Risk Factors Comparison 2024-03-14 to 2023-02-27 Form: 10-K

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You should carefully consider the risks described below together with the other information included in this Annual Report on Form 10- K. Our business, financial condition ~~or~~ **and** results of operations could be adversely affected by any of these risks. **The risks described below include forward- looking statements, and actual events and our actual results may differ materially from these forward- looking statements. Additional risks and uncertainties not currently known to us or that we currently deem immaterial may also impair our business, results of operations and financial condition. Furthermore, additional risks and uncertainties are described under other captions in this Annual Report on Form 10- K.** If any of these risks occur, the value of our common stock could decline. **A** ~~For a~~ summary of the risk factors included in this Item 1A ~~and~~ **are set** ~~for~~ **forth below followed by a full set of risk factors described in greater detail. For** further details on our forward- looking statements, see " **Cautionary Statement Regarding** Forward- Looking Statements ~~and Summary of Risk Factors~~ " on page 1. **Summary of Risk Factors Risks Related to the Commercialization and Continued Approval of our Products ● We currently depend heavily on the generation of revenues from the sales of our products. Any current products or future product candidates may cause serious adverse events or undesirable side effects. There may be safety issues regarding our products that were not known at the time of approval are discovered. Physicians, patients, third party payors and others in the medical community might not accept and use our current or future products. Coverage and reimbursement may not be available for our current or future products in all territories. Risks Related to Our Business We have a limited commercial operating history. We may fail to supply drug substance to Chiesi or Pfizer. We may be unable to enhance our portfolio of product candidates. We or our providers may experience manufacturing problems. Reliance on third parties for final processing of our products and product candidates exposes us to a number of risks. Developments by competitors may render our products or technologies obsolete or non- competitive. If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. Our internal computer systems, or those used by our third- party contractors or consultants, may fail or suffer security breaches and expose our company to liabilities. We may face product liability claims. Our ability to utilize net operating loss carryforwards may be limited.** Risks Related to Clinical Trials and Regulatory Matters We ~~authorities~~ **Related to the Commercialization of Drug Products There has been continued non-compliance with the terms and conditions of the Brazil Agreement** . ~~If problems are identified during~~ **We do not control and may not be able to effectively influence Fiocruz' s ability to distribute BioManguinhos alfataliglicerase in Brazil.Any failure by Fiocruz to comply with the purchase requirements of the Brazil Agreement,or any** ~~the~~ **other** ~~review~~ **material breach by Fiocruz of the agreement,may have a material adverse effect on** ~~or~~ **our business** ~~inspection of these manufacturers or manufacturing facilities~~ , ~~it could result~~ **results of operations and financial condition.We face the risk of lower than anticipated purchases of BioManguinhos alfataliglicerase by the Brazilian MoH.In addition,we may fail to supply the intended amounts on time,if at all.We also cannot accurately predict the amount of revenues we will generate under the Brazil Agreement** in **future periods,if any.Any failure by the Brazilian MoH to purchase BioManguinhos alfataliglicerase,by us to supply BioManguinhos alfataliglicerase for purchase or by Fiocruz to distribute BioManguinhos alfataliglicerase in Brazil,or the experience of significant delays in any of the foregoing,may have a material adverse effect on our business,results of operations and financial condition.We have limited experience in selling,marketing or distributing products and limited internal capability to do so.We currently have very limited sales,marketing or distribution capabilities and no experience in building a sales force and distribution capabilities.Under our arrangements with Pfizer and Chiesi,we have out- licensed the marketing rights to Elelyso and pegunigalsidase alfa,except that we retained the marketing rights to BioManguinhos alfataliglicerase in 49Brazil.We have not licensed the marketing or commercialization rights to any of our** ~~the~~ **other** ~~facility becoming unable to manufacture the~~ product ~~or~~ **candidates to any party.The commercialization of** a ~~determination~~ **drug product requires** that ~~inventories are~~ **we commit significant financial and managerial resources to develop a marketing and sales force with technical expertise and with supporting distribution capabilities.We may elect to pursue arrangements regarding the sales and marketing and distribution of one or more of our other product candidates.Our future revenues may depend,in part,on our ability to enter into and maintain arrangements with our existing partners and other companies having sales,marketing and distribution capabilities and the ability of such companies to successfully market and pharmaceutical products on a global scale.Commercialization,marketing,distribution and other similar alliances with respect to our product and product candidate will subject us to a number of risks,including the following:● we may be required to relinquish important rights to our products or product candidates;● we may** not ~~safe~~ **be able to control the amount and timing of resources that our distributors** ~~for~~ **or** ~~commercial~~ **collaborators may devote to the commercialization of our product candidates;● our distributors or collaborators may experience financial difficulties;● our distributors or collaborators may not devote sufficient time to the marketing and** ~~sale~~ **sales of our products;and ● business combinations or significant changes in a collaborator' s business strategy may adversely affect a collaborator' s willingness or ability to complete its obligations under any arrangement.Factors that may inhibit our efforts to commercialize our products directly and without strategic partners include:● the inability to recruit and retain adequate numbers of effective sales and marketing personnel;● the inability of sales personnel to obtain access to an adequate number of physicians or to pursuade them to prescribe our products;● the lack of complementary products to be offered by sales personnel;and ●**

unforeseen costs and expenses.We may not be successful in recruiting or retaining the sales and marketing personnel necessary to sell BioManguinhos alfataliglicerase in Brazil or any of our products upon approval,if at all ,which ~~may~~ **would** have a material adverse effect on our business,results of operations and financial condition.If physicians,patients,third party payors and others in the medical community do not accept and use ~~Elfabrio~~ **taliglucerase alfa** , ~~Elelyso~~ **pegunigalsidase alfa or any of** ~~or~~ **our** ~~any~~ other ~~future products~~ **product candidates,if approved** ,our ability to generate revenue from product sales will be materially impaired.Physicians and patients,and other healthcare providers,may not accept and use **any of** ~~Elfabrio,Elelyso or~~ **our products** ~~any other future of our~~ **or** ~~other~~ **any** product candidates **,if approved for marketing** .Future acceptance and use of any of our products **or any product candidates,if approved,** will depend upon a number of factors including:● perceptions by physicians,patients,third party payors and others in the medical community about the safety and effectiveness of ~~Elfabrio~~ **taliglucerase alfa,pegunigalsidase alfa or** ~~or~~ **our other drug candidates** ~~Elelyso,or any future product,if any~~ ;● the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies; ~~36~~ ● the prevalence and severity of any side effects,including any limitations or warnings contained in our products' approved labeling ~~,including the boxed warning associated with Elfabrio in the United States~~ ; **50** ● pharmacological benefits of ~~Elfabrio~~ **taliglucerase alfa,pegunigalsidase alfa or** ~~or~~ **our other drug candidates** ~~Elelyso,or any future product,if any~~ relative to competing products and products under development;● the efficacy and potential advantages relative to competing products and products under development;● relative convenience and ease of administration;● effectiveness of education,marketing and distribution efforts by **us** ~~Chiesi,Pfizer~~ and **our** ~~any other relevant~~ licensees and distributors **,if any** ;● publicity concerning ~~Elfabrio~~ **taliglucerase alfa,pegunigalsidase alfa or** ~~or~~ **our** ~~Elelyso,~~ **other drug candidates** or ~~any future product,if any,or concerning~~ competing products and treatments; ~~and~~ ● **coverage and reimbursement of our products by third party payors;and ●** the price for our products and competing products **.A lack of market acceptance of BioManguinhos alfataliglicerase in Brazil,or globally for any of our other products candidates,if approved,would have a material adverse effect on our business,results of operations and financial condition** .If the market opportunities for ~~Elfabrio,Elelyso or any~~ other ~~future products~~ **product candidates,and for BioManguinhos alfataliglicerase in Brazil,** are smaller than we believe they are,our revenues may be adversely affected and our business may suffer.To date,our development efforts have focused mainly on relatively rare disorders with ~~relatively~~ small patient populations,in particular Gaucher disease and Fabry disease. ~~Estimation~~ **Currently,most reported estimates** of the prevalence of these diseases are based on studies of small subsets of the population of specific geographic areas ~~and~~ **,which** are **then extrapolated** ~~often inexact and prone~~ to ~~error~~ **estimate the prevalence of the diseases in the broader world population** .As new studies are performed,the estimated prevalence of these diseases may change.There can be no assurance that the prevalence of Gaucher disease or Fabry disease in the study populations,particularly in these newer studies,accurately reflect the prevalence of these diseases in the broader world population.If the market opportunities for our **current** ~~products or~~ product candidates are smaller than we believe they are,our revenues may be adversely affected and our business may suffer.Coverage and reimbursement may not be available for ~~Elfabrio,Elelyso~~ **one or more of** ~~or~~ **our** ~~any other future products~~ **product candidates,if approved,** in all territories,which could diminish **our** sales ~~of our~~ **or** ~~products or adversely~~ affect ~~the~~ **our ability to sell any such products** profitably ~~of such sales~~ .Market acceptance and sales of ~~Elfabrio,Elelyso~~ **any one or more of** ~~or~~ **our** ~~any other future products~~ **product candidates** ,if ~~any~~ **approved** ,will depend on coverage and reimbursement policies in the countries in which they are approved for sale.Government authorities and third- party payors,such as private health insurers and health maintenance organizations,decide which drugs they will pay for and establish reimbursement levels.Obtaining reimbursement approval for an approved product from ~~individual~~ governments and other third party payors is a time consuming ~~(six to 12 months or longer)~~ and costly process that requires our collaborators or us,as the case may be,to provide supporting scientific,clinical and cost-effectiveness data for the use of our products,if and when approved,to every payor. **We may not be able to provide** ~~Data~~ **data** sufficient to gain acceptance with respect to coverage and reimbursement **or we** might **need to conduct** ~~not be available,or~~ post-marketing studies ~~may be required~~ in order to demonstrate the cost- effectiveness of approved products,if any,to such payors' satisfaction.Such studies might require our collaborators or us to commit a significant amount of management time and financial and other resources.Even if a payor determines that an approved product is eligible for reimbursement,the payor may impose coverage limitations that preclude payment for some uses that are approved by the FDA or other regulatory authorities. ~~For example,the U.S.Inflation Reduction Act allows Medicare to negotiate the prices of the prescription drugs.Such initiatives and legislation may cause added pricing pressure on our products.Proposals that could impact coverage and reimbursement of our products,including giving states more flexibility to manage drugs covered under the Medicaid program and permitting the re-importation of prescription medications from other countries,could have a material adverse effect by limiting our products' use and coverage.To the extent that private insurers or managed care programs in the United States or elsewhere follow Medicaid coverage and payment developments,they could use the enactment of these increased rebates to exert pricing pressure on our products,and the adverse effects may be magnified by their adoption of lower payment schedules.~~ In addition,full reimbursement may not be available for high priced products.Moreover,eligibility for coverage does not imply that any approved product will be reimbursed in all cases or at a rate ~~37that~~ **that** allows us to make a profit or even cover our costs.Limited reimbursement amounts may reduce the demand for,or the price of, ~~Elfabrio,Elelyso or~~ **our** ~~any other future products~~ **product candidates** .If coverage and reimbursement are not available or are available only to limited levels,the sales of ~~Elfabrio,Elelyso or~~ **our** ~~other future~~ products,if ~~any~~ **approved** ,may be diminished or we may not be able to sell such products profitably. **51We** ~~The pricing of our products in different countries may vary widely,thus creating the potential for third- party trade in our products in an attempt to exploit price differences between countries.This third- party trade of our products could undermine our sales in markets with higher prices which could have a material adverse effect on our business,results of operations and financial condition.Fioeruz is not complying,and we expect they will continue to not comply,with the terms and conditions of the Brazil Agreement.We do not control and may not be able to effectively influence Fioeruz' s ability to distribute~~

~~BioManguinhos alfataliglicerase in Brazil.Fioeruz has not complied with the purchase requirements of the Brazil Agreement in the past,and we expect Fioeruz will continue to not comply and may otherwise materially breach the agreement.Continued non- compliance may have a material adverse effect on our business,results of operations and financial condition.We face the risk of lower than anticipated purchases of BioManguinhos alfataliglicerase by the Brazilian MoH.In addition,we may fail to supply the intended amounts on time,if at all.We also cannot accurately predict the amount of revenues we will generate under the Brazil Agreement in future periods,if any.Any failure by the Brazilian MoH to purchase BioManguinhos alfataliglicerase,by us to supply BioManguinhos alfataliglicerase for purchase or by Fioeruz to distribute BioManguinhos alfataliglicerase in Brazil,or the experience of significant delays in any of the foregoing,may have a material adverse effect on our business,results of operations and financial condition.We~~ and our collaborating partners may be subject,directly or indirectly,to federal and state healthcare fraud and abuse and false claims laws and regulations.If we or our collaborating partners are unable to comply,or have not fully complied,with such laws,we could face substantial penalties.All marketing activities associated with **drug** products that are approved for sale in the United States,if any,will be,directly or indirectly through our customers,subject to numerous federal and state laws governing the marketing and promotion of pharmaceutical products in the United States,including,without limitation,the federal Anti- Kickback Law,the federal False Claims Act and HIPAA.These laws may adversely impact,among other things,our proposed sales,marketing and education programs.The federal Anti- Kickback Law prohibits persons from knowingly and willfully soliciting,receiving,offering or paying remuneration,directly or indirectly,to induce either the referral of an individual,or the furnishing,recommending,or arranging for a good or service,for which payment may be made under a federal healthcare program,such as the Medicare and Medicaid programs.The term " remuneration " has been broadly interpreted to include anything of value,including for example,gifts,discounts,the furnishing of supplies or equipment,credit arrangements,payments of cash,waivers of co- payments and deductibles,ownership interests and providing anything at less than its fair market value.Despite a series of narrow safe harbors,the federal Anti- Kickback Law prohibits many arrangements and practices that are lawful in businesses outside of the healthcare industry.Penalties for violations of the federal Anti- Kickback Law include criminal penalties and civil sanctions such as fines,imprisonment and possible exclusion from Medicare,Medicaid and other state or federal healthcare programs.Many states have also adopted laws similar to the federal Anti- Kickback Law,some of which apply to the referral of patients for healthcare items or services reimbursed by any source,not only the Medicare and Medicaid programs,and do not contain identical safe harbors.The federal False Claims Act imposes liability on any person who,among other things,knowingly presents,or causes to be presented,a false or fraudulent claim for payment by a federal healthcare program.In addition,various states have enacted false claims laws analogous to the False Claims Act.Many of these state laws apply where a claim is submitted to any third- party payer and not merely a federal healthcare program.Violations of the federal False Claims Act and the analogous state laws may result in substantial financial penalties,some as much as three times the actual damages sustained by the government. ~~38HIPAA --~~ **HIPAA** created several new federal crimes,including health care fraud,and false statements relating to health care matters.The health care fraud statute prohibits knowingly and willfully executing a scheme to defraud any health care benefit program,including private third- party payers.The false statements statute prohibits knowingly and willfully falsifying,concealing or covering up a material fact or making any materially false,fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits,items or services.We are unable to predict whether we could be subject to actions under any of these or other fraud and abuse laws,or the impact of such actions.Moreover,to the extent that ~~Elfabrio~~ **taliglucerase alfa** , ~~Elelyso~~ **pegunigalsidase alfa or any of** ~~or~~ **our** ~~any other future products~~ - **product candidates** ,if ~~any~~ **approved for marketing** , ~~are~~ **will be** sold in a foreign country,we and our **future** collaborators may be subject to similar foreign laws and regulations.If we or any of our **future** collaborators are found to be in violation of any of the laws described above and other applicable state and federal fraud and abuse laws,we may be subject to penalties,including civil and criminal penalties,damages,fines,exclusion from government healthcare reimbursement programs and the curtailment or restructuring or our operations,any of which could have a material adverse effect on our business,results of operations and financial condition.Risks ~~Related to Our BusinessWe have a limited commercial operating history which may limit the ability of investors to make an informed investment decision.Elfabrio and Elelyso are our only commercial products both of which are marketed by our commercialization partners.Our operations to date have been limited to acquiring,developing and securing our proprietary technology and undertaking,through third parties,preclinical and clinical trials of our drug candidates and advancing our drug candidates through the regulatory approval processes.These operations provide a limited basis for investors to assess our ability to commercialize our drug candidates and whether to invest in our company.Any failure by us to supply drug substance to Chiesi or Pfizer may have a material adverse effect on our business,results of operations and financial condition.We have agreed to sell drug substance to Pfizer and Chiesi for the production of Elelyso and Elfabrio.With respect to Elelyso,our drug substance supply commitment is for a 15- year period after the execution of the Amended Pfizer Agreement,subject to certain terms and conditions.As part of that obligation,we agreed to substantial financial penalties if we fail to comply with the supply commitments,or are delayed in doing so.The amounts of the penalties depend on when any such failure occurs and for how long it persists,if at all,and~~ may not obtain the necessary U. S., EMA or other worldwide regulatory approvals to commercialize our drug candidates in a timely manner, if at all, which would have a material adverse effect on our business, results of operations and financial condition. To commercialize our drug candidates worldwide, we need FDA approval, EMA approval and approvals from other countries' regulators to commercialize our drug candidates elsewhere, as applicable. In order to obtain FDA approval of any of our drug candidates, we must submit to the FDA a BLA or an NDA demonstrating that the drug candidate is safe and effective for its intended use. This demonstration requires significant research and animal tests, which are referred to as preclinical studies, as well as human tests, which are referred to as clinical trials. In the European Union, we must submit an MAA to the EMA. Satisfaction of the regulatory requirements of the FDA, EMA and other countries' regulatory authorities typically takes many years, depends upon the type, complexity and novelty of the drug candidate and requires substantial resources for research, development and testing.

