other vendors are required to comply with all applicable laws, regulations, and guidelines, including those required by the FDA, EMA and comparable foreign regulatory authorities for all of our product candidates in clinical development. If we or any of our CROs or vendors fail to comply with applicable and evolving laws, regulations, and guidelines, the results generated in our clinical trials may be deemed insufficient or unreliable, and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses. Our operations, and those of our contract research organizations, CMO, suppliers, and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, acts of war, medical pandemics or epidemics, such as the novel coronavirus, and other natural or man- made disasters or business interruptions. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. If we fail to develop and commercialize additional product candidates, we may be unable to grow our business. Although the development and commercialization of pegozafermin is currently our primary focus, as part of our longer- term growth strategy, we plan to evaluate the development and commercialization of other therapies related to ~~NASH~~ **MASH** and other liver and cardio-metabolic diseases. The success of this strategy depends primarily upon our ability to identify and validate new therapeutic candidates, and to identify, develop and commercialize new drugs and biologics. Our research efforts may initially show promise in discovering potential new drugs and biologics yet fail to yield product candidates for clinical development for a number of reasons. We may use our limited financial and human resources to pursue a particular research program or product candidate that is ultimately unsuccessful or less successful than other programs or product candidates that we may have forgone or delayed. Because we have limited personnel and financial resources, we may forego or delay the development of certain programs or product candidates that later prove to have greater commercial potential than the programs or product candidates that we do pursue. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for product candidates may not yield any commercially viable products. Similarly, our decisions to delay or terminate drug development programs may also be incorrect and could cause us to miss valuable opportunities. We may seek to establish commercial collaborations for our product candidates, and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans. Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. We may decide to collaborate with other pharmaceutical and biotechnology companies for the development and potential commercialization of our product candidates. Collaborations are complex and time- consuming to negotiate and document. We may not be able to negotiate collaborations on a timely basis,

on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities or increase our expenditures and undertake development or commercialization activities at our own expense. We may not be successful in our efforts to identify, in- license or acquire, discover, develop or commercialize additional product candidates. We may seek to identify, in- license or acquire, discover, develop and commercialize additional product candidates. We cannot assure you that our effort to in- license or acquire additional product candidates will be successful. Even if we are successful in in- licensing or acquiring additional product candidates, their requisite development activities may require substantial resources, and we cannot assure you that these development activities will result in regulatory approvals. Our international operations may expose us to business, regulatory, political, operational, financial, pricing and reimbursement risks associated with doing business outside of the United States. Our use of our international facilities subjects us to U. S. and foreign governmental trade, import and export, and customs regulations and laws including various economic and trade sanctions regulations administered by the U. S. Treasury Department' s Office of Foreign Assets Controls and the U. S. Export Administration Regulations. Compliance with these regulations and laws is costly and exposes us to penalties for non- compliance. Doing business internationally potentially involves a number of risks, any of which could harm our ongoing international clinical operations and supply chain, as well as any future international expansion and operations and, consequently, our business, financial condition, prospects and results of operations. Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop. We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercialize any resulting products. Product liability claims may be brought against us by subjects enrolled in our clinical trials, patients, or others using our products. Our clinical trial liability insurance coverage may not adequately cover all liabilities that we may incur. Our employees, contractors, vendors, principal investigators, consultants and future partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading. We are exposed to the risk of fraud or other misconduct by our employees, contractors, vendors, principal investigators, consultants or future partners. Misconduct by these parties could include failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with federal and state healthcare fraud and abuse laws and regulations, to report financial information or data timely, completely or accurately, or to disclose unauthorized activities to us. Most states also have statutes or regulations similar to these federal laws, which may apply to items such as pharmaceutical products and services reimbursed by private insurers. We and / or our future partners may be subject to administrative, civil and criminal sanctions for violations of any of these laws. We depend on our information technology systems and those of our third- party collaborators, service providers, contractors or consultants. Our internal computer systems, or those of our third- party collaborators, service providers, contractors or consultants, may fail or suffer security breaches, disruptions, or incidents, which could result in a material disruption of our development programs or loss of data or compromise the privacy, security, integrity or confidentiality of sensitive information related to our business and have a material adverse effect on our reputation, business, financial condition or results of operations. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. Our internal technology systems and infrastructure, and those of our current or future third- party collaborators, service providers, contractors and consultants are vulnerable to damage from computer viruses, unauthorized access or use resulting from malware, natural disasters, terrorism, war and **information technology,** telecommunication and electrical failures, denial- of- service attacks, cyber- attacks or cyber- intrusions over the Internet, hacking, phishing and other social engineering attacks, persons inside our organizations (including employees or contractors), loss or theft, or persons with access to systems inside our organization. From time to time, we are subject to periodic phishing attempts. In ~~the third quarter of~~ 2021, we ~~discovered~~ **implemented remedial measures promptly following** a business email compromise caused by phishing ~~. The phishing attack did not result in the misappropriation of any funds and we do not believe that it had a material adverse effect on our business. We implemented remedial measures promptly following this incident~~ , however, we cannot guarantee that our implemented remedial measures will prevent additional related, as well as unrelated, incidents. If a material system failure, accident or security breach were to occur and cause interruptions in our operations or the operations of third- party collaborators, service providers, contractors and consultants, it could result in a material disruption of our development programs and significant reputational, financial, legal, regulatory, business or operational harm. To the extent that any real or perceived security breach affects our systems (or those of our third- party collaborators, service providers, contractors or consultants), or results in the loss of or accidental, unlawful or unauthorized access to, use of, release of, or other processing of personally identifiable information or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed. Any failure or perceived failure by us or any third- party collaborators, service providers, contractors or consultants to comply with our privacy, confidentiality, data security or similar obligations, or any data security incidents or other security breaches that result in the accidental, unlawful or unauthorized access to, use of, release of, processing of, or transfer of sensitive information, including personally identifiable information, may result in negative publicity, harm to our reputation, governmental investigations, enforcement actions, regulatory fines, litigation or public statements against us, could cause third parties to lose trust in us or could result in claims by third parties, including those that assert that we have breached our privacy, confidentiality, data security or similar obligations, any of which could have a material adverse effect on our reputation, business, financial condition or results of operations **. If the market opportunities for our approved product candidates, if any, are smaller than we expect, it could materially and adversely affect our financial condition and results of operation. If the market opportunity for our products, if approved, is smaller than we expect, we may never become or remain profitable nor**

generate sufficient revenue growth to sustain our business even if we obtain significant market share for them. The potentially addressable patient population for our products may be limited or may not be amenable to treatment with our products, and new patients may become increasingly difficult to identify or access, which would adversely affect our results of operations and our business . Risks Related to Regulatory Approvals We do not expect pegozafermin or any future product candidate to be commercially available for several years, if at all. Pegozafermin is and any future product candidate will be subject to strict regulation by regulatory authorities in the United States and in other countries. We cannot market any product candidate until we have completed all necessary preclinical studies and clinical trials and have obtained the necessary regulatory approvals. We do not know whether regulatory agencies will grant approval for pegozafermin or any future product candidate. Even if we complete preclinical studies and clinical trials successfully, we may not be able to obtain regulatory approvals or we may not receive approvals to make claims about our products that we believe to be necessary to effectively market our products. Data obtained from preclinical studies and clinical trials is subject to varying interpretations that could delay, limit or prevent regulatory approval, and failure to comply with regulatory requirements or inadequate manufacturing processes are examples of other problems that could prevent approval. **While** ~~The regulatory authorities in~~ the **FDA has** ~~United States and the EU have not~~ approved ~~any~~ **a** ~~products~~ **product** for the treatment of ~~NASH~~ **MASH** ~~,~~ and ~~while~~ there are guidelines issued by the FDA for the development of drugs for the treatment of ~~NASH~~ **MASH** , it is unclear whether the requirements for approval will change in the future or whether the FDA will rely on regulatory precedent for future regulatory approvals. Any such changes may require us to conduct new trials that could delay our timeframe and increase the costs of our programs related to pegozafermin or any future product candidate for the treatment of ~~NASH~~ **MASH** or SHTG. Even if we are able to obtain regulatory approvals for pegozafermin or any future product candidate, if they exhibit harmful side effects after approval, our regulatory approvals could be revoked or otherwise negatively impacted, and we could be subject to costly and damaging product liability claims. Even if we receive regulatory approval for pegozafermin or any future product candidates, we will have tested them in only a small number of patients during our clinical trials. If our applications for marketing are approved and more patients begin to use our product, new risks and side effects associated with our products may be discovered. As a result, regulatory authorities may revoke their approvals. Based on guidelines issued by the FDA for the development of drugs for the treatment of ~~NASH~~ **MASH** , if pegozafermin is approved by the FDA based on a surrogate endpoint pursuant to section 506 (c) of the Federal Food, Drug, and Cosmetic Act and the accelerated approval regulations (21 C. F. R. part 314, subpart H; 21 C. F. R. part 601, subpart E), consistent with FDA guidance, we will be required to conduct additional clinical trials establishing clinical benefit on the ultimate outcome of ~~NASH~~ **MASH** . Under the Food and Drug Omnibus Reform Act of 2022, the FDA may require, as appropriate, that such studies be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. If pegozafermin is approved by the FDA for the treatment of SHTG based on an endpoint of the reduction of triglycerides, the FDA may still require a cardiovascular outcomes study as part of a post- marketing