

Risk Factors Comparison 2024-07-11 to 2023-07-10 Form: 10-K

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An investment in our common stock involves various risks, and prospective investors are urged to carefully consider the matters discussed in the section titled “ Risk Factors ” prior to making an investment in our common stock. These risks include, but are not limited to, the following:

- We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability. • ~~Our limited operating history~~ **We are a clinical stage company which** may make it difficult to evaluate the success of our business to date and to assess our future viability.
- We will need substantial additional funding. If we are unable to raise capital when needed, we may need to delay, reduce or eliminate our product development programs or commercialization efforts.
- If we are unable to successfully develop and commercialize one or more of our compounds, or if we experience significant delays in doing so, the business will be materially harmed.
- Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.
- If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented and expenses for development of our product candidates could increase.
- If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.
- **Our operations and relationships with healthcare providers, healthcare organizations, customers and third- party payors will be subject to applicable anti-bribery, anti- kickback, fraud and abuse, transparency and other healthcare laws and regulations, which could expose us to, among other things, enforcement actions, criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.**
- We may seek orphan drug exclusivity for some of our product candidates, and we may be unsuccessful.
- A ~~Fast track~~ **Fast track** designation by the FDA may not lead to a faster development or regulatory review or approval process and does not increase the likelihood that our product candidates will receive marketing approval.
- Failure to obtain marketing approval in international jurisdictions would prevent our product candidates from being marketed abroad.
- Even if any of our product candidates receives marketing approval, we may fail to achieve the degree of market acceptance by physicians, patients, third party payors and others in the medical community necessary for commercial success.
- We face substantial competition, which may result in others discovering, developing or commercializing competing products before or more successfully than we do.
- The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue.
- We contract with third parties for the manufacture of our product candidates for preclinical and clinical testing and we expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products at an acceptable cost and quality, which could delay, prevent or impair our development or commercialization efforts.
- If we are unable to obtain and maintain intellectual property protection for our technology and products or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired.
- Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements.
- Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.
- We expect to expand our development ~~and~~, regulatory ~~capabilities and potentially implement~~ sales, marketing and distribution capabilities, and as a result ~~we~~ may encounter difficulties in managing our growth, which could disrupt our operations.
- Our stock price is volatile and our stockholders may not be able to resell shares of our common stock at or above the price they paid.
- Shareholder activism could cause material disruption to our business.
- Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.
- Unstable or unfavorable global market and economic conditions may have adverse consequences on our business, financial condition and stock price.

Investing in our common stock involves a high degree of risk. You should consider carefully the risks and uncertainties described below, together with all of the other information in this Annual Report on Form 10- K, including the consolidated financial statements, the notes thereto and the section entitled “ Management’ s Discussion and Analysis of Financial Condition and Results of Operations ” included elsewhere in this Annual Report on Form 10- K before deciding whether to invest in shares of our common stock. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties that we are unaware of or that we deem immaterial may also become important factors that adversely affect our business. If any of the following risks actually occur, our business, financial condition, results of operations and future prospects could be materially and adversely affected. In that event, the market price of our stock could decline, and you could lose part or all of your investment. Risks Related to Our Business Since inception, we have incurred significant operating losses as we focused on our discovery efforts and developing our product candidates. We expect that it ~~will~~ **could** be ~~several as much as a years~~ **year**, if ever, before we have a product candidate ready for commercialization. To date, we have financed our operations primarily through sales of our **common stock and warrants** and a previous option agreement with Merck and associated private placement. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue clinical development

of our current product candidates; • seek to identify additional product candidates; • acquire or in-license other products and technologies or enter into collaboration arrangements with regards to product discovery; • initiate clinical trials for additional product candidates; • seek marketing approvals for our product candidates that successfully complete clinical trials; • establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval; • maintain, expand and protect our intellectual property portfolio; • hire additional personnel; • add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and • continue to incur increased costs as a result of operating as a public company. To become and remain profitable, we must develop and eventually commercialize a product or products with significant market potential. This will require us to be successful in a range of challenging activities, including completing clinical trials of our product candidates, obtaining marketing approval for these product candidates and manufacturing, marketing and selling those products for which we may obtain marketing approval. **For example, we submitted an NDA to the FDA in June of 2024 for sebetralstat as an on-demand HAE therapy for adults as well as adolescents over age 12 with HAE.** We may never succeed in these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our business and could impair our ability to raise capital, maintain our discovery and preclinical development efforts, expand our business or continue our operations and may require us to raise additional capital that may dilute the ownership interest of common stockholders. A decline in the value of our business could also cause stockholders to lose all or part of their investment. We are a clinical stage company and our operations to date have been limited to organizing and staffing, business planning, raising capital, acquiring and developing the technology, identifying potential product candidates, and undertaking up to Phase 3 clinical studies of our most advanced product candidates. ~~candidate~~. We have not yet demonstrated our ability to ~~successfully complete large-scale, pivotal clinical trials~~, obtain marketing approvals, manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Substantial time is required to develop a new medicine from the time it is discovered to when it is available for treating patients. Consequently, any predictions made about our future success or viability based on our limited operating history to date may not be as accurate as they could be if we had a longer operating history. In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. Upon regulatory approval of our product candidates, we will need to transition from a company with a research focus to a company capable of supporting and scaling commercial activities. We may not be successful in such a transition. We expect our expenses to increase in parallel with our ongoing activities, particularly as we continue our discovery and preclinical development collaborations to identify new clinical candidates and initiate clinical trials of, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, we will need to obtain substantial additional funding for our continuing operations. If we are unable to raise capital when needed or on attractive terms, we may be forced to delay, reduce or eliminate our discovery and preclinical development programs or any future commercialization efforts. Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings and debt financings. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of common stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Risks Related to the Discovery and Development of Our Product Candidates We currently do not have any products that have gained regulatory approval. We have invested substantially all of our efforts and financial resources in identifying potential drug candidates and funding our preclinical and clinical studies. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our clinical stage product candidates. We have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. For example, to execute our business plan, we will need to successfully: • execute ongoing clinical development activities; ~~• complete any clinical trials beyond Phase 2~~; • move other product candidates into late-stage development; • obtain required regulatory approvals for the development and commercialization of one or more of our product candidates **such as approval by the FDA of the NDA we submitted in June 2024 for the on-demand treatment of HAE attacks in adults and pediatric patients aged 12 years and older**; • maintain, leverage and expand our intellectual property portfolio; • manufacture a commercial scale product or arrange for a third party to do so on our behalf; • build and maintain robust sales, distribution and marketing capabilities for successful product commercialization, either on our own or in collaboration with strategic partners; • gain market acceptance for one or more of our product candidates; • develop and maintain any strategic relationships we elect to enter into; and • manage our spending as costs and expenses increase due to drug discovery, preclinical development, clinical trials, regulatory approvals and commercialization. If we are unsuccessful in accomplishing these objectives, we may not be able to successfully develop and commercialize sebetralstat or other product candidates, and our business will suffer. **Moreover, it is possible that some or all of our product candidates will never obtain marketing authorization even if we expend substantial time and resources seeking such approval.** We have not yet commercialized our product candidates and the historical failure rate in clinical drug development of product candidates in our industry is high. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must

complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of its product candidates in humans. Clinical testing is expensive, difficult to design and implement and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Further, the results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. We may experience delays in our clinical trials and we do not know whether planned clinical trials will begin or enroll subjects on time, need to be redesigned or be completed on schedule, if at all. There can be no assurance that the FDA, Medicines & Healthcare products Regulatory Agency (the “MHRA”), the U. K. regulatory authority, or the European Medicines Agency (the “EMA”) will not put any of our product candidates on clinical hold in the future. We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates. Clinical trials may be delayed, suspended or prematurely terminated for a variety of reasons, such as:

- delay or failure in reaching agreement with the FDA, MHRA, EMA or a comparable foreign regulatory authority on a trial design that we want to execute;
- delay or failure in obtaining authorization to commence a trial or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a clinical study;
- delays in reaching, or failure to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- inability, delay, or failure in identifying and maintaining a sufficient number of trial sites, many of which may already be engaged in other clinical programs;
- delay or failure in recruiting and enrolling suitable subjects to participate in a trial;
- delay or failure in having subjects complete a trial or return for post-treatment follow-up;
- delay or failure in data collections in connection with a clinical trial;
- clinical sites and investigators deviating from trial protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial;
- lack of adequate funding to continue the clinical trial, including the incurrence of unforeseen costs due to enrollment delays, requirements to conduct additional clinical studies and increased expenses associated with the services of its clinical research organizations (“CROs”) and other third parties;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- we may experience delays or difficulties in the enrollment of patients that our product candidates are designed to target;
- our third party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may have difficulty partnering with experienced CROs that can identify patients that our product candidates are designed to target and run our clinical trials effectively;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- there may be political factors surrounding the approval process, such as government shutdowns or political instability;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; or
- there may be changes in governmental regulations or administrative actions.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings that would reduce the potential market for our products or inhibit our ability to successfully commercialize our products;
- be subject to additional post-marketing restrictions and / or testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or marketing approvals. We do not know whether any of our preclinical studies or clinical trials will need to be restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials to demonstrate safety and efficacy. We do not know whether planned or ongoing clinical trials will enroll subjects in a timely fashion, require redesign of essential trial elements or be completed on our projected schedule. In particular, because we are focused on patients with HAE, which is a rare disease, our ability to enroll eligible patients in trials may be limited or may result in slower enrollment than we anticipate. In addition, competitors have ongoing clinical trials for product candidates that treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors’ product candidates. Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Patient enrollment is affected by many factors including:

- the eligibility criteria for the study in question;
- the perceived risks and benefits of the product candidate under study;
- the efforts to facilitate timely enrollment in clinical trials;
- the inability to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs, including some that may be for the same disease indication;
- the patient referral practices of physicians;
- the proximity and availability of clinical trial sites for prospective patients;
- ambiguous or negative interim results of our clinical trials, or results that are inconsistent with earlier results;
- feedback from the FDA, MHRA, EMA, IRBs, data safety monitoring boards, or a

comparable foreign regulatory authority, or results from earlier stage or concurrent preclinical and clinical studies, that might require modifications to the protocol; • decisions by the FDA, MHRA, EMA, IRBs, a comparable foreign regulatory authority or us, or recommendations by data safety monitoring boards, to suspend or terminate clinical trials at any time for safety issues or for any other reason; and • unacceptable risk- benefit profile or unforeseen safety issues or adverse effects. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of the company to decline and limit our ability to obtain additional financing. If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of our products may be delayed and, as a result, our stock price may decline. From time to time, we estimate the timing of the anticipated accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are and will be based on numerous assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet these milestones as publicly announced, or at all, the commercialization of our products may be delayed or never achieved and, as a result, our stock price may decline. If serious adverse events or unacceptable side effects are identified during the development of our product candidates, we may need to abandon or limit the development of some of our product candidates. If our product candidates are associated with undesirable effects in preclinical or clinical trials or have characteristics that are unexpected, we may need to interrupt, delay or abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk- benefit perspective. ~~In October 2022, we terminated a Phase 2 clinical trial of KVD824, which was being developed as a potential HAE prophylaxis therapy, due to elevated liver enzymes observed in multiple study patients. Although we have not conclusively determined that KVD824 was the cause of, or a significant contributor to, these elevations, we do not anticipate further development of KVD824.~~ Our on- demand HAE program sebetralstat is still in clinical testing ~~and we have not yet determined what, if any, significant side effects may occur from dosing~~. Additional or more severe side effects may be identified for all our programs through further clinical studies. These or other drug- related side effects could affect patient recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Any of these occurrences may significantly harm our business, financial condition and prospects.

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters Our product candidates must be approved by the FDA pursuant to an NDA in the U. S. and by the EMA and similar regulatory authorities outside the U. S. prior to commercialization. **We initiated an NDA submission in June 2024 for sebetralstat for the on-demand treatment of HAE attacks in adults and pediatric patients aged 12 years and older.** The process of obtaining marketing approvals, both in the U. S. and abroad, is expensive and takes many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates and therapeutic indications involved. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. Securing marketing approval requires the submission of extensive chemistry, manufacturing and preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate’ s safety and efficacy. Securing marketing approval also usually requires inspection of manufacturing facilities by the regulatory authorities and also audits of the clinical trial sites, data and CROs that have supported KalVista in the clinical development. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude us from obtaining marketing approval or prevent or limit commercial use. Regulatory authorities have substantial discretion in the approval process and may refuse to accept an application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. **For example, we submitted an NDA to the FDA in June of 2024 for sebetralstat as an on-demand HAE therapy for adults as well as adolescents over age 12 with HAE, and the FDA must inform us within 60 days of submission if it has not filed our NDA for regulatory review. If the FDA determines that our NDA submission is incomplete or insufficient for filing, the FDA may refuse to file the NDA. Any such refusal by the FDA could require use to expend additional time and resources to revise and resubmit our NDA or harm our business and reputation. Furthermore, there is no guarantee that any revised or resubmitted NDA submission we make will be accepted by the FDA.** In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may also cause delays in or prevent the approval of an application. For example, the U. K. formally left the E. U. on January 31, 2020, often referred to as Brexit, and the transition period ended on December 31, 2020. Brexit has caused uncertainty in the current regulatory framework in Europe. For instance, Brexit has resulted in the EMA, moving from the U. K. to the Netherlands. The U. K. has now put in place legislation to cover the approval of new medicinal products in the U. K., including designations such as orphan designation, and a pediatric investigational plan. The requirements are similar to those in the E. U. and in many cases have adopted the same requirements. However, there are still adjustments being made to legislation. Any of these adjustments as a result of Brexit could result in significant delays and additional expense to our business. Any of the foregoing factors could have a material adverse effect on our business, results of operations, or financial condition. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post- approval commitments that render the approved product not commercially viable. If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired. **Our current and future arrangements with healthcare providers, healthcare organizations, third- party payors**

and customers expose us to broadly applicable anti-bribery, fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research, market, sell and distribute any of our product candidates, if approved. Restrictions under applicable federal and state anti-bribery and healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, individuals and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under a federal and state healthcare program such as Medicare and Medicaid. The term remuneration has been broadly interpreted to include anything of value. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal criminal and civil false claims and civil monetary penalties laws, including the federal False Claims Act, which can be enforced through civil whistleblower or qui tam actions against individuals or entities, and the Federal Civil Monetary Penalties Law, which prohibit, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. Moreover, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act;
- HIPAA and its implementing regulations, which imposes criminal and civil liability, prohibits, among other things, knowingly and willfully executing, or attempting to execute a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by HITECH, and their respective implementing regulations, which impose obligations on certain healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, as well as their business associates that perform certain services involving the storage, use or disclosure of individually identifiable health information for or on behalf of a covered entity and their covered subcontractors, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information;
- the federal Physician Payments Sunshine Act, which requires certain manufacturers of covered drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program, with certain exceptions, to report annually to CMS information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other health care professionals (such as physician assistants and certain advance practice nurses), and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members, with the information made publicly available on a searchable website;
- the Foreign Corrupt Practices Act, which prohibits U.S. businesses and their representatives from offering to pay, paying, promising to pay or authorizing the payment of money or anything of value to a foreign official in order to influence any act or decision of the foreign official in his or her official capacity or to secure any other improper advantage in order to obtain or retain business;
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; and
- certain state laws that require biopharmaceutical companies to comply with the biopharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and drug pricing information, and state and local laws that require the registration of biopharmaceutical sales representatives. Efforts to ensure that our current and future business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any such requirements, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA, exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, integrity oversight and reporting obligations, or reputational harm, any of which could adversely affect our financial results. These risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources.