The ~~We cannot assure you that the FDA will approve the BLA submitted for pegunigalsidase alfa by the PDUFA date or at all, or that the EMA will approve the MAA in a timely manner or at all. We also cannot assure you that the~~ results of clinical trials of our ~~other~~ product candidates ~~will~~ **may fail to** demonstrate that the candidates are safe and effective for their intended uses. Companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced or late- stage clinical trials, even after obtaining promising earlier trial results or in preliminary findings or other comparable authorities for such clinical trials. Further, even if favorable testing data is generated by the clinical trials of a drug candidate, the applicable regulatory authority may not accept or approve a marketing application we file for the drug candidate or may require us to conduct additional clinical testing or perform post- marketing studies which would cause us to incur additional costs. Failure to obtain approval of the FDA, EMA or comparable foreign authorities of ~~pegunigalsidase alfa or~~ any of our **product** ~~other drug~~ candidates in a timely manner, if at all, will severely undermine our business, **results of operations and** financial condition ~~and results of operation~~ by **decreasing** ~~reducing our potential marketable products and~~ our ability to generate ~~corresponding~~ product revenues ~~. In light of our receipt of a CRL~~ from the **sales** ~~FDA regarding our BLA for pegunigalsidase alfa, the U. S. regulatory requirements and timing for pegunigalsidase alfa approval are uncertain; we are substantially dependent on receipt~~ of **such** ~~regulatory approvals for pegunigalsidase alfa, our most advanced~~ product ~~candidate~~ **candidates** ~~. The CRL issued by the FDA in response to the pegunigalsidase alfa BLA did not report any concerns relating to the potential safety or efficacy of pegunigalsidase alfa in the submitted data package. Although the FDA, at the Type A meeting held on September 9, 2021, in principle, agreed that the data package that was subsequently included in the BLA resubmission has the potential to support a traditional approval of pegunigalsidase alfa for the treatment of Fabry disease, we cannot guarantee when, or if, we will be successful in receiving regulatory approval for pegunigalsidase alfa. If we do not obtain approval for pegunigalsidase alfa or are delayed in obtaining such approval, it would have a material and adverse effect on our operations and financial condition. The FDA may request additional data or impose other conditions in connection with an approval of the BLA. We cannot assure you that the FDA will eventually approve pegunigalsidase alfa on a resubmission. In addition, we may incur significant additional expenditures in order to obtain or maintain FDA approval. If the resubmitted BLA is approved, the FDA may subject pegunigalsidase alfa to post- marketing commitments or requirements, and we may need to develop and / or improve certain antibody or additional assays as post- marketing requirements or commitments. Even if we comply with all the requests of regulatory authorities, the FDA and other authorities may ultimately reject the BLA or any other marketing application that we file for a product candidate in the future, if any, or we might not obtain regulatory clearance in a timely manner~~ . We are subject to extensive governmental regulation including the requirements of the FDA and other comparable regulatory authorities before our drug candidates may be marketed. Both before and after marketing approval of our drug candidates, if at all, we, our drug candidates, our suppliers, our contract manufacturers and our contract testing laboratories are subject to extensive regulation by the FDA and comparable foreign regulatory authorities. Failure to comply with applicable requirements of the FDA or comparable foreign regulatory authorities could result in, among other things, any of the following actions: ● warning letters; ● fines and other monetary penalties; ● unanticipated expenditures; ● delays in the FDA' s or other foreign regulatory authorities' approving, or the refusal of any regulatory authority to approve, any drug candidate; ● product recall or seizure; ● interruption of manufacturing or clinical trials; ● operating restrictions; ● injunctions; and ● criminal prosecutions. ~~In~~ **46In** addition to the approval requirements, other numerous and pervasive regulatory requirements apply, both before and after approval, to us, our drug candidates, our suppliers, contract manufacturers, and contract testing laboratories. These include requirements related to: ● testing; ● manufacturing; ● quality control; ● labeling; ● advertising; ● promotion; ● distribution; ● export; ● reporting to the FDA certain adverse experiences associated with use of the drug candidate; and ● obtaining additional approvals for certain modifications to the drug candidate or its labeling or claims. ~~36We~~ **We** also are subject to inspection by the FDA and comparable foreign regulatory authorities, to determine our compliance with regulatory requirements, as are our suppliers, contract manufacturers, and contract testing laboratories, and there can be no assurance that the FDA, or any other comparable foreign regulatory authority, will not identify compliance issues that may disrupt production or distribution, or require substantial resources to correct. We may be required to make modifications to our manufacturing operations in response to these inspections which may require significant resources and may have a material adverse effect upon our business, results of operations and financial condition. The approval process for any drug candidate may also be delayed by changes in government regulation, future legislation or administrative action or changes in policy of the FDA and comparable foreign authorities that occur prior to or during their respective regulatory reviews of such drug candidate. Delays in obtaining regulatory approvals with respect to any drug candidate will materially and adversely affect our prospects, business, results of operations and financial condition. Delays in obtaining regulatory approvals with respect to any drug candidate may: ● delay commercialization of, and our ability to derive product revenues from, such drug candidate; ● delay any regulatory- related milestone payments payable under outstanding collaboration agreements; ● require us to perform costly procedures with respect to such drug candidate; or ● otherwise diminish any competitive advantages that we may have with respect to such drug candidate. Delays in the approval process for any drug candidate ~~will~~ **may** have a material adverse effect upon our prospects, business, results of operations and financial condition. ~~Clinical~~ **47Clinical** trials are very expensive, time- consuming and difficult to design and implement and may result in unforeseen costs, which may have a material adverse effect on our business, results of operations and financial condition. Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. Preliminary and initial results from a clinical trial do not necessarily predict final results, and failure can occur at any stage of the trial. We may encounter problems that could cause us to abandon or repeat preclinical studies or clinical trials. The clinical trial process is also time- consuming. Failure or delay in the commencement or completion of our clinical trials may be caused by several factors, including: ● slower than expected rates of patient recruitment, particularly with respect to trials of rare diseases; ● determination of dosing issues; ● unforeseen safety issues; ● lack of effectiveness during clinical trials; ● disagreement by applicable regulatory bodies over our trial protocols, the interpretation of

data from preclinical studies or clinical trials or conduct and control of clinical trials; ● determination that the patient population participating in a clinical trial may not be sufficiently broad or representative to assess efficacy and safety for our target population; ● inability to monitor patients adequately during or after treatment; ● inability or unwillingness of medical investigators and institutional review boards to follow our clinical protocols; ~~and37 --~~ **and** ● lack of sufficient funding to finance the clinical trials. Any failure or delay in commencement or completion of any clinical trials of our product candidates will have a material adverse effect on our business, results of operations and financial condition. In addition, we, the FDA or other regulatory authorities may suspend any clinical trial at any time if it appears that we are exposing participants in the trial to unacceptable safety or health risks or if the FDA or such other regulatory authorities, as applicable, find deficiencies in our IND submissions or the conduct of the trial. Any suspension of a clinical trial may have a material adverse effect on our business, results of operations and financial condition. If the results of our clinical trials do not support our claims relating to a drug candidate, or if serious side effects are identified, the completion of development of such drug candidate may be significantly delayed or we may be forced to abandon development altogether, which will significantly impair our ability to generate product revenues. The results of our clinical trials with respect to any drug candidate might not support our claims of safety or efficacy, the results of our clinical trials may fail to conclusively show superiority over other commercially available treatments for the same or similar indications, the effects of our drug candidates may not be the desired effects or may include undesirable side effects or the drug candidates may have other unexpected characteristics. Data obtained from tests are susceptible to varying interpretations which may delay, limit or prevent regulatory approval. The clinical trial process may fail to demonstrate that our drug candidates are safe for humans and effective for indicated uses. In addition, our clinical trials, may involve specific and small patient populations. Results of early clinical trials conducted on a small patient population may not be indicative of future results. Adverse or inconclusive results may cause us to abandon a drug candidate and may delay development of other drug candidates. Any delay in, or termination of, our clinical trials will delay the filing of BLAs and NDAs with the FDA, or other filings with other foreign regulatory authorities, and, ultimately, significantly impair our ability to commercialize our drug candidates and generate product revenues which would have a material adverse effect on our business, results of operations and financial condition. ~~Interim~~ **48Interim** , ~~topline~~ **top- line** or preliminary data from clinical trials that we announce or publish may change as more patient data becomes available and are subject to audit and verification procedures that could result in material changes in the final data. We may publicly disclose interim, ~~topline~~ **top- line** or preliminary data from our clinical trials, which is based on a preliminary analysis of then- available data. The results and related findings and conclusions are subject to change following a full analysis of all data related to the particular trial. We also may 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, any interim, ~~topline~~ **top- line** or preliminary results that we report may differ from future results of the same trials, or different conclusions or considerations may qualify such results once additional data have been received and fully evaluated. ~~Topline~~ **Top- line** data also remain subject to audit and verification procedures that may result in the final data being materially different than the preliminary data we previously published. As a result, any ~~topline~~ **top- line** data should be viewed with caution until final data are available. 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 data becomes available. Further, regulatory agencies may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses, or may interpret or ascribe different weight to the data, which may impact the value of the clinical trial and may affect the particular clinical program and the approvability or commercialization of the particular product candidate and our business in general. If regulatory authorities disagree with the conclusions we reach, we may not be able to obtain approval for and commercialize our product candidates, which will have a material adverse effect on our business, results of operations and financial condition. We may find it difficult to enroll patients in our clinical trials, or patients may discontinue their participation in our clinical trials, which could cause significant delays in the completion of such trials or may negatively impact the results of these studies and extend the timeline for completion of our development programs or cause us to abandon one or more clinical trials. Some of the diseases or disorders that our drug candidates **under evaluation** are intended to treat are relatively rare and we expect only a subset of the patients with these diseases to be eligible for our clinical trials. Our clinical trials generally mandate that a ~~38patient --~~ **patient** cannot be involved in another clinical trial for the same indication. Therefore, subjects that participate in ongoing clinical trials for products that are competitive with our drug candidates are not available for our clinical trials. An inability to enroll a sufficient number of patients for any of our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. In addition, patients who enroll in our clinical trials may discontinue their participation at any time during the study as a result of a number of factors, **related to the trials or not,** including withdrawing their consent, experiencing adverse clinical events, which may or may not be judged related to our drug candidates ~~under evaluation~~ , or due to **personal reasons, such as** planned or actual pregnancies. The discontinuation of patients in any one of our studies may delay the completion of the study or cause the results from the study not to be positive or to not support a filing for regulatory approval of the applicable drug candidate. Any failure to enroll a sufficient number of patients in our clinical trials in a timely manner, if at all, may have a material adverse effect on our business, results of operations and financial condition. **Our** ~~Because our~~ clinical trials depend upon third- party ~~researchers~~ **service providers and, accordingly** , the results of our clinical trials and such research activities are subject to delays and other risks which are, to a certain extent, beyond our control, which could impair our clinical development programs and our competitive position. We depend upon independent investigators and collaborators, such as universities and medical institutions, to conduct our preclinical and clinical trials. These collaborators are not our employees, and we cannot control the amount or timing of resources that they devote to our clinical development programs. The investigators may not prioritize to our clinical development programs or pursue them as diligently as we would if we were undertaking such programs directly. If outside collaborators fail to devote sufficient time and resources to our clinical development programs, or if their performance is substandard, the approval of anticipated NDAs, BLAs

and other marketing applications, and our introduction of new drugs, if any, may be delayed which could impair our clinical development programs and would have a material adverse effect on our business, results of operations and financial condition. Our collaborators may also have relationships with other commercial entities, some of whom may compete with us. If our collaborators also assist our competitors, our competitive position could be harmed. ~~We~~ **49We** have only limited experience in regulatory affairs, and some of our drug candidates may be based on new technologies. These factors may affect our ability or the time we require to obtain necessary regulatory approvals. We have only limited experience in filing and prosecuting the applications necessary to gain regulatory approvals for medical devices and drug candidates. Moreover, some of the drug candidates that are likely to result from our development programs may be based on new technologies that have not been extensively tested in humans. The regulatory requirements governing these types of drug candidates may not be well defined or more rigorous than for conventional products. As a result, we may experience a longer regulatory process in obtaining regulatory approvals of any products that we develop, which may have a material adverse effect on our business, results of operations and financial condition. We may seek orphan drug designation for some or all of our product candidates across various indications, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug designation, including market exclusivity, which may cause our revenue, if any, to be reduced. We may seek orphan drug **or other comparable** ~~designation~~ **designations** for our product candidates in specific ~~orphan~~ indications in which there is a medically plausible basis for the use of these products. Even if we obtain orphan drug designation, exclusive marketing rights in the United States **or other applicable jurisdictions** may be limited if we seek approval for an indication broader than the orphan designated indication, and may be lost if the FDA **, or other applicable regulatory authorities** later ~~determines~~ **determine** that the request for designation was materially defective, if we are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition, or if a subsequent applicant demonstrates clinical superiority over our products, if approved. In addition, more than one drug can have orphan designation for the same indication. Although we may seek orphan drug designation for other product candidates, we might not receive such designations. ~~39Risks Related to the COVID- 19 PandemicThe COVID- 19 pandemic, or any other pandemic, epidemic or outbreak of an infectious disease, could adversely impact our business, including our clinical trials, and financial condition. In December 2019, a novel strain of coronavirus, COVID- 19, was reported to have surfaced in Wuhan, China. Since then, the COVID- 19 coronavirus and its variants have spread to multiple countries, including the United States, Australia and European and Asia- Pacific countries, including countries where we have planned or active clinical trial sites. As the COVID- 19 coronavirus and its variants continue to spread around the globe, we may experience disruptions that could potentially impact our business and clinical trials. While the extent of the impact of the current COVID-19 pandemic on our business and financial results depends on future developments that are highly uncertain and cannot be predicted, including new information which may emerge concerning the severity of the coronavirus and its variants and the actions to contain them or treat their impact, among others, a continued and prolonged public health crisis such as the COVID-19 pandemic may adversely affect our business, results of operations and financial condition.~~ Risks Related to Our BusinessWe have a limited..... of operations and financial condition. 46Risks Related to our Financial Condition and Capital RequirementsServicing our debt and settling conversion requests may require a significant amount of cash, and we may not have sufficient cash flow from our business to pay our debt. Furthermore, restrictive covenants governing our indebtedness may restrict our ability to raise additional capital. ~~We currently~~ **As of December 31, 2023, we** have outstanding $ ~~28~~ **20** . ~~75~~ **4** million aggregate principal amount of our 2024 Notes which are secured with a perfected lien on all of our assets. Under the terms of the indenture governing the 2024 Notes, or the 2024 Indenture, we are required to maintain a minimum cash balance of at least $ 7. 5 million. Our ability to make payments with respect to the 2024 Notes and to satisfy any other debt obligations depends on our future operating performance and our ability to generate significant cash flow in the future, which will be affected by prevailing economic conditions and financial, business, competitive, legislative and regulatory factors as well as other factors affecting our company and industry, many of which are beyond our control. If, when required, we are unable to comply with the terms of the 2024 Notes, we may be required to adopt one or more alternatives, such as selling assets, restructuring debt or obtaining additional equity capital on terms that may be onerous or highly dilutive. In addition, certain terms of the 2024 Notes regarding the security interest or future indebtedness may restrict us from adopting any of these alternatives. We may be unable to obtain amendments and waivers of such restrictions. If there is a default ~~of~~ **on** such notes, the note holders could, among other things, elect to declare all amounts owed immediately due and payable, which could cause all or a large portion of our available cash flow to be used to pay such amounts and thereby reduce the amount of cash available to pursue our business plans or force us into bankruptcy or liquidation, or, with respect to our indebtedness that is secured, result in the foreclosure on the assets that secure the debt, which would force us to relinquish rights to assets that we may believe are critical to our business. Any default on our debt will have a material adverse effect on our business, results of operations and financial condition. Our significant level of indebtedness could adversely affect our business, results of operations and financial condition and prevent us from fulfilling our obligations under our convertible notes and our other indebtedness. Our 2024 Notes represent a significant amount of indebtedness with substantial debt service requirements. We may also incur additional indebtedness to meet future financing needs. Our substantial indebtedness could have material adverse effects on our business, results of operations and financial condition. For example, it could: **50** ● make it more difficult for us to satisfy our financial obligations, including with respect to the 2024 Notes; ● result in an event of default under **the 2024 Indenture** ~~our outstanding convertible notes~~ if we fail to comply with the financial and other restrictive covenants contained in agreements governing any future indebtedness, which event of default could result in all of our debt becoming immediately due and payable; ● increase our vulnerability to general adverse economic, industry and competitive conditions; ● reduce the availability of our cash flow to fund working capital, capital expenditures, acquisitions and other general corporate purposes because we will be required to dedicate a substantial portion of our cash flow from operations to the payment of principal and interest on our indebtedness; ● limit our flexibility in planning for, or reacting to, and increasing our