authorization commitment. Such a study would be time consuming and costly and we cannot guarantee that we will see positive results, which could result in the revocation of the approval. Additionally, we may be required to conduct additional clinical trials, make changes in labeling of our product, reformulate our product or make changes and obtain new approvals for our and our suppliers' manufacturing facilities for pegozafermin and any future product candidates. We might have to withdraw or recall our products from the marketplace. We may also experience a significant drop in the potential sales of our product if and when regulatory approvals for such product are revoked. As a result, we may experience harm to our reputation in the marketplace or become subject to lawsuits, including class actions. Any of these results could decrease or prevent any sales of our approved product or substantially increase the costs and expenses of commercializing and marketing our product. The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time- consuming and inherently unpredictable. Our inability to obtain regulatory approval for pegozafermin or any future product candidates would substantially harm our business. Currently, we do not have any product candidates that have received regulatory approval. The time required to obtain approval from the FDA and comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of preclinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate' s development and may vary among jurisdictions. It is possible that none of pegozafermin or any future product candidates will ever obtain regulatory approval. Pegozafermin or any future product candidate could fail to receive regulatory approval from the FDA or comparable foreign regulatory authorities for many reasons, including those referenced in Part I, Item 1. " Business — Government Regulation and Product Approval " in this Annual Report on Form 10- K. If we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may grant approval contingent on the performance of costly post- marketing clinical trials or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of the product candidate. We have received ~~breakthrough~~ **Breakthrough** ~~therapy~~ **Therapy** designation for pegozafermin in ~~NASH~~ **MASH** from the FDA **and PRIME designation for pegozafermin in MASH from the EMA** , but such designation may not actually lead to a faster development or regulatory review or approval process **, and does not increase the likelihood that pegozafermin will receive marketing approval** . In addition, we may seek ~~breakthrough~~ **Breakthrough** ~~therapy~~ **Therapy , Fast Track or PRIME** designation for other indications or future product candidates, but we might not receive such designation. In September 2023, we received Breakthrough Therapy designation for pegozafermin in ~~NASH~~ **MASH** from the FDA ~~. However~~ **and in March 2024** , the **EMA granted PRIME status to** ~~receipt of Breakthrough Therapy designation for~~ pegozafermin in **patients with** ~~NASH~~ **MASH** ~~may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA~~ . **We** ~~In addition, we~~ may **in the future** seek Breakthrough Therapy designation **, Fast Track designation or PRIME designation** for other indications or future product

candidates. **However** ~~Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly~~ , even if we believe **a particular product candidate is eligible for these designations, we cannot assure you** that ~~a current~~ **the FDA, EMA** or ~~future product candidate meets~~ **similar regulatory agency would decide to grant** ~~the~~ **them . In addition,** ~~criteria for designation as a~~ breakthrough ~~therapy~~ **Therapy** , ~~the~~ **Fast Track and PRIME designations may not result in a faster development process, review or approval compared to conventional** FDA **or EMA procedures, respectively** ~~may disagree and instead determine not to make such designation~~ . In addition, even though pegozafermin is designated as a ~~breakthrough~~ **Breakthrough** ~~therapy~~ **Therapy** in ~~NASH~~ **MASH** , the FDA may later decide that the product candidate no longer meets the conditions for designation and the designation may be rescinded **. The Breakthrough Therapy, Fast Track and PRIME designations do not assure ultimate regulatory approval by the FDA or the EMA. Many drugs and biologics that have received Breakthrough Therapy, Fast Track or PRIME designation have failed to obtain approval** . See Part I, Item 1. " Business — Expedited Programs for Serious Conditions " in this Annual Report on Form 10- K. We ~~plan to~~ conduct clinical trials for pegozafermin at sites outside the United States, and the FDA may not accept data from trials conducted in such locations. We have conducted and expect ~~in the future~~ to **continue** ~~conduct~~ **conducting** one or more of our clinical trials outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data is subject to conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with ethical principles. The trial population must also adequately represent the U. S. population, and the data must be applicable to the U. S. population and U. S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will depend on its determination that the trials also complied with all applicable U. S. laws and regulations. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time- consuming and would delay or permanently halt our development of the applicable product candidates. Even if the FDA accepted such data, it could require us to modify our planned clinical trials to receive clearance to initiate such trials in the United States or to continue such trials once initiated. Further, conducting international clinical trials presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs that could restrict or limit our ability to conduct our clinical trials, the administrative burdens of conducting clinical trials under multiple sets of foreign regulations, foreign exchange fluctuations, diminished protection of intellectual property in some countries, as well as political and economic risks relevant to foreign countries **. Disruptions at the FDA and other government agencies could negatively affect the review of our regulatory submissions, which could negatively impact our business. The ability of the FDA to review and approve regulatory submissions can be affected by a variety of factors, including disruptions caused by government shutdowns and public health crises, or layoffs of federal workers by the federal government. Such disruptions could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business** . Even if pegozafermin or any future product candidate receives regulatory approval, it may still face future development and regulatory difficulties. Even if we obtained regulatory approval for a product candidate, it would be subject to ongoing requirements by the FDA and comparable foreign regulatory authorities governing the manufacture, quality control, further development, labeling, packaging, storage, distribution, safety surveillance, import, export, advertising, promotion, recordkeeping and reporting of safety and other post- market information. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP, regulations and standards. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. If we, our product candidates or the manufacturing facilities for our product candidates fail to comply with applicable regulatory requirements, or undesirable side effects caused by such products are identified, a regulatory agency may: issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings about such product; mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners; require that we conduct post- marketing studies; require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance; seek an injunction or impose civil or criminal penalties or monetary fines; suspend marketing of, withdraw regulatory approval of or recall such product; suspend any ongoing clinical studies; refuse to approve pending applications or supplements to applications filed by us; suspend or impose restrictions on operations, including costly new manufacturing requirements; or seize or detain products, refuse to permit the import or export of products or require us to initiate a product recall. The occurrence of any event or penalty described above may inhibit our ability to commercialize our products and generate product revenue. We expect the product candidates we develop will be regulated as biologics, and therefore they may be subject to competition sooner than anticipated. The BPCIA was enacted as part of the **ACA** ~~Affordable Care Act~~ to establish an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as " interchangeable " based on its similarity to an approved biologic. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the reference product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when processes intended to implement BPCIA may be fully adopted by the FDA, any of these processes could have a material adverse effect on the future commercial prospects for our biological products. We believe that any of the product candidates we develop that is approved in the United

States as a biological product under a BLA should qualify for the 12- year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider the subject product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of the reference products in a way that is similar to traditional generic substitution for non- biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. In addition, the first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against other biologics submitted under the abbreviated approval pathway for the lesser of (i) one year after the first commercial marketing, (ii) 18 months after approval if there is no legal challenge, (iii) 18 months after the resolution in the applicant' s favor of a lawsuit challenging the biologics' patents if an application has been submitted, or (iv) 42 months after the application has been approved if a lawsuit is ongoing within the 42- month period. The approval of a biologic product biosimilar to one of our product candidates could have a material adverse impact on our business as it may be significantly less costly to bring to market and may be priced significantly lower than our product candidates. Current and future legislation may increase the difficulty and cost for us, and any collaborators, to obtain marketing approval of and commercialize our drug candidates and affect the prices we, or they, may obtain. Heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare therapies, which could result in reduced demand for our product candidates or additional pricing pressures. **The** ~~On August 16, 2022, President Biden signed into law the~~ Inflation Reduction Act of 2022 (" IRA ") ~~, which, among other provisions, included~~ **includes** several measures intended to lower the cost of prescription drugs and related healthcare reforms. We cannot be sure whether additional legislation or rulemaking related to the IRA will be issued or enacted, or what impact, if any, such changes will have on the profitability of any of our drug candidates, if approved for commercial use, in the future. Healthcare insurance coverage and reimbursement may be limited or unavailable for our product candidate, if approved, which could make it difficult for us to sell our product candidate or other therapies profitably. The success of pegozafermin, if approved, depends on the availability of coverage and adequate reimbursement from third- party payors including governmental healthcare programs, such as Medicare and Medicaid, commercial payors, and health maintenance organizations. We cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates or assure that coverage and reimbursement will be available for any product that we may develop. Governments outside the United States tend to impose strict price controls, which may adversely affect our revenue, if any. In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost- effectiveness of our drug candidate to other available procedures. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially. Risks Related to Intellectual Property Our success will depend in significant part on our current or future licensors', licensees' or collaborators' ability to establish and maintain adequate protection of our owned and licensed intellectual property covering the product candidates we plan to develop, and the ability to develop these product candidates and commercialize the products resulting therefrom, without infringing the intellectual property rights of others. In addition to taking other steps to protect our intellectual property, we hold issued patents, we have applied for patents, and we intend to continue to apply for patents with claims covering our technologies, processes and product candidates when and where we deem it appropriate to do so. We have filed numerous patent applications both in the United States and in certain foreign jurisdictions to obtain patent rights to inventions we have discovered, with claims directed to compositions of matter, methods of use and other technologies relating to our programs. There can be no assurance that any of these patent applications will issue as patents or, for those applications that do mature into patents, that the claims of the patents will exclude others from making, using or selling our product candidates or products that compete with or are similar to our product candidates. In countries where we have not sought and do not seek patent protection, third parties may be able to manufacture and sell our product candidates without our permission, and we may not be able to stop them from doing so. With respect to patent rights, we do not know whether any of the pending patent applications for any of our product candidates will result in the issuance of patents that effectively protect our technologies, processes and product candidates, or if any of our issued patents or our current or future licensors', licensees' or collaborators' issued patents will effectively prevent others from commercializing competitive technologies, processes and products. We cannot be certain that we or our current or future licensors, licensees or collaborators were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our current or future licensors, licensees or collaborators were the first to file for patent protection of such inventions. Any changes we make to our pegozafermin or any future product candidates to cause them to have what we view as more advantageous properties may not be covered by our existing patents and patent applications, and we may be required to file new applications and / or seek other forms of protection for any such altered product candidates. The patent landscape surrounding the technology underlying our product candidates is crowded, and there can be no assurance that we would be able to secure patent protection that would adequately cover an alternative to pegozafermin or any future product candidates. We and our current or future licensors, licensees or collaborators may not be able to prepare, file and

prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our current or future licensors, licensees or collaborators will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection for them. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain or enforce the patents, covering technology that we license from or license to third parties and may be reliant on our current or future licensors, licensees or collaborators to perform these activities, which means that these patent applications may not be prosecuted, and these patents enforced, in a manner consistent with the best interests of our business. If our current or future licensors, licensees or collaborators fail to establish, maintain, protect or enforce such patents and other intellectual property rights, such rights may be reduced or eliminated. If our current or future licensors, licensees or collaborators are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. Similar to the patent rights of other biotechnology companies, the scope, validity and enforceability of our owned and licensed patent rights generally are highly uncertain and involve complex legal and factual questions. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. **Historically** ~~In recent years~~ , these areas have been the subject of much litigation in the industry. As a result, the issuance, scope, validity, enforceability and commercial value of our and our current or future licensors', licensees' or collaborators' patent rights are highly uncertain. Our and our current or future licensors', licensees' or collaborators' pending and future patent applications may not result in patents being issued that protect our technology or product candidates, or products resulting therefrom, in whole or in part, or that effectively prevent others from commercializing competitive technologies and products. The patent examination process may require us or our current or future licensors, licensees or collaborators to narrow the scope of the claims of pending and future patent applications, which would limit the scope of patent protection that is obtained, if any **. Accordingly, even if we or our licensors are able to obtain patents, the patents might be substantially narrower than anticipated. Thus, there is no assurance as to the degree and range of protections any of our patents, if issued, may afford us or whether patents will be issued** . Our and our current or future licensors', licensees' or collaborators' patent applications cannot be enforced against third parties practicing the technology that is currently claimed in such applications unless and until a patent issues from such applications, and then only to the extent the claims that issue are broad enough to cover the technology being practiced by those third parties. Furthermore, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after the resulting products are commercialized. As a result, our owned and in- licensed patents may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. We expect to seek extensions of patent terms for our issued patents, where available. The applicable authorities, including the FDA in the United States, and any comparable foreign regulatory authorities, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. In addition, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to the expiration of relevant patents or otherwise failing to satisfy applicable requirements. We may not be able to protect our intellectual property rights throughout the world. The legal protection afforded to inventors and owners of intellectual property in countries outside of the United States may not be as protective or effective as that in the United States and we may, therefore, be unable to acquire and enforce intellectual property rights outside the United States to the same extent as in the United States. Whether filed in the United States or abroad, our patent applications may be challenged or may fail to result in issued patents. Filing, prosecuting, enforcing and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States are less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and certain state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with pegozafermin or any future product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. In April 2018, we entered into ~~an Asset Transfer and License Agreement (~~ the ~~"~~ FGF21 Agreement ~~")~~ with Teva under which we acquired certain patents, intellectual property and other assets relating to Teva' s glycoPEGylated FGF21 program, including pegozafermin. Under this agreement, we were granted a perpetual, non- exclusive (but exclusive as to pegozafermin), non- transferable, worldwide license to patents and know- how related to glycoPEGylation technology used in the development, manufacture and commercialization of pegozafermin and products containing pegozafermin. The FGF21 Agreement also contains numerous covenants with which we must comply, including the utilization of commercially reasonable efforts to develop and ultimately commercialize pegozafermin, as well as certain reporting covenants and the obligation to make royalty payments, if and when pegozafermin is approved for commercialization. Our failure to satisfy any of these covenants could result in the termination of the FGF21 Agreement. In addition, we entered into a Sublicense Agreement with ratiopharm (the " ratiopharm Sublicense "), under which we were granted a perpetual, exclusive, worldwide sublicense to patents and know- how related to glycoPEGylation technology used in the development, manufacture and commercialization of pegozafermin and products containing pegozafermin. Termination of the FGF21 Agreement or the ratiopharm Sublicense will impact our rights under the intellectual property licensed to us by Teva and ratiopharm, respectively, including our license to glycoPEGylation technology, but will not affect our rights under the assets assigned to us. Beyond this agreement, our commercial success will also depend upon our ability, and the ability of our licensors, to develop, manufacture, market and sell our product candidates and use our proprietary technologies

without infringing the proprietary rights of third parties. A third party may hold intellectual property rights, including patent rights, that are important or necessary to the development of our product candidates. As a result, we may enter into additional license agreements in the future. If we fail to comply with the obligations under these agreements, including payment and diligence obligations, our licensors may have the right to terminate these agreements, in which event we may not be able to develop, manufacture, market or sell any product that is covered by these agreements or to engage in any other activities necessary to our business that require the freedom to operate afforded by the agreements, or we may face other penalties under the agreements. We may be unable to obtain intellectual property rights or technology necessary to develop and commercialize pegozafermin and any future product candidates. The patent landscape around our programs is complex, and we are aware of several third- party patents and patent applications containing subject matter that might be relevant to pegozafermin. Depending on what claims ultimately issue from these patent applications, and how courts construe the issued patent claims, as well as depending on the ultimate formulation and method of use of pegozafermin or any future product candidates, we may need to obtain a license to practice the technology claimed in such patents. There can be no assurance that such licenses will be available on commercially reasonable terms, or at all. We may become involved in lawsuits or other proceedings to protect or enforce our intellectual property, which could be expensive, time- consuming and unsuccessful and have a material adverse effect on the success of our business. Third parties may infringe our patents or misappropriate or otherwise violate our intellectual property rights. In the future, we may initiate legal proceedings to enforce or defend our intellectual property rights, to protect our trade secrets or to determine the validity or scope of intellectual property rights we own or control. Also, third parties may initiate legal proceedings against us to challenge the validity or scope of intellectual property rights we own, control or to which we have rights. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, narrowed, held unenforceable or interpreted in such a manner that would not preclude third parties from entering the market with competing products. Third- party pre- issuance submission of prior art to the USPTO, or opposition, derivation, revocation, reexamination, inter partes review or interference proceedings, or other pre- issuance or post- grant proceedings or other patent office proceedings or litigation in the United States or other jurisdictions provoked by third parties or brought by us, may be necessary to determine the inventorship, priority, patentability or validity of inventions with respect to our patents or patent applications. An unfavorable outcome could leave our technology or product candidates without patent protection, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or could require us to obtain license rights from the prevailing party in order to be able to manufacture or commercialize our product candidates without infringing third- party patent rights. Our business could be harmed if the prevailing party in such a case does not offer us a license on commercially reasonable terms, or at all. Even if we obtain a license, it may be non- exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Even if we successfully defend such litigation or proceeding, we may incur substantial costs and our defense may distract our management and other employees. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, many foreign jurisdictions have rules of discovery that are different than those in the United States and that may make defending or enforcing our patents extremely difficult. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of shares of our common stock. Third parties may initiate legal proceedings against us alleging that we infringe their intellectual property rights or we may initiate legal proceedings against third parties to challenge the validity or scope of intellectual property rights controlled by third parties. Third parties may initiate legal proceedings against us alleging that we infringe their intellectual property rights or we may initiate legal proceedings against third parties to challenge the validity or scope of intellectual property rights controlled by third parties, including in oppositions, interferences, revocations, reexaminations, inter partes review or derivation proceedings before the USPTO or its counterparts in other jurisdictions. These proceedings can be expensive and time- consuming and many of our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. We could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent of a third party. A finding of infringement could prevent us from commercializing our pegozafermin or any future product candidates or force us to cease some of our business operations, which could materially harm our business. Although we have reviewed certain third- party patents and patent filings that we believe may be relevant to our therapeutic candidates or products, we have not conducted a freedom- to- operate search or analysis for any of our therapeutic candidates or products, and we may not be aware of patents or pending or future patent applications that, if issued, would block us from commercializing our product candidates. Thus, we cannot guarantee that our product candidates, or our commercialization thereof, do not and will not infringe any third party' s intellectual property. Risks Related to Ownership of Our Common Stock The price of our common stock may be volatile and fluctuate significantly and results announced by us and our collaborators or competitors could cause our stock price to decline, and you may lose all or part of your investment. The market price of our common stock could fluctuate significantly, and you may not be able to resell your shares at or above the price you paid for your shares. Our stock price could fluctuate significantly due to various factors in addition to those otherwise described in this Annual Report on Form 10- K, including those described in these " Risk Factors, " including business developments announced by us and by our collaborators and competitors, or as a result of market trends and daily trading volume. The business developments that could affect our stock price include announcements or disclosures from competitors in the same class or category, new collaborations, clinical advancement, commercial launch or discontinuation of product candidates in the same class or category and regulatory approvals for our product candidates or product candidates in the same class or category. Our stock price could also fluctuate significantly with the level of overall

investment interest in small- cap biotechnology stocks or for other reasons unrelated to our business. Any of these factors may result in large and sudden changes in the volume and trading price of our common stock. In the past, following periods of volatility in the market price of a company' s securities, stockholders have often instituted securities class action litigation against that company. Sales of our common stock, or the perception that such sales may occur, or issuance of shares of our common stock upon exercise of warrants could depress the price of our common stock. Sales of a substantial number of shares of our common stock in the public market, or the perception that such sales may occur, could depress the market price of our common stock. In addition, we have filed a registration statement registering under the Securities Act the shares of our common stock reserved for issuance under our 2019 Plan and **the Amended and Restated** 2023 Inducement Plan, including shares issuable upon exercise of outstanding options. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates. Further, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt or equity securities. In addition, **if** we ~~must~~ **issue warrants in the future, we may need to** settle exercises of **such** ~~our outstanding~~ warrants in shares of our common stock. The issuance of shares of our common stock upon exercise of ~~the~~ warrants will dilute the ownership interests of our stockholders, which could depress the trading price of our common stock. In addition, the market' s expectation that exercises may occur could depress the trading price of our common stock even in the absence of actual exercises. Moreover, the expectation of exercises could encourage the short selling of our common stock, which could place further downward pressure on the trading price of our common stock. Certain of our executive officers and directors have entered or may enter into Rule 10b5- 1 plans providing for sales of shares of our common stock from time to time. Under a Rule 10b5- 1 plan, a broker executes trades pursuant to parameters established by the executive officer or director when entering into the plan, without further direction from the executive officer or director. A Rule 10b5- 1 plan may be amended or terminated in some circumstances. Our executive officers and directors also may buy or sell additional shares outside of a Rule 10b5- 1 plan when they are not in possession of material nonpublic information. Raising additional capital may cause dilution to existing stockholders, restrict our operations or require us to relinquish rights to our technologies. Existing stockholders could suffer dilution or be negatively affected by fixed payment obligations we may incur if we raise additional funds through the issuance of additional equity securities, including under the **2023** ATM Facility (defined ~~above~~ **below**), or debt. Furthermore, these securities may have rights senior to those of our common stock and could contain covenants or protective rights that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. **We may issue warrants in the future, and** ~~Hedging~~ **hedging** activity by investors in ~~the~~ **such** warrants could depress the trading price of our common stock. We ~~expect that many~~ **may issue warrants in the future and** investors in ~~our~~ **such** warrants ~~will~~ **may** seek to employ an arbitrage strategy. Under this strategy, investors typically short sell a certain number of shares of our common stock and adjust their short position over time while they continue to hold the warrants. Investors may also implement this type of strategy by entering into swaps on our common stock in lieu of, or in addition to, short selling shares of our common stock. This market activity, or the market' s perception that it will occur, could depress the trading price of our common stock. General Risk Factors Our directors, executive officers and current holders of 5 % or more of our capital stock have substantial control over our company, which could limit your ability to influence the outcome of matters subject to stockholder approval, including a change of control. As of December 31, ~~2023~~ **2024** , our executive officers, directors and other holders of 5 % or more of our common stock beneficially owned a majority of our outstanding common stock. As a result, our executive officers, directors and other holders of 5 % or more of our common stock, if they act, will be able to influence or control matters requiring approval by our stockholders, including the election of directors and the approval of mergers, acquisitions or other extraordinary transactions. In addition, our current directors, executive officers and other holders of 5 % or more of our common stock, acting together, would have the ability to control the management and affairs of our company. They may also have interests that differ from yours and may vote in a way with which you disagree and that may be adverse to your interests. This concentration of ownership may have the effect of delaying, preventing or deterring a change of control of our company, could deprive our stockholders of an opportunity to receive a premium for their shares of our common stock as part of a sale of our company. Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud. If we are unable to maintain effective internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our stock may decrease. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well- conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision- making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected. The Sarbanes- Oxley Act of 2002 (the " Sarbanes- Oxley Act ") requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, we are required to perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting, as required by Section 404 (a) of the Sarbanes- Oxley Act. Section 404 (b) of the Sarbanes- Oxley Act (" Section 404 ") also requires our independent auditors to express an opinion on our internal control over financial reporting. Ensuring that we have adequate internal controls in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that will need to be evaluated frequently. If we are unable to maintain effective internal control over financial

reporting, we may not have adequate, accurate or timely financial information, our independent registered public accounting firm may issue a report that is adverse, and we may be unable to meet our reporting obligations as a public company or comply with the requirements of the SEC or Section 404. This could result in a restatement of our financial statements, the imposition of sanctions, including the inability of registered broker dealers to make a market in our common stock, or investigation by regulatory authorities. Any such action or other negative results caused by our inability to meet our reporting requirements or comply with legal and regulatory requirements or by disclosure of an accounting, reporting or control issue could adversely affect the trading price of our securities and our business. Material weaknesses in our internal control over financial reporting could also reduce our ability to obtain financing or could increase the cost of any financing we obtain. If we are not able to comply with the requirements of Section 404 or if we or our independent registered public accounting firm are unable to express an opinion as to the effectiveness of our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC, or other regulatory authorities, which would require additional financial and management resources. Our amended and restated certificate of incorporation, amended and restated bylaws and Delaware law could prevent a third party from acquiring us (even if an acquisition would benefit our stockholders), may limit the ability of our stockholders to replace our management and limit the price that investors might be willing to pay for shares of our common stock. Our amended and restated certificate of incorporation and our amended and restated bylaws could have the effect of making it more difficult for a third party to acquire, or of discouraging a third party from attempting to acquire, control of us. These provisions could delay or prevent a change in control of the Company and could limit the price that investors might be willing to pay in the future for shares of our common stock. In addition, as a Delaware corporation, we are subject to the anti- takeover provisions of Section 203 of the Delaware General Corporation Law, which prohibits a Delaware corporation from engaging in a business combination specified in the statute with an interested stockholder (as defined in the statute) for a period of three years after the date of the transaction in which the person first becomes an interested stockholder, unless the business combination is approved in advance by a majority of the independent directors or by the holders of at least two- thirds of the outstanding disinterested shares. The application of Section 203 of the Delaware General Corporation Law could also have the effect of delaying or preventing a change of control of us. Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and the federal district courts of the United States will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees. Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for certain actions or proceedings under Delaware statutory or common law. Our amended and restated certificate of incorporation provides further that the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. These choice of forum provisions may limit a stockholder' s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees. If a court were to find the choice of forum provision contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable, we may incur additional costs associated with resolving such action in other jurisdictions. Our ability to use our net operating loss carryforwards and other tax attributes may be limited. If we are required to pay any tax assessment, it could impact our net operating loss carryforwards, as well as our results of operations and financial condition. As of December 31, ~~2023~~ **2024**, we had U. S. federal and state net operating loss (" NOL ") carryforwards of $ ~~195~~ **255**. ~~0~~ **5** million and $ ~~302~~ **496**. ~~8~~ **5** million, respectively, which may be available to offset future taxable income. As of December 31, ~~2023~~ **2024**, we also had gross federal tax credits of $ **19.** 7 ~~.5~~ million, which may be used to offset future tax liabilities. Certain NOLs and tax credit carryforwards will begin to expire in 2039. Use of our NOL carryforwards and tax credit carryforwards depends on many factors, including having current or future taxable income, which cannot be assured. In addition, in December 2023, the Israeli Tax Authorities issued a tax assessment claiming our 2019 reorganization and intercompany transaction to license the intellectual property rights from our subsidiary in Israel should be treated as a sale of intellectual property rights **. As of December 31, 2024, discussions with the Israel Tax Authorities are ongoing**. If this matter is litigated and the Israeli Tax Authorities are able to successfully sustain their position and we are required to pay a tax assessment, it could impact our NOL carryforwards and our results of operations and financial condition could be materially and adversely affected. See further discussion in Part II, Item 7 " Management' s Discussion and Analysis of Financial Condition and Results of Operations — Critical Accounting Estimates — Income Taxes " and in Note 9 to our consolidated financial statements appearing under Part II, Item 8 of this Annual Report on Form 10- K. Litigation costs and the outcome of litigation could have a material adverse effect on our business. From time to time we may be subject to litigation claims through the ordinary course of our business operations regarding, but not limited to, securities litigation, employment matters, security of patient and employee personal information, contractual relations with collaborators and licensors and intellectual property rights. Litigation to defend ourselves against claims by third parties, or to enforce any rights that we may have against third parties, could result in substantial costs and diversion of our resources, causing a material adverse effect on our business, financial condition, results of operations or cash flows. ~~57~~