An Orphan Drug Designation by the FDA or EMA or MHRA does not increase the likelihood that our product candidates will receive marketing exclusivity. Regulatory authorities in some jurisdictions, including the U.S. and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a disease with

a prevalence of fewer than 200,000 individuals in the U. S. Generally, if a product with an orphan drug designation in a particular jurisdiction subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the authority in that jurisdiction from approving another marketing application for the same drug for the same indication during the period of exclusivity. The applicable period is seven years in the U. S. and ten years in Europe. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective, the criteria on which the orphan designation was originally issued no longer apply or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. The FDA has granted orphan drug designation for sebetralstat. This designation may not effectively protect sebetralstat (or other drug products for which KalVista seeks Orphan orphan Designation designation) from competition because the designation does not preclude different drugs from being approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that it is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. The FDA has granted fast track designation for sebetralstat for the treatment of HAE. We may also seek fast track designation for other indications or for some of our other product candidates. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA fast track designation. The FDA has broad discretion whether or not to grant this designation. Even if we believe a particular product candidate is eligible for this designation, we cannot assure that the FDA would decide to grant it. Even though we have received fast track designation for sebetralstat for the treatment of HAE, or even if we receive fast track designation for other indications or for our other product candidates, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Many drugs that have received fast track designation have failed to obtain drug approval. **In Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction. For example, even if the FDA grants marketing approval of a product candidate, in** order to market and sell our products- **product candidates** in the U. K., E. U. and many other jurisdictions **outside of the U. S.**, we or our third party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the U. S. generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the U. S., it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We, or our third party collaborators, may not obtain approvals from regulatory authorities outside the U. S. on a timely basis, if at all. Approval in any one jurisdiction does not ensure approval by regulatory authorities in other countries or jurisdictions, and likewise approval by one regulatory authority outside the U. S. does not ensure approval by regulatory authorities in any other countries or jurisdictions including the U. S. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market. Any product candidate for which we obtain marketing approval will be subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved. Our product candidates and the activities associated with their development and commercialization, including their testing, manufacture, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA, E. U., MHRA, Swiss and other regulatory authorities. In the U. S., these requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, including periodic inspections by the FDA and other regulatory authority, requirements regarding the distribution of samples to physicians and recordkeeping. The FDA, or other regulatory authorities, may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding use of their products and if we promote our products beyond their approved indications, we may be subject to enforcement action for off-label promotion. Violations of the FDC Act relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws. In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including: • restrictions on the labeling or marketing of a product; • restrictions on product distribution or use; • requirements to conduct post-marketing studies or clinical trials; • warning or untitled letters; • withdrawal of the products from the market; • refusal to approve pending applications or supplements to approved applications that we submit; • recall of products; • fines, restitution or disgorgement of profits or revenues; • suspension or withdrawal of marketing approvals; • refusal to permit the import or export of our products; • product seizure; or • injunctions or the imposition of civil or criminal penalties. Non-compliance with U. S., U. K. and E. U. requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the U. K. and E. U.'s requirements regarding the protection of personal information can also lead to significant penalties and sanctions. Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain. In the U. S. and some foreign jurisdictions, there have been a number of

legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post- approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval .As an example, the ACA, was signed into law in 2010 but has been the subject of legislative and judicial efforts to modify, repeal or otherwise invalidate all or certain aspects of its provisions. The ACA mandated a substantial number of major changes to the healthcare system that impact our business, and several other pieces of legislation since then, as well as ongoing efforts, have continued to create a complicated planning and operating environment for companies in our industry. We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Legislative and regulatory proposals have been made to expand post- approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U. S. Congress of the FDA’s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post- marketing testing and other requirements. **In addition, in the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs, including costs of pharmaceuticals. There has been heightened governmental scrutiny over the manner in which sponsors set prices for their products, which has resulted in several presidential executive orders, 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, reduce the costs of drugs under Medicare and Medicaid, and reform government program reimbursement methodologies for drug products. Recently, several healthcare reform initiatives culminated in the enactment of the IRA in August 2022, which, among other things, allows United States Department of Health and Human Services (“ HHS ”) to directly negotiate the selling price of a statutorily specified number of drugs and biologics each year that CMS reimburses under Medicare Part B and Part D. Only high- expenditure single- source drugs that have been approved for at least seven years (11 years for single- source biologics) are eligible to be selected for negotiation by CMS, with the negotiated price taking effect two years after the selection year. Negotiations for Medicare Part D products begin in 2024 with the negotiated price taking effect in 2026, and negotiations for Medicare Part B products begin in 2026 with the negotiated price taking effect in 2028. In August 2023, HHS announced the ten Medicare Part D drugs and biologics that it selected for negotiations. HHS will announce the negotiated maximum fair prices by September 1, 2024. This price cap, which cannot exceed a statutory ceiling price, will come into effect on January 1, 2026, and will represent a significant discount from average prices to wholesalers and direct purchasers. The IRA also imposes rebates on Medicare Part D and Part B drugs whose prices have increased at a rate greater than the rate of inflation. In addition, the law eliminates the “ donut hole ” under Medicare Part D beginning in 2025 by significantly lowering the beneficiary maximum out- of- pocket cost and requiring manufacturers to subsidize, through a newly established manufacturer discount program, 10 % of Part D enrollees’ prescription costs for brand drugs below the out- of- pocket maximum, and 20 % once the out- of- pocket maximum has been reached. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in Patient Protection and Affordable Care Act (“ ACA ”) marketplaces through plan year 2025. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including significant civil monetary penalties. These provisions may be subject to legal challenges. For example, the provisions related to the negotiation of selling prices of high- expenditure single- source drugs and biologics have been challenged in multiple lawsuits brought by pharmaceutical manufacturers. The outcome of these lawsuits is uncertain, and some IRA drug discount provisions have not been challenged in litigation. Thus, while it is unclear how the IRA will be implemented, it will likely have a significant impact on the pharmaceutical industry and the pricing of sebetralstat or any future product candidates. At the state level, legislatures are increasingly enacting laws and implementing regulations designed to control pharmaceutical and biological product pricing, including restrictions or prohibitions on certain marketing practices, reporting of specified categories of remuneration provided to health care practitioners, and reporting and justification of price increases greater than a specified level. In some cases, states have designed programs to encourage importation from other countries and bulk purchasing, though the federal government has not yet approved any such plans. 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 pharmaceuticals and other healthcare products and services, which could result in reduced demand for sebetralstat or any future product candidates or additional pricing pressures. We expect that other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products.**

Governments outside the U. S. tend to impose strict price controls, which may adversely affect our revenues, if any. In some countries, particularly the countries of the E. U. and the U. K., 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 product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost- effectiveness of our product candidate to other available therapies. If

reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed. If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business. We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from its use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed its resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with the storage or disposal of biological, hazardous or radioactive materials. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our discovery, preclinical development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions. Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements. As with all companies, we are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, provide accurate information to the FDA, comply with manufacturing standards we may establish, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a material and adverse effect on our business, financial condition, results of operations and prospects, including the imposition of significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA, exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, integrity oversight and reporting obligations, or reputational harm.