vulnerability to changes in our business, the industry in which we operate and the general economy; ● prevent us from raising funds necessary to purchase 2024 Notes surrendered to us by holders upon a fundamental change (as described in the 2024 Indenture ~~governing the notes~~), which failure would result in an event of default with respect to the 2024 Notes; ● place us at a competitive disadvantage compared to our competitors that have less indebtedness or are less highly leveraged and that, therefore, may be able to take advantage of opportunities that our debt levels or leverage prevent us from exploiting; and ● limit our ability to obtain additional financing. ~~47Each~~ -- **Each** of these factors may have a material and adverse effect on our business, results of operations and financial condition and our ability to meet our payment obligations ~~under~~ **relating to** the 2024 Notes and our other indebtedness. We are required to comply with a number of covenants under the 2024 Indenture governing our outstanding 2024 Notes that could hinder our growth. The 2024 Indenture contains a number of restrictive affirmative and negative covenants, which limit our ability to incur additional debt; exceed certain limits; pay dividends or distributions; or merge, consolidate or dispose of substantially all of our assets, including all of our intellectual property assets and other material assets securing the 2024 Notes. A breach of these covenants could result in default, and if such default is not cured or waived, the holders of the indebtedness could, among other things, elect to declare all amounts owed immediately due and payable, which could cause all or a large portion of our available cash flow to be used to pay such amounts and thereby reduce the amount of cash available to pursue our business plans or force us into bankruptcy or liquidation, or, result in the foreclosure on the assets that secure the debt, including all of our intellectual property assets, which would force us to relinquish rights to such assets that we may believe are critical to our business. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations. Any default on our debt will have a material adverse effect on our business, results of operations and financial condition. Any conversion of our outstanding 2024 Notes into common stock will dilute the ownership interest of our existing stockholders, including holders who had previously converted their notes. The conversion of some or all of our 2024 Notes into shares of our common stock will dilute the ownership interests of our existing stockholders. Any sales in the public market of our common stock issuable upon such ~~conversion~~ **conversions** could adversely affect prevailing market prices of our common stock. In addition, the existence of our outstanding 2024 Notes may encourage short selling by market participants because the conversion of 2024 Notes could depress the market price of our common stock. ~~The~~ **51The** fundamental change purchase feature of our outstanding 2024 Notes may delay or prevent an otherwise beneficial attempt to take over our company. The terms of our outstanding 2024 Notes require us to offer to purchase the notes for cash in the event of a fundamental change. A non- stock takeover of our company may trigger the requirement that we purchase the notes. This feature may have the effect of delaying or preventing a takeover of our company that would otherwise be beneficial to our stockholders. We may fail to meet the continued market capitalization- based listing requirement or other continued listing requirements of the NYSE American. The stock market in general, and the market for pharmaceutical companies in particular, have experienced extreme price and volume fluctuations that may have been unrelated or disproportionate to the operating performance of the listed companies. The trading price of our common stock has been volatile and has been subject to wide price fluctuations in response to various factors, many of which are beyond our control. The volatility of our stock price has from time to time in recent periods affected our market capitalization. Adverse fluctuations in the price per share of our common stock or our market capitalization may result in our failure to meet the continued listing requirements of the NYSE American, which would require us to take steps to gain compliance with alternate listing standards or take remedial steps to bring us into compliance. A failure to maintain or regain compliance with applicable listing standards could adversely affect the liquidity of our common stock and could result in an event of default under the 2024 Indenture, which would have a material adverse effect on our business, results of operations and financial condition. We **may** ~~currently have no significant product revenues and~~ need to raise additional capital to operate our business, which may not be available on favorable terms, or at all, and which will have a dilutive effect on our stockholders. ~~To date, we have not generated significant revenues from product sales and only minimal revenues from research and development services and other fees, other than the milestone and other payments we have received in connection with our agreements with Pfizer and Chiesi.~~ For the years ended December 31, 2022 ~~,~~ **and** 2021 ~~and 2020~~ , we had net losses from continuing operations of $ 14. 9 million ~~,~~ **and** $ 27. 6 million **, respectively,** and **, in the year ended December 31, 2023, we had a net income of** $ ~~6~~ **8** . ~~5~~ **3** million **. The net losses for the years ended December 31** , ~~respectively,~~ **2022 and 2021 were** primarily **the** ~~as a~~ result of expenses ~~48incurred~~ -- **incurred** through a combination of research and development activities and expenses supporting those activities, which includes share- based compensation expense. **We may incur losses in future fiscal years as we continue to execute on our strategic goals as** ~~Drug~~ **drug** development and commercialization is very capital intensive. We ~~fund all of our~~ **expect to continue to incur significant** ~~operations~~ - **operating expenditures,** and **we anticipate that our expenses will increase in the foreseeable future as we seek to in- license additional technologies, continue to undertake preclinical development and clinical trials for our current and new drug candidates and seek regulatory approvals for our drug candidates. In addition, changes may occur that could consume our existing** capital ~~expenditures~~ **at a faster rate than projected, including, among others, the cost and timing of regulatory approvals, changes in the progress of our research and development efforts and the costs of protecting our intellectual property rights. Currently, our source of potential revenues will be** from **royalties and commercial milestone payments generated from Pfizer, Fiocruz and Chiesi. We have also generated revenues from research and development services and milestone and** ~~the~~ **other payments we received in connection with our agreements with our commercialization partners, and generated capital from equity and debt offerings and other sources. The** revenues we generate from **royalties** ~~licensing fees~~ and **commercial milestone payments** ~~grants, the net proceeds of equity and debt offerings~~ and other sources ~~. In addition, changes~~ may **not be sufficient to fund** ~~occur~~ -- **our planned operations and** ~~that could consume our existing~~ capital **expenditures** ~~at a faster rate than projected, including, among others, the cost and timing of regulatory approvals, changes in the progress of our research and development efforts and the costs of protecting our intellectual property rights~~ . ~~We will~~ **Accordingly, we may** need to finance our future cash needs through corporate collaboration, licensing

or similar arrangements, public or private equity offerings or debt financings. If we are unable to secure additional financing in the future on acceptable terms, or at all, we may be unable to **expand our portfolio of product candidates,** commence or complete planned preclinical and clinical trials or obtain approval of our drug candidates from the FDA and other regulatory authorities. In addition, we may be forced to reduce or discontinue product development or product licensing, reduce or forego sales and marketing efforts and other commercialization activities or forego attractive business opportunities in order to improve our liquidity and to enable us to continue operations which would have a material adverse effect on our business and results of operations. Furthermore, any additional source of financing will likely involve the issuance of our equity securities, which will have a dilutive effect on our stockholders. ~~We are not currently profitable and delays in achieving profitability, if at all, will have a material adverse effect on our business and results of operations and could negatively impact the value of our common stock. We may incur losses for the foreseeable future. We expect to continue to incur significant operating expenditures, and we anticipate that our expenses will increase in the foreseeable future as we: ● continue to undertake preclinical development and clinical trials for our current and new drug candidates; ● seek regulatory approvals for our drug candidates; and ● seek to in-license additional technologies. We also may continue to experience negative cash flow for the foreseeable future as we fund our operating losses and capital expenditures. As a result, we will need to generate significant revenues in order to achieve and maintain profitability. We may not be able to generate these revenues or achieve profitability in the foreseeable future, if at all. Delays in achieving profitability, or subsequent failures to maintain profitability, will have a material adverse effect on our business and results of operations and could negatively impact the value of our common stock. Risks~~ **52Risks** Related to the Commercialization of Drug Products..... of operations and financial condition. Risks Related to Intellectual Property MattersThe intellectual property and assets owned by our subsidiaries are subject to security agreements that secure our payment and other obligations under our convertible notes, and our subsidiaries have guaranteed all of those obligations. In connection with the issuance of our 2024 Notes, we entered into new security agreements pursuant to which our subsidiaries provided first priority security interests in all of their assets, which consist of all of our intellectual property and other material assets. The security agreements secure certain payment, indemnification and other obligations under the 2024 Notes. If we were to default on certain of our obligations, or in certain other circumstances generally related to ~~52a~~ **a** bankruptcy or insolvency, holders of our outstanding 2024 Notes could seek to foreclose on the collateral under the security agreements to obtain satisfaction of our obligations, and our business could be materially and adversely impacted, which would in turn have a material adverse effect on our results of operations and financial condition. Furthermore, in connection with the issuance of the 2024 Notes, our subsidiaries guaranteed all of our obligations under the 2024 Indenture. If we were to default on our obligations under the 2024 Indenture, the holders could require our subsidiaries to satisfy all of those obligations under the guarantees. If we fail to adequately protect or enforce our intellectual property rights or secure rights to third party patents, the value of our intellectual property rights would diminish and our business, competitive position and results of operations would suffer. As of December 31, ~~2022~~ **2023** , we had **approximately 50** ~~more than 30~~ pending patent applications. However, the filing of a patent application does not mean that we will be issued a patent, or that any patent eventually issued will be as broad as requested in the patent application or sufficient to protect our technology. Any modification required to a current patent application may delay the approval of such patent application which ~~would~~ **may** have a material adverse effect on our business, results of operations and financial condition. In addition, there are a number of factors that could cause our patents, if granted, to become invalid or unenforceable or that could cause our patent applications to not be granted, including known or unknown prior art, deficiencies in the patent application or the lack of originality of the technology. Our competitive position and future revenues will depend in part on our ability and the ability of our licensors and collaborators to obtain and maintain patent protection for our products, methods, processes and other technologies, to preserve our trade secrets, to prevent third parties from infringing on our proprietary rights and to operate without infringing the proprietary rights of third parties. We have filed U. S. and international patent applications for process patents, as well as composition of matter patents, for **Elfabrio** ~~taliglucerase alfa~~ , **Elelyso** ~~pegunigalsidase alfa~~ and our product candidates. However, we cannot predict: ● the degree and range of protection any patents will afford us against competitors and those who infringe upon our patents, including whether third parties will find ways to invalidate or otherwise circumvent our licensed patents; ● if and when patents will issue; ● whether or not others will obtain patents claiming aspects similar to those covered by our licensed patents and patent applications; or ● whether we will need to initiate litigation or administrative proceedings, which may be costly, whether we win or lose. As of December 31, ~~2022~~ **2023** , we held, or had license rights to, **approximately 90** ~~more than 80~~ patents. If patent rights covering our products or technologies are not sufficiently broad, they may not provide us with sufficient proprietary protection or competitive advantages against competitors with similar products and technologies. Furthermore, if the USPTO or foreign patent offices issue patents to us or our licensors, others may challenge the patents or circumvent the patents, or the patent office or the courts may invalidate the patents. Thus, any patents we own or license from or to third parties may not provide any protection against our competitors and those who infringe upon our patents. ~~Furthermore~~ **53Furthermore** , the life of our patents is limited. The patents we hold, and the patents that may be issued in the future based on patent applications from the patent families, relating to our ProCellEx protein expression system are expected to expire by 2025. We rely on confidentiality agreements that could be breached and may be difficult to enforce which could have a material adverse effect on our business and competitive position. Our policy is to enter agreements relating to the non- disclosure of confidential information with third parties, including our contractors, consultants, advisors and research collaborators, as well as agreements that purport to require the disclosure and assignment to us of the rights to the ideas, developments, discoveries and inventions of our employees and consultants while we employ them. However, these agreements can be difficult and costly to enforce. Moreover, to ~~53the~~ -- **the** extent that our contractors, consultants, advisors and research collaborators apply or independently develop intellectual property in connection with any of our projects, disputes may arise as to the proprietary rights to the intellectual property. If a dispute arises, a court may determine that the right belongs to a third party, and enforcement of our rights can be costly and unpredictable. In addition, we rely on

trade secrets and proprietary know- how that we seek to protect in part by confidentiality agreements with our employees, contractors, consultants, advisors and others. Despite the protective measures we employ, we still face the risk that: ● these agreements may be breached; ● these agreements may not provide adequate remedies for the applicable type of breach; or ● our trade secrets or proprietary know- how will otherwise become known. Any breach of our confidentiality agreements or our failure to effectively enforce such agreements may have a material adverse effect on our business and competitive position. If we infringe the rights of third parties we could be prevented from selling products, forced to pay damages and required to defend against litigation which could result in substantial costs and may have a material adverse effect on our business, results of operations and financial condition. We have not received to date any claims of infringement by any third parties. However, as our drug candidates progress into clinical trials and commercialization, if at all, our public profile and that of our drug candidates may be raised and generate such claims. Defending against such claims, and occurrence of a judgment adverse to us, could result in unanticipated costs and may have a material adverse effect on our business and competitive position. If our products, methods, processes and other technologies infringe the proprietary rights of other parties, we may incur substantial costs and we may have to: ● obtain licenses, which may not be available on commercially reasonable terms, if at all; ● redesign our products or processes to avoid infringement; ● stop using the subject matter claimed in the patents held by others, which could cause us to lose the use of one or more of our drug candidates; ● defend litigation or administrative proceedings that may be costly whether we win or lose, and which could result in a substantial diversion of management resources; or ● pay damages. Any costs incurred in connection with such events or the inability to sell our products may have a material adverse effect on our business, results of operations and financial condition. ~~If~~ **54If** we cannot meet requirements under our license agreements, we could lose the rights to our products, which could have a material adverse effect on our business. We depend on licensing agreements with third parties to maintain the intellectual property rights to certain of our product candidates. Our license agreements require us to make payments and satisfy performance obligations in order to maintain our rights under these agreements. All of these agreements last either throughout the life of the patents that are the subject of the agreements, or with respect to other licensed technology, for a number of years after the first commercial sale of the relevant product. In addition, we are responsible for the cost of filing and prosecuting certain patent applications and maintaining certain issued patents licensed to us. If we do not meet our obligations under our license agreements in a timely manner, we could lose the rights to our proprietary technology which could have a material adverse effect on our business, results of operations and financial condition. ~~54Risks --~~ **Risks** Relating to our Operations in IsraelSignificant parts of our operations are located in Israel and, therefore, our results may be adversely affected by political, economic and military conditions in Israel. Our executive office and operations are located in the State of Israel. Accordingly, ~~political,~~ economic **, geopolitical** and military conditions in Israel **and the surrounding region could** directly affect our business. Any armed conflicts, political instability, terrorism, cyberattacks or any other hostilities involving Israel or the interruption or curtailment of trade between Israel and its present trading partners could **adversely** affect **our operations. Since the establishment of Israel in 1948, a number of armed conflicts have occurred between Israel and its Arab neighbors, Hamas and Hezbollah. In October 2023, terrorists from the Hamas organization infiltrated Israel' s southern border from the Gaza Strip and in other areas within the State of Israel attacking a number of civilian and military targets while simultaneously launching extensive rocket attacks on the Israeli population and industrial centers. At the same time, clashes between Israel and Hezbollah in Lebanon have increased. In response, Israel' s security cabinet declared war against the Hamas and a military campaign against these terrorist organizations commenced in parallel to their continued rocket and terror attacks. The attacks by Hamas and Hezbollah, and Israel' s defensive measures, as well as actions that could be taken in the future by NATO, the United States, the United Kingdom the European Union or Israel' s neighboring states and other countries have created global security concerns that may result in a greater or lasting regional conflict. To date, our operations have not been** adversely ~~our operations~~ **affected by this situation** . ~~For example,~~ **Hostilities have not taken place where** our facilities ~~in northern Israel~~ are **located and we do not anticipate any disruption to the supply of Elfabrio or Elelyso. However, our facilities are** in range of **certain of the** rockets that ~~were~~ **are being** fired from Lebanon ~~into Israel during a 2006 war with the Hizbollah in Lebanon,~~ and **elsewhere. We** suffered minimal damages during **a** ~~one of the~~ rocket ~~attacks~~ **attack in 2006** . Our insurance policies do not cover damages incurred in connection with these conflicts or for any resulting disruption in our operations. The Israeli government, as a matter of law, provides coverage for the reinstatement value of direct damages that are caused by terrorist attacks or acts of war; however, the government may cease providing such coverage or the coverage might not be enough to cover potential damages. ~~If~~ **Any damage to** our facilities ~~are damaged~~ as a result of **war or other** hostile action ~~,~~ **may have a material adverse effect on** our **business, results of** operations **and financial condition** ~~may be materially adversely affected~~ . Ongoing and revived hostilities or other Israeli political or economic factors, could prevent or delay shipments of our products, harm our operations and product development and cause any future sales to decrease. **If** ~~In the event that~~ hostilities disrupt the ongoing operation of our facilities or the airports and seaports on which we depend to import and export our supplies, materials, drug substance and other products, our **business, results of** operations **and financial condition** may be materially **and adversely affected. Parties with whom we do business may sometimes decline to travel to Israel during periods of heightened unrest or tension, forcing us to make alternative arrangements when necessary to meet our business partners face to face. Further, shifting economic and political conditions in the United States and in other countries may result in changes in how the United States and other countries conduct business and other relations with Israel, which may have an** adverse ~~affected~~ **impact on our Israeli operations and a material adverse impact on our business. In addition, several countries, principally in the Middle East, restrict doing business with Israel, and additional countries may impose restrictions on doing business with Israel and Israeli companies whether as a result of hostilities in the region or otherwise. Moreover, there have been 55increased efforts by organizations and movements to cause companies and consumers to boycott Israeli goods based on Israeli government policies** . Our operations may be disrupted by the obligations of our personnel to perform military

service which could have a material adverse effect on our business. Many of our male employees in Israel, including members of senior management, are obligated to perform up to one month (in some cases more) of annual military reserve duty until they reach the age of 45 and, in the event of a military conflict, could be called to active duty. ~~Our~~ **To date, we have not suffered any disruptions to our operations from the absence of employees in connection with the current military action. However, we continue to face the risk that our** operations could be disrupted by the absence of a significant number of our employees related to military service or the absence for extended periods of military service of one or more of our key employees. ~~A~~ **Any such** disruption may have a material adverse effect on our business, results of operations and financial condition. **A** ~~Because a~~ certain portion of our expenses is incurred in New Israeli Shekels **and, accordingly** , our results of operations may be seriously harmed by currency fluctuations and inflation. We report our financial statements in U. S. dollars, our functional currency. Although most of our expenses are incurred in U. S. dollars, we pay a portion of our expenses in New Israeli Shekels, or NIS, and as a result, we are exposed to risk to the extent that the inflation rate in Israel exceeds the rate of devaluation of the NIS in relation to the U. S. dollar or if the timing of these devaluations lags behind inflation in Israel. In that event, the U. S. dollar cost of our operations in Israel will increase and our U. S. dollar- measured results of operations will be adversely affected. To the extent that the value of the NIS increases against the U. S. dollar, our expenses on a dollar cost basis increase. Our operations also could be adversely affected if we are unable to guard against currency fluctuations in the future. To date, we have not engaged in hedging transactions. In the future, we may enter into currency hedging transactions to decrease the risk of financial exposure from fluctuations in the exchange rate of the U. S dollar against the NIS. These measures, however, may not adequately protect us from material adverse effects. The tax benefits available to us require that we meet several conditions and may be terminated or reduced in the future, which would increase our taxes. We are able to take advantage of tax exemptions and reductions resulting from the " Approved Enterprise " status of our facilities in Israel. To remain eligible for these tax benefits, we must continue to meet certain conditions, including making specified investments in property and equipment, and financing at least 30 % of such investments with share capital. If we fail to meet these conditions in the future, the tax benefits would be canceled and we may be required to refund any tax benefits we already have enjoyed. These tax benefits are subject to investment policy by the Investment Center and may not be continued in the future at their current levels or at any level. In recent years the Israeli government has reduced the benefits available and has indicated that it may further reduce or eliminate some of these ~~55benefits~~ -- **benefits** in the future. The termination or reduction of these tax benefits or our inability to qualify for additional " Approved Enterprise " approvals may increase our tax expenses in the future, which would reduce our expected profits and adversely affect our business and results of operations. Additionally, if we increase our activities outside of Israel, for example, by future acquisitions, such increased activities generally may not be eligible for inclusion in Israeli tax benefit programs. The Israeli government grants we have received for certain research and development expenditures restrict our ability to manufacture products and transfer technologies outside of Israel and require us to satisfy specified conditions. If we fail to satisfy these conditions, we may be required to refund grants previously received together with interest and penalties which could have a material adverse effect on our business and results of operations. In the past, our research and development efforts have been financed, in part, through grants that we have received from NATI. We, therefore, must comply with the requirements of the Research Law. Under the Research Law we are prohibited from manufacturing products developed using these grants outside of the State of Israel without special approvals, although the Research Law does enable companies to seek prior approval for conducting manufacturing activities outside of Israel without being subject to increased royalties. We may not receive the required approvals for any proposed transfer of manufacturing activities. Even if we do receive approval to manufacture products developed ~~with~~ **56with** government grants outside of Israel, we may be required to pay an increased total amount of royalties (possibly up to ~~300~~ **600** % of the grant amounts plus interest), depending on the manufacturing volume that is performed outside of Israel, as well as ~~at~~ a possibly increased royalty rate. This restriction may impair our ability to outsource manufacturing or engage in similar arrangements for those products or technologies. Additionally, under the Research Law, Protalix Ltd. is prohibited from transferring NATI- financed technologies and related intellectual property rights outside of the State of Israel, except under limited circumstances and only with the approval of NATI Council or the Research Committee. Protalix Ltd. may not receive the required approvals for any proposed transfer and, if received, Protalix Ltd. may be required to pay NATI a portion of the consideration that it receives upon any sale of such technology by a non- Israeli entity. The scope of the support received, the royalties that Protalix Ltd. has already paid to NATI, the amount of time that has elapsed between the date on which the know- how was transferred and the date on which NATI grants were received and the sale price and the form of transaction will be taken into account in order to calculate the amount of the payment to NATI. Approval of the transfer of technology to residents of the State of Israel is required, and may be granted in specific circumstances only if the recipient abides by the provisions of applicable laws, including the restrictions on the transfer of know- how and the obligation to pay royalties. No assurance can be made that approval to any such transfer, if requested, will be granted. These restrictions may impair our ability to sell our technology assets or to outsource manufacturing outside of Israel. The restrictions will continue to apply for a certain period of time even after we have repaid the full amount of royalties payable for the grants. If we fail to satisfy the conditions of the Research Law, we may be required to refund certain grants previously received together with interest and penalties, and may become subject to criminal charges, any of which could have a material adverse effect on our business, results of operations and financial condition. Investors may have difficulties enforcing a U. S. judgment, including judgments based upon the civil liability provisions of the U. S. federal securities laws against us, our executive officers and most of our directors or asserting U. S. securities laws claims in Israel. ~~Most~~ **A majority** of our directors and all of our executive officers are residents of Israel, and accordingly, most of their assets and our assets are located outside the United States. Service of process upon us or our non- U. S. resident directors and officers and enforcement of judgments obtained in the United States against us or our non- U. S. resident directors and executive officers may be difficult to obtain within the United States. We have been informed by our legal counsel in Israel that it may be difficult to assert claims under U.

S. securities laws in original actions instituted in Israel or obtain a judgment based on the civil liability provisions of U. S. federal securities laws. Israeli courts may refuse to hear a claim based on a violation of U. S. securities laws against us or our non- U. S. resident officers and directors because Israel may not be the most appropriate forum to bring such a claim. In addition, even if an Israeli court agrees to hear a claim, it may determine that Israeli law and not U. S. law is applicable to the claim. If U. S. law is found to be applicable, the content of applicable U. S. law must be proved as a fact, which can be a time-consuming and costly process. Certain matters of procedure will also be governed by Israeli law. There is little binding case law in Israel addressing the matters ~~56described~~ -- **described** above. Israeli courts might not enforce judgments rendered outside Israel, which may make it difficult to collect on judgments rendered against us or our non- U. S. resident officers and directors. Moreover, among other reasons, including but not limited to, fraud or absence of due process, or the existence of a judgment which is at variance with another judgment that was given in the same matter if a suit in the same matter between the same parties was pending before a court or tribunal in Israel, an Israeli court will not enforce a non- Israeli judgment if it was given in a state whose laws do not provide for the enforcement of judgments of Israeli courts (subject to exceptional cases) or if its enforcement is likely to prejudice the sovereignty or security of the State of Israel. Risks Related to Investing in our Common StockThe market price of our common stock may fluctuate significantly. The market price of our common stock has experienced significant volatility. The securities of life sciences companies often experience significant volatility in connection with clinical trial and regulatory announcements. ~~We~~ **57We** anticipate that the market price of our common stock is likely to continue to fluctuate significantly in response to numerous factors, some of which are beyond our control, such as: ● ~~the timing of and any delays in anticipated marketing approvals for pegunigalsidase alfa; ●~~ sales of **Elfabrio by Chiesi** ~~pegunigalsidase alfa, if approved for marketing~~ ; ● our sale of shares of our common stock under our ATM program, or market expectations that such sales are to be executed; ● purchases of BioManguinhos alfataliglicerase in Brazil; ● the progress and results of the studies of our ~~other~~ product candidates **under development; ● the announcement of new products or product enhancements by us or our competitors** ; ● developments concerning intellectual property rights and regulatory approvals; ● ~~the announcement of new products or product enhancements by us or our competitors; ●~~ variations in our and our competitors' results of operations; ● changes in earnings estimates or recommendations by securities analysts; ● developments in the biotechnology industry; and ● general market conditions and other factors, including factors unrelated to our operating performance **, such as the Israel-Hamas war** . Continued market fluctuations could result in extreme volatility in the price of our common stock, which could cause a decline in the value of our common stock. Price volatility of our common stock may be worse when the trading volume of our common stock is low. We have not paid, and do not expect to pay, any cash dividends on our common stock as any earnings generated from future operations will be used to finance our operations. As a result, investors will not realize any income from an investment in our common stock until and unless their shares are sold at a profit. Future sales of our common stock could reduce our stock price. If our stockholders sell substantial amounts of our common stock, including shares of our common stock **underlying** ~~issuable upon conversion of~~ our outstanding convertible notes ~~or~~ **and** warrants, or if we sell a substantial amount of our common stock under our ATM program, the market price of our common stock could decrease significantly. The perception in the public market that our existing stockholders might sell shares of common stock ~~could~~ **may** also depress the trading price of our common stock. ~~57A~~ **A** substantial majority of our outstanding shares of our common stock are freely tradable without restriction or further registration under the federal securities laws. In addition, we may sell additional shares of our common stock in the future to raise capital. A substantial number of shares of our common stock are reserved for issuance upon the exercise of stock options, upon conversion of our outstanding convertible notes and upon the exercise of our outstanding warrants. At December 31, ~~2022~~ **2023** , there were outstanding options to purchase common stock issued covering approximately ~~5~~ **7** . ~~5~~ **0** million shares of our common stock with a weighted average exercise price of $ 2. ~~28~~ **13** per share. Also at December 31, ~~2022~~ **2023** , there were ~~136~~ **633** , ~~738~~ **409** shares of common stock available for future for issuance in connection with future grants of incentives under our Amended and Restated ~~Pro~~ **Protalix** BioTherapeutics, Inc. 2006 Stock Incentive Plan, as amended, approximately ~~21~~ **15** . ~~5~~ **2** million shares of common stock reserved for issuance upon conversion of our outstanding 2024 Notes and approximately ~~14~~ **13** . ~~6~~ **4** million shares of common stock reserved for issuance upon the exercise of our outstanding warrants. The issuance and sale of substantial amounts of common stock, or the perception that such issuances and sales may occur, could adversely affect the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. ~~If securities analysts stop publishing research or reports about us or our business or if they downgrade our common stock, the market price of our common stock could decline. The market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. We do not control these analysts. If any analyst who covers us downgrades our stock or lowers its future stock price targets or estimates of our operating results, the market price for our common stock could decline rapidly. Furthermore, if any analyst ceases to cover us, we could lose visibility in the market, which in turn could cause the market price of our common stock to decline. Our common stock is listed to trade on more than one stock exchange, and this may result in price variations. Our common stock is listed for trade on both the NYSE American and the TASE, although we will be delisting from the TASE effective as of March 22, 2023. Dual- listing may result in price variations between the exchanges due to a number of factors. First, our common stock is traded in U. S. dollars on the NYSE American and in NIS on the TASE. In addition, the exchanges are open for trade at different times of the day and on different days. For example, the TASE opens generally during Israeli business hours, Sunday through Thursday, while the NYSE American opens generally during U. S. business hours, Monday through Friday. The two exchanges also have differing vacation schedules. Differences in the trading schedules, as well as volatility in the exchange rate of the two currencies, among other factors, may result different trading prices for our common stock on the two exchanges. Other external influences may have different effects on the trading price of our common stock on the two exchanges. Compliance with changing regulation of corporate governance and public disclosure may result in additional expenses, divert management' s attention from operating our business which could have a material adverse effect on our~~

~~business. The laws, rules, regulations and standards including the rules promulgated by the national securities exchanges, including the NYSE American, to which we are subject are changed and / or amended from time to time. New or changed laws, rules, regulations and standards are subject to varying interpretations in many cases due to their lack of specificity, and as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies, which could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. As a result, our efforts to comply with evolving laws, rules, regulations and standards are likely to continue to result in increased general and administrative expenses and a diversion of management time and attention from revenue- generating activities to compliance activities. Members of our Board of Directors and our executive officers, could face an increased risk of personal liability in connection with the performance of their duties. As a result, we may have difficulty attracting and retaining qualified directors and executive officers, which could have a material adverse effect on our business. If our efforts to comply with new or changed laws, regulations and standards differ from the activities intended by regulatory or governing bodies, we may incur additional expenses to comply with standards set by regulatory authorities or governing bodies which would have a material adverse effect on our business, results of operations and financial condition.~~