Disruptions at the FDA, the SEC and other government agencies or comparable regulatory authorities caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, otherwise prevent new products and services from being developed, approved or commercialized in a timely manner or at all, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business. The ability of the FDA or other regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, statutory, regulatory and policy changes, and other events that may otherwise affect the FDA's or comparable foreign regulatory authorities' ability to perform routine functions. In addition, government funding of the SEC and other government agencies or comparable foreign regulatory authorities on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA or other regulatory authorities may also slow the time necessary for new drugs to be reviewed and / or approved, which would adversely affect our business. For example, in 2024, the U. S. government was on the verge of a shutdown and has previously shut down several times, and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, or if geopolitical or global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it 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. Further, future government shutdowns or delays could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Risks Related to the Commercialization of Our Product Candidates If any of our product candidates receives marketing approval, we may nonetheless fail to gain sufficient market acceptance by physicians, patients, third party payors and others in the medical community. In addition, physicians, patients and third party payors may prefer other novel products to ours. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety and potential advantages and disadvantages compared to alternative treatments;
- the ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of our marketing and distribution support;
- the

availability of third party coverage and adequate reimbursement, including patient cost-sharing programs such as copays and deductibles; • the ability to develop or partner with third-party collaborators to develop companion diagnostics; • FDA-approved labeling which may include restrictive safety and efficacy data, or may not include aspects of safety and efficacy that we believe are important; • the prevalence and severity of any side effects; and • any restrictions on the use of our products together with other medications. In addition, in order to commercialize any product candidates, we must build marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. If we are unable to enter into such arrangements when needed on acceptable terms or at all, we may not be able to successfully commercialize any of our product candidates that receive regulatory approval or any such commercialization may experience delays or limitations. If we are not successful in commercializing our product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we may incur significant additional losses. Our estimates of the potential market opportunities for our products are informed by work that is not definitive and future analyses may lead to estimates that are higher or lower than these estimates than those provided at any given time, with respect to addressable patient populations. If our market opportunity is lower than anticipated, our business may suffer. The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we are developing our product candidates. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. In addition, our ability to compete may be affected in many cases by insurers or other third party payors seeking to encourage the use of generic products. Generic products are expected to become available over the coming years, potentially creating pricing pressure. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic products. Many of the companies against which we are competing or we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford expensive treatments. Sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the U. S., the principal decisions about reimbursement for new medicines are typically made by the CMS, an agency within **HHS** the U. S. Department of Health and Human Services, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these new products. Reimbursement agencies in Europe may be more conservative than CMS. Outside the U. S., international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries has and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the U. S. Other countries allow companies to fix their own prices for medicines, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the U. S., the reimbursement for our products may be reduced compared with the U. S. and may be insufficient to generate commercially reasonable revenues and profits. Moreover, increasing efforts by governmental and third party payors, in the U. S. and abroad, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products into the healthcare market. In

addition, many private payors contract with commercial vendors who sell software that provide guidelines that attempt to limit utilization of, and therefore reimbursement for, certain products deemed to provide limited benefit to existing alternatives. Such organizations may set guidelines that limit reimbursement or utilization of our products. Our ability to obtain services, reimbursement or funding may be impacted by possible reductions in federal spending in the U. S. as well as globally. U. S. federal government agencies currently face potentially significant spending reductions. Under the Budget Control Act of 2011, the failure of Congress to enact deficit reduction measures of at least \$ 1. 2 trillion for the years 2013 through 2021 triggered automatic cuts to most federal programs. These cuts would include aggregate reductions to Medicare payments to providers of up to two percent per fiscal year, which went into effect beginning on April 1, 2013 and will stay in effect through 2030 unless additional Congressional action is taken. ~~The American Taxpayer Relief Act of 2012, which was enacted on January 1, 2013, among other things, reduced Medicare payments to several providers, including hospitals and imaging centers. The full impact on our business of these automatic cuts is uncertain. Additionally, the Coronavirus Aid, Relief, and Economic Security (“ CARES ”) Act enacted in 2020 provides financial support and resources to individuals and businesses affected by the COVID-19 pandemic, suspended and reduced the 2 % Medicare sequester from May 1, 2020 through June 30, 2022, and extended the sequester policy, through 2031, in order to offset the added expense of the 2020 cancellation. Moreover, the American Taxpayer Relief Act of 2012 among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. The IRA, which was enacted in August 2022, will, among other things, allow HHS to negotiate the selling price of certain drugs and biologics that CMS reimburses under Medicare Part B and Part D, although only high-expenditure single-source drugs that have been approved for at least 7 years (11 years for biologics) can be selected by CMS for negotiation, with the negotiated price taking effect two years after the selection year. The negotiated prices, which will first become effective in 2026, will be capped at a statutory ceiling price. Beginning in January 2023 for Medicare Part B and October 2022 for Medicare Part D, the IRA will also penalize drug manufacturers that increase prices of Medicare Part B and Part D drugs at a rate greater than the rate of inflation. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. These provisions will take effect progressively starting in 2023, although they may be subject to legal challenges. For example, in June 2023, the drug price negotiation program for Medicare Parts B and D was challenged in federal court. It is unclear whether such litigation or other litigation, if brought, will be successful.~~ If government spending is reduced, anticipated budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA or the National Institutes of Health to continue to function at current levels. Amounts allocated to federal grants and contracts may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve drug research and development, manufacturing, and marketing activities, which may delay our ability to develop, market and sell any products we may develop. Any reductions in government spending in countries outside the U. S. may also impact us negatively, such as by limiting the functioning of international regulatory agencies in countries outside the U. S. or by eliminating programs on which we may rely. 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 commercially sell any products that we may develop. If we cannot successfully defend against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in: • decreased demand for any product candidates or products that we may develop; • injury to our reputation and significant negative media attention; • withdrawal of clinical trial participants; • significant costs to defend the related litigation; • substantial monetary awards to trial participants or patients; • loss of revenue; • reduced resources of our management to pursue our business strategy; and • the inability to commercialize any products that we may develop. We currently hold \$ 10 million in product liability insurance coverage in the aggregate, with a per incident limit of \$ 10 million which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Our Dependence on Third Parties We do not own or operate facilities for the manufacture of our product candidates, and we do not have any manufacturing personnel. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing and **commercial supply and** we do not have backup sources of supply established for our candidates. We review the manufacturing process for each of our candidates and assess the risk to supply and, as appropriate, establish multiple manufacturers and / or establish stock levels to support future activities and do not believe we are currently substantially dependent on any one third party. Despite the drug substance and product risk management, this reliance on third parties presents a risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. Any performance failure on the part of our existing or future manufacturers of drug substance or drug products could delay clinical development or marketing approval. If current suppliers cannot supply us with our **Phase 2 clinical trial or commercial** requirements as agreed, we may be required to identify alternative manufacturers, which would lead us to incur added costs and delays in identifying and qualifying any such replacement. Even if we choose to self-manufacture, the formulation used in early studies frequently is not a final formulation for commercialization. Additional changes may be required by the FDA or other regulatory authorities on specifications and storage conditions. These may require additional studies and may delay our clinical trials. We expect to rely on third party manufacturers or third party collaborators

for the manufacture of commercial supply of any other product candidates for which our collaborators or we obtain marketing approval. 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 or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue. We may be unable to establish any agreements with third party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third party manufacturers, reliance on third party manufacturers entails additional risks, including: • reliance on the third party for regulatory compliance and quality assurance; • the possible breach of the manufacturing agreement by the third party; • the possible misappropriation of our proprietary information, including trade secrets and know-how; and • the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us. Third party manufacturers may not be able to comply with cGMP, regulations or similar regulatory requirements outside the U. S. ~~Our~~ **If the FDA determines that our third party manufacturers are not in compliance with FDA laws and regulations, including those governing cGMPs, the FDA may not approve an NDA until the deficiencies are corrected or we replace the manufacturer in our application with a manufacturer that is in compliance. Moreover, our** failure, or the failure of our third party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. **In addition, approved products and the facilities at which they are manufactured are required to maintain ongoing compliance with extensive FDA requirements and the requirements of other similar agencies, including ensuring that quality control and manufacturing procedures conform to cGMP requirements. As such, our third party manufacturers are subject to continual review and periodic inspections to assess compliance with cGMPs. Furthermore, although we do not have day- to- day control over the operations of our third party manufacturers, we are responsible for ensuring compliance with applicable laws and regulations, including cGMPs. In addition, certain Chinese biotechnology companies may become subject to trade restrictions, sanctions, other regulatory requirements, or proposed legislation by the U. S. government, which could restrict or even prohibit our ability to work with such entities, thereby potentially disrupting the supply of material to us. For example, the recently proposed BIOSECURE Act introduced in the U. S. House of Representatives, as well as a substantially similar bill in the U. S. Senate, target U. S. government contracts, grants and loans for entities that use equipment and services from certain named Chinese biotechnology companies, and authorizes the U. S. government to name additional Chinese biotechnology companies of concern. If these bills become law, or similar laws are passed, they would have the potential to severely restrict our ability to work with Chinese biotechnology manufacturing companies without losing the ability to contract with, or otherwise receive funding from, the U. S. government. We cannot predict what actions may ultimately be taken with respect to trade relations between the United States and China or other countries, what products and services may be subject to such actions or what actions may be taken by China or the other countries in retaliation. If we are required to change third party manufacturers for any reason, we will be required to verify that the new third party manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product candidate or product according to the specifications previously submitted to the FDA or another regulatory authority. The delays associated with the verification of a new third party manufacturers could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget.** Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis. We may not successfully engage in strategic transactions, including any additional collaborations we seek, which could adversely affect our ability to develop and commercialize product candidates, impact our cash position, increase our expenses and present significant distractions to our management. The terms of any collaborations may also have impacts on other aspects of our business. From time to time, we may consider strategic transactions, such as collaborations, acquisitions of companies, asset purchases and out- or in- licensing of product candidates or technologies that we believe will complement or augment our existing business. In particular, we will evaluate and, if strategically attractive, seek to enter into additional collaborations, including with major biotechnology or biopharmaceutical companies. The competition for collaborators is intense, and the negotiation process is time- consuming and complex. Any new collaboration may be on terms that are not optimal for us, and we may not be able to maintain any new collaboration if, for example, development or approval of a product candidate is delayed, sales of an approved product candidate do not meet expectations or the collaborator terminates the collaboration. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future strategic partners. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the strategic partner' s resources and expertise, the terms and conditions of the proposed collaboration and the proposed strategic partner' s evaluation of a number of factors. These factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the U. S., the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. Moreover, even if we acquire assets with promising markets or technologies, we may not be able to realize

the benefit of acquiring such assets due to an inability to successfully integrate them with our existing technologies and we may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that following any such collaboration, or other strategic transaction, we will achieve the expected synergies to justify the transaction. For example, such transactions may require us to incur non-recurring or other charges, increase our near- and long-term expenditures and pose significant integration or implementation challenges or disrupt our management or business. These transactions would entail numerous operational and financial risks, including exposure to unknown liabilities, disruption of our business and diversion of our management's time and attention in order to manage a collaboration or develop acquired products, product candidates or technologies, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected collaboration, acquisition or integration costs, write-downs of assets or goodwill or impairment charges, increased amortization expenses, difficulty and cost in facilitating the collaboration or combining the operations and personnel of any acquired business, impairment of relationships with key suppliers, manufacturers or customers of any acquired business due to changes in management and ownership and the inability to retain key employees of any acquired business. Also, such strategic alliance, joint venture or acquisition may be prohibited. Collaborations may also have potential impact on other aspects of our business. Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks that would have a material and adverse effect on our business, financial condition, results of operations and prospects. We have entered, and may in the future seek to enter, into collaborations with third parties for the development and commercialization of our product candidates. If we fail to enter into such collaborations, or such collaborations are not successful, we may not be able to capitalize on the market potential of our product candidates. Biopharmaceutical companies are our prior and likely future collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements. We expect that in any future collaboration agreements, we would have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Moreover, our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for any collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay our development program or one or more of our other development programs, delay our potential development schedule or reduce the scope of research activities, or increase our expenditures and undertake discovery or preclinical development activities at our own expense. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development activities, we may not be able to further develop our product candidates or continue to develop our product candidates and our business may be materially and adversely affected. Future collaborations we may enter into may involve the following risks: • collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations; • collaborators may not perform their obligations as expected; • changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, may divert resources or create competing priorities; • collaborators may delay discovery and preclinical development, provide insufficient funding for product development of targets selected by us, stop or abandon discovery and preclinical development for a product candidate, repeat or conduct new discovery and preclinical development for a product candidate; • collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed than our products; • product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the development of its product candidates; • collaborators may not properly maintain or defend their intellectual property rights or intellectual property rights licensed to us or may use their proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation; • collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and • collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates. Additionally, subject to its contractual obligations to us, if a collaborator is involved in a business combination, the collaborator might deemphasize or terminate the development of any of our product candidates. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and the perception of us in the business and financial communities could be adversely affected. If our collaborations do not result in the successful development of products or product candidates, product candidates could be delayed and we may need additional resources to develop product candidates. All of the risks relating to product development, regulatory approval and commercialization described in this proxy statement also apply to the activities of our collaborators.

We rely, and intend to continue to rely, on third parties to support or conduct our clinical trials and perform some of our research and preclinical studies. If these third parties do not satisfactorily carry out their contractual duties, fail to comply with applicable regulatory requirements or do not meet expected deadlines, our development programs may be delayed or subject to increased costs or we may be unable to obtain regulatory approval, each of which may have an adverse effect on our business, financial condition, results of operations and prospects. We do not have the ability to independently conduct all aspects of our clinical trials ourselves. As a result, we are dependent on third parties to conduct our ongoing and planned clinical trials of sebetralstat, including our ongoing KONFIDENT- KID clinical trial of

sebetralstat in pediatric patients with HAE, and any future product candidates, as well as potentially preclinical studies of future product candidates. The timing of the initiation and completion of these trials will therefore be partially controlled by such third parties and may result in delays to our development programs. For example, we expect CROs, independent clinical investigators and consultants to play a significant role in the conduct of these trials and the subsequent collection and analysis of data. However, these investigators, CROs and other third parties are not our employees, and we will not be able to control all aspects of their activities. Nevertheless, we are responsible for ensuring that each clinical trial is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the investigators, CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs and other third parties are required to comply with Good Clinical Practice (“GCP”) requirements, which are regulations and guidelines enforced by the FDA for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical trial investigators and clinical trial sites. If we or any of our CROs or clinical trial sites fail to comply with applicable GCP requirements, the data generated in our clinical trials may be deemed unreliable, and the FDA or other regulators may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA or other regulators will determine that our clinical trials comply with GCPs. In addition, our clinical trials must be conducted with product manufactured under cGMP regulations. Our failure or the failure of third parties on whom we rely to comply with these regulations may require us to stop and / or repeat clinical trials, which would delay the regulatory approval process. There is no guarantee that any such CROs, clinical trial investigators or other third parties on which we rely will devote adequate time and resources to our development activities or perform as contractually required. In addition, these third parties may be subject to supply chain or inflationary pressures that limit their ability to achieve anticipated timelines or result in a greater cost to us. For example, we are aware of recurrent shortages of non-human primates available for preclinical studies and although that is not expected to impact our current business, if we begin new product development programs we could be subject to longer development times or difficulty completing necessary research. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, otherwise perform in a substandard manner, or terminate their engagements with us, the timelines for our development programs may be extended or delayed or our development activities may be suspended or terminated. If a clinical trial site terminates for any reason, we may experience the loss of follow-up information on subjects enrolled in such clinical trial site unless we are able to transfer those subjects to another qualified clinical trial site, which may be difficult or impossible. In addition, with respect to investigator-sponsored trials that may be conducted, we would not control the design or conduct of these trials, and it is possible that the FDA will not view these investigator-sponsored trials as providing adequate support for future clinical trials or market approval, whether controlled by us or third parties, for any one or more reasons, including elements of the design or execution of the trials or safety concerns or other trial results. We expect that such arrangements will provide us certain information rights with respect to the investigator-sponsored trials, including access to and the ability to use and reference the data, including for our own regulatory submissions, resulting from the investigator-sponsored trials. However, we would not have control over the timing and reporting of the data from investigator-sponsored trials, nor would we own the data from the investigator-sponsored trials. If we are unable to confirm or replicate the results from the investigator-sponsored trials or if negative results are obtained, we would likely be further delayed or prevented from advancing further clinical development. Further, if investigators or institutions breach their obligations with respect to the clinical development of our product candidates, or if the data proves to be inadequate compared to the firsthand knowledge we might have gained had the investigator-sponsored trials been sponsored and conducted by us, then our ability to design and conduct any future clinical trials ourselves may be adversely affected. The investigators may design clinical trials with clinical endpoints that are more difficult to achieve, or in other ways that increase the risk of negative clinical trial results compared to clinical trials that we may design on our own. Negative results in investigator-sponsored clinical trials could have a material adverse effect on our efforts to obtain regulatory approval for our product candidates and the public perception of our product candidates. Additionally, the FDA or other regulators may disagree with the sufficiency of our right of reference to the preclinical, manufacturing or clinical data generated by these investigator-sponsored trials, or our interpretation of preclinical, manufacturing or clinical data from these investigator-sponsored trials. If so, the FDA or other regulators may require us to obtain and submit additional preclinical, manufacturing, or clinical data. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors for whom they may also be conducting clinical trials or other pharmaceutical product development activities that could harm our competitive position. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, regulatory approval for sebetralstat and any future product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our products.

Risks Related to Our Intellectual Property Our success depends in large part on our ability to obtain and maintain patent protection in the U. S., the E. U., and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing patent applications in the U. S. and abroad related to our novel technologies and product candidates. This patent portfolio includes issued patents and pending patent applications covering compositions of matter and methods of use. The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We may choose not to seek patent protection for certain innovations and may choose not to pursue patent protection in certain jurisdictions, and under the laws of certain jurisdictions, patents or other intellectual property rights may be unavailable or

limited in scope. It is also possible that we will fail to identify patentable aspects of our discovery and preclinical development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the U. S. For example, India and China do not allow patents for methods of treating the human body. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U. S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. If a third party has also filed a U. S. patent application prior to the effective date of the relevant provisions of the America Invents Act (i. e. before March 16, 2013) covering our product candidates or a similar invention, we may have to participate in an adversarial proceeding, known as an interference, declared by the USPTO to determine priority of invention in the U. S. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the E. U., the U. S. and other countries may diminish the value of our patents or narrow the scope of our patent protection. Moreover, we may be subject to a third party preissuance submission of prior art to the USPTO, or become involved in opposition, derivation, reexamination, inter partes review, post- grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third party patent rights. 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 our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non- infringing manner. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the U. S. and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. 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 such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. The risks described elsewhere pertaining to our patents and other intellectual property rights also apply to the intellectual property rights that we license, and any failure to obtain, maintain and enforce these rights could have a material adverse effect on our business. In some cases we may not have control over the prosecution, maintenance or enforcement of the patents that we license, and our licensors may fail to take the steps that we believe are necessary or desirable in order to obtain, maintain and enforce the licensed patents. Any inability on our part to protect adequately our intellectual property may have a material adverse effect on our business, operating results and financial position. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and / or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the U. S. in several stages over the lifetime of the patents and / or applications. We employ an outside firm and rely on our outside counsel to pay these fees due to non- U. S. patent agencies. The USPTO and various non- U. S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business. We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful. Because competition in our industry is intense, competitors may infringe or otherwise violate our issued patents, patents of our licensors or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringed their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent' s claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. We may also elect to enter into license agreements in order to settle patent infringement claims or to resolve disputes prior to litigation, and any such license agreements may require us to pay royalties and other fees that could be significant. 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. Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference or derivation proceedings before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business. If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We seek to protect our confidential proprietary information, in part, by entering into confidentiality and invention or patent assignment agreements with our employees and consultants, however, we cannot be certain that such agreements have been entered into with all relevant parties. Moreover, to the extent we enter into such agreements, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the U. S. are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate them, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed. Risks Related to Employee Matters, Facilities, Managing Growth and Macroeconomic Conditions We are highly dependent on the research and development, clinical and business development expertise of the principal members of our management, scientific and clinical team. Although we have entered into employment letter agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of our management team, other key employees and other scientific and medical advisors, and our inability to find suitable replacements, could result in delays in product development and harm our business. Recruiting and retaining qualified scientific, clinical, manufacturing, sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our discovery and preclinical development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to provide services to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited. We expect to **expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations. We expect to** experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and, if any of our product candidates receive marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations. Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses. Our operations, and those of our CROs and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme

weather conditions, **medical health epidemics and**, such as the **COVID-19 pandemic pandemics**, and other natural or man-made disasters or business interruptions, for which we may not have insurance coverage. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce and process our product candidates. Our ability to obtain supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. Our operations and financial condition could suffer in the event of a natural or man-made disaster near our headquarters in Cambridge, Massachusetts or our research facility in Porton Down, United Kingdom. Our failure to comply with privacy and data security laws, regulations and standards may cause our business to be materially adversely affected. We are, and may increasingly become, subject to various laws and regulations, as well as contractual obligations, relating to data privacy and security in the jurisdictions in which we operate. Personal privacy and data security have become significant issues in the U. S., Europe and in many other jurisdictions. The regulatory framework for privacy and security issues worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. We maintain a large quantity of sensitive information, including confidential business **information** and patient health information in connection with our clinical development regarding the patients enrolled in our clinical trials. Any violations of these rules by us could subject us to civil and criminal penalties and adverse publicity and could harm our ability to initiate and complete clinical trials. We cannot provide assurance that current or future legislation will not prevent us from generating or maintaining personal data or that patients will consent to the use of their personal data (as necessary); either of these circumstances may prevent us from undertaking or publishing essential research and development, manufacturing, and commercialization, which could have a material adverse effect on our business, results of operations, financial condition, and prospects. The myriad international and U. S. privacy and data breach laws are not consistent, and compliance in the event of a widespread data breach is difficult and may be costly. In many jurisdictions, enforcement actions and consequences for noncompliance are also rising. **For instance, companies that violate the European Union's General Data Protection Regulation, including as implemented in the United Kingdom (collectively, the "GDPR"), can face fines of up to the greater of 20 million Euros under the E. U. GDPR / 17.5 million pounds under the U. K. GDPR, or 4 % of their worldwide annual revenue, whichever is higher. In addition, we may be unable to transfer personal data from Europe and other jurisdictions to the United States or other countries due to data localization requirements or limitations on cross-border data flows. If there is no lawful manner for us to transfer personal data from the E. U., the U. K., or other jurisdictions to the United States, or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions (such as the E. U. and / or U. K.) at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business.** In addition to government regulation, privacy advocates and industry groups may propose new and different self-regulatory standards that either legally or contractually applies to us. Any inability to adequately address privacy and security concerns, even if unfounded, or comply with applicable privacy and data security laws, regulations and policies, could result in additional cost and liability to us, damage our reputation, and adversely affect our business. Additionally, all of these evolving compliance and operational requirements impose significant costs, such as costs related to organizational changes, implementing additional protection technologies, training employees and engaging consultants, which are likely to increase over time. In addition, such requirements may require us to modify our data processing practices and policies, distract management or divert resources from other initiatives and projects, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Enforcement actions and investigations by regulatory authorities related to data security incidents and privacy violations continue to increase. Any failure or perceived failure by us (or the third parties with whom we have contracted to process such information) to comply with applicable privacy and data security laws, policies or related contractual obligations, or any compromise of security that results in unauthorized access, use or transmission of, personal user information, could result in a variety of claims against us, including governmental enforcement actions and investigations, class action privacy litigation in certain jurisdictions and proceedings by data protection authorities, potentially amounting to significant compensation or damages liabilities, as well as associated costs, diversion of internal resources, and reputational harm. When such events occur, our reputation may be harmed, we may lose current and potential users and the competitive positions of our brand might be diminished, any or all of which could materially adversely affect our business, operating results, and financial condition. In addition, if our practices are not consistent or viewed as not consistent with legal and regulatory requirements, including changes in laws, regulations and standards or new interpretations or applications of existing laws, regulations and standards, we may become subject to audits, inquiries, whistleblower complaints, adverse media coverage, investigations, loss of export privileges, or severe criminal or civil sanctions, all of which may have a material adverse effect on our business, operating results, reputation, and financial condition. Our business and operations would suffer in the event of system failures, cyberattacks or a deficiency in our cybersecurity. Our internal computer systems and those of our CROs, collaborators and third parties on whom we rely are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Furthermore, we have little or no control over the security measures and computer systems of our third party collaborators. The risk of a security breach or disruption, particularly through cyberattacks or cyber intrusion, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity, and sophistication of attempted attacks and intrusions from around the world have increased. In addition, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information or other intellectual property. The costs to us or our CROs or other contractors or consultants we may utilize to mitigate network security problems, bugs, viruses, worms, **cyberattacks**, phishing attempts,

malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position. For example, the loss of research data could delay development of our product candidates and the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and we may incur substantial costs to attempt to recover or reproduce the data. If any disruption or security breach resulted in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and / or the further development of our product candidates could be delayed or impaired. In addition, such a breach may require notification to governmental agencies, the media or individuals pursuant to various federal and state privacy and security laws, if applicable, including the Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing rules and regulations, as well as regulations promulgated by the Federal Trade Commission and state breach notification laws. We would also be exposed to a risk of loss or litigation and potential liability under laws, regulations and contracts that protect the privacy and security of personal information. We would also be exposed to a risk of loss or litigation and potential liability, which could materially adversely affect our business, reputation, results of operations, financial condition and prospects.

Activities outside of the U. S. implicate local and national data protection standards, impose additional compliance requirements and generate additional risks of enforcement for non-compliance. The GDPR and other data protection, privacy and similar national, state / provincial and local laws may restrict the access, use, storage, disclosure and other processing activities concerning patient health information abroad. Compliance efforts will likely be an increasing and substantial cost in the future. Further, on July 26, 2023, the SEC adopted new cybersecurity disclosure rules for public companies that require disclosure regarding cybersecurity risk management (including the board's role in overseeing cybersecurity risks, management's role and expertise in assessing and managing cybersecurity risks and processes for assessing, identifying and managing cybersecurity risks) in annual reports on Form 10-K. These new cybersecurity disclosure rules also require the disclosure of material cybersecurity incidents by Form 8-K, within four business days of determining an incident is material.

We also depend on our information technology infrastructure for communications among our personnel, contractors, consultants and vendors. System failures or outages could also compromise our ability to perform these functions in a timely manner, which could harm our ability to conduct business or delay our financial reporting.

Risks Related to Ownership of Our Common Stock

The trading price of our common stock is highly volatile and could be subject to wide fluctuations in response to various factors, many of which are beyond our control. Factors affecting the market price of our common stock include those discussed in this “Risk Factors” section of this Annual Report on Form 10-K and others such as:

- announcement of a strategic transaction or other significant events for us or our competitors;
- our decision to initiate a clinical trial or not to initiate a clinical trial;
- announcements of significant changes in our business or operations, including the decision not to pursue drug development programs;
- additions or departures of key personnel;
- adverse results or delays in clinical trials;
- changes in reimbursement or third party coverage of treatments, or changes to treatment recommendations or guidelines applicable to treatment;
- announcements relating to collaboration partnerships or other strategic transactions undertaken by us;
- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;
- changes or developments in laws or regulations applicable to any of our product candidates;
- any adverse changes to our relationship with any manufacturers or suppliers;
- the success of our testing and clinical trials;
- the success of our efforts to acquire or license or discover additional product candidates;
- any intellectual property infringement actions in which we may become involved;
- announcements concerning our competitors or the pharmaceutical industry in general;
- achievement of expected product sales and profitability;
- manufacture, supply or distribution shortages;
- actual or anticipated fluctuations in our operating results;
- FDA or other regulatory actions affecting us or our industry or other healthcare reform measures in the U. S., the U. K. or the E. U.;
- changes in financial estimates or recommendations by securities analysts;
- trading volume of our common stock;
- sales of our common stock by us, our executive officers and directors or our stockholders in the future;
- general economic and market conditions and overall fluctuations in the U. S. equity markets, including due to rising inflation and interest rates, labor shortages, supply chain issues, and global conflicts such as the war in Ukraine; and
- other events or factors, many of which are beyond our control.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that may have been unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our management would be diverted from the operation of our business, which could seriously harm our financial position. Any adverse determination in litigation could also subject us to significant liabilities. We incur significant costs as a result of operating as a public company, and our management devotes substantial time to compliance initiatives. We may fail to comply with the rules that apply to public companies, including Section 404 of the Sarbanes-Oxley Act of 2002, which could result in sanctions or other penalties that would harm our business. We incur significant legal, accounting and other expenses as a public company, including costs resulting from public company reporting obligations under the Exchange Act, and regulations regarding corporate governance practices. The listing requirements of The NASDAQ Global Market require that we satisfy certain corporate governance requirements relating to director independence, distributing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel have devoted, and will continue to need to devote, a substantial amount of time to ensure that we comply with all of these requirements. Moreover,

the reporting requirements, rules and regulations increase our legal and financial compliance costs and make some activities more time consuming and costly. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as executive officers, or to obtain certain types of insurance, including directors' and officers' insurance, on acceptable terms. We are subject to Section 404 of The Sarbanes- Oxley Act of 2002 (" Section 404 "), and the related rules of the SEC which generally require our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. Section 404 requires an annual management assessment of the effectiveness of our internal control over financial reporting. Effective April 27, 2020, the SEC adopted amendments to the " accelerated filer " and " large accelerated filer " definitions in Rule 12b- 2 under the Securities and Exchange Act of 1934. The amendments exclude from the " accelerated filer " and " large accelerated filer " definitions an issuer that is eligible to be a smaller reporting company and that had annual revenues of less than \$ 100 million in the most recent fiscal year for which audited financial statements are available. We determined that our Company does not meet the accelerated or large accelerated filer definitions as of April 30, 2023-2024. For so long as we remain a smaller reporting company and a non- accelerated filer, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to public companies, including, but not limited to, not being required as a non- accelerated filer to comply with the auditor attestation requirements of Section 404 (b). An independent assessment by our independent registered public accounting firm of the effectiveness of internal control over financial reporting could detect problems that our management' s assessment might not. Undetected material weaknesses in our internal control over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation. During the course of the review and testing of our internal control for the purpose of providing the reports required by these rules, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal control over financial reporting, we may not detect errors on a timely basis and our financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we are required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The NASDAQ Global Market or other adverse consequences that would materially harm our business. In addition, if we lose our status as a " non- accelerated filer, " we will be required to have our independent registered public accounting firm attest to the effectiveness of internal control over financial reporting. If our independent registered public accounting firm is unable to express an opinion as to the effectiveness of our internal control over financial reporting once we are an accelerated filer or a large accelerated filer, investors may lose confidence in the accuracy and completeness of our financial reports, and the market price of our common stock could be negatively affected.

Shareholder Activism Could Cause Material Disruption to Our Business. Publicly traded companies have increasingly become subject to campaigns by activist investors advocating corporate actions such as actions related to environment, social and governance (" ESG ") matters, financial restructuring, increased borrowing, dividends, share repurchases or even sales of assets or the entire company. Responding to proxy contests and other actions by such activist investors or others in the future could be costly and time- consuming, disrupt our operations and divert the attention of our board of directors and senior management from the pursuit of our business strategies, which could adversely affect our results of operations and financial condition.

Investors' expectations of our performance relating to environmental, social and governance factors may impose additional costs and expose us to new risks. There is an increasing focus from certain regulators, investors, employees, users and other stakeholders concerning corporate responsibility, specifically related to environmental, social and governance (" ESG ") matters both in the U. S. and internationally. Some investors may use these non- financial performance factors to guide their investment strategies and, in some cases, may choose not to invest in us if they believe our policies and actions relating to corporate responsibility are inadequate. We may face reputational damage in the event that we do not meet the ESG standards set by various constituencies. Further, ESG initiatives, goals or commitments could be difficult to achieve or costly to implement. If our competitors' corporate social responsibility performance is perceived to be better than ours, potential or current investors may elect to invest with our competitors instead. Moreover, California recently adopted two new climate- related bills, which require companies doing business in California that meet certain revenue thresholds to publicly disclose certain greenhouse gas emissions data and climate- related financial risk reports, and compliance with such requirements could require significant effort and resources. Additionally, in March 2024, the SEC enacted comprehensive climate change disclosure rules, although the SEC has since issued an order to stay the rules pending the completion of judicial review of multiple petitions challenging the rules. Our business may face increased scrutiny related to these activities and our related disclosures, including from the investment community, and our failure to achieve progress or manage the dynamic public sentiment and legal landscape in these areas on a timely basis, or at all, could adversely affect our reputation, business, and financial performance.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could significantly reduce the value of our shares to a potential acquirer or delay or prevent changes in control or changes in our management without the consent of our board of directors. The provisions in our charter documents include the following:

- a classified board of directors with three- year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors

or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors; • the required approval of at least 66 2 / 3 % of the shares entitled to vote to remove a director for cause, and the prohibition on removal of directors without cause; • the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer; • the ability of our board of directors to alter our bylaws without obtaining stockholder approval; • the required approval of at least 66 2 / 3 % of the shares entitled to vote at an election of directors to adopt, amend or repeal certain provisions of our bylaws and our amended and restated certificate of incorporation regarding the election and removal of directors; • a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders; • the requirement that a special meeting of stockholders may be called only by or at the direction of our board of directors pursuant to a resolution adopted by a majority of the total number of directors that our board of directors would have if there were no vacancies, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and • advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer' s own slate of directors or otherwise attempting to obtain control of us. In addition, these provisions would apply even if we were to receive an offer that some stockholders may consider beneficial. We are also subject to the anti- takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15 % or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction. Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third party claims against us and may reduce the amount of money available to us. Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law. In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that: • we will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person' s conduct was unlawful. • we may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law. • we are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification. • we will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification. • the rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons. • we may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents. Our ability to use our net operating losses to offset future taxable income, if any, may be subject to certain limitations. **Under the Tax Cuts and Jobs Act of 2017, (“ TCJA ”), net operating loss carryforwards generated in years after 2017 will only be available to offset up to 80 % of our taxable income in any single year (before taking into certain deductions) but will not expire.** In ~~general addition~~, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an “ ownership change ” (generally defined as a greater than 50- percentage- point cumulative change (by value) in the equity ownership of certain stockholders over a rolling three- year period) is subject to limitations on its ability to utilize its pre- change net operating losses, or NOLs, to offset future taxable income. We have experienced ownership changes **in the past** that substantially limit our use of the NOLs available to us for U. S. federal income tax purposes. ~~For example, we believe we experienced an and “ ownership change ” within the meaning of Section 382 of the Internal Revenue Code of 1986, as a result amended, in December 2022, and we continue to analyze the impact if any on~~ **currently expect that approximately \$ 76. 7 million of** our ability to utilize NOLs ~~in the future will go unutilized~~. If we undergo additional ownership changes (some of which changes may be outside our control), our ability to utilize our NOLs could be further limited by Section 382 of the Code. Our NOLs may also be impaired under state law **and there may be periods in which certain states suspend our ability to use our NOLs**. Accordingly, we may not be able to utilize a material portion of our NOLs **against future taxable income**. Furthermore, our ability to utilize our NOLs is conditioned upon our attaining profitability and generating U. S. federal taxable income. We have incurred net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; thus, we do not know whether or when we will generate the U. S. federal taxable income necessary to utilize our NOLs. ~~The Tax Cuts and Jobs Act of 2017, or the TCJA, changed both the federal deferred tax value of the net operating loss carryforwards and the rules of utilization of federal net operating loss carryforwards. Under the TCJA, net operating loss carryforwards generated in years after 2017 will only be available to offset 80 % of future taxable income in any single year but will not expire. However, the Coronavirus Aid, Relief, and Economic Security Act (the “ CARES Act ”) temporarily repealed the 80 % taxable income limitation for tax years beginning before January 1, 2021; net operating loss carried forward generated from 2018 or later and carryforwards to taxable years beginning after December 31, 2020 will be subject to the 80 % limitation. Also, under the CARES Act, net operating losses arising in 2018, 2019 and 2020 can be carried back 5 years.~~ General Risk Factors Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets.

Challenging or uncertain economic conditions including those related to global epidemics, pandemic, or contagious diseases, **regional geopolitical turmoil conflicts**, inflation, fluctuation in interest rates and foreign exchange rates, **uncertainty with respect to the federal debt ceiling and budget and government shutdowns related thereto, actual or perceived** instability in the global banking system, disruptions in supply chains may adversely affect our general business strategy and stock price. In addition, a recession, depression or other sustained adverse market event could materially and adversely affect our business and the value of our common stock. ~~For example, on March 10, 2023, Silicon Valley Bank (“SVB”) was closed by the California Department of Financial Protection & Innovation and the Federal Deposit Insurance Corporation (the “FDIC”) was named receiver. Similarly, on March 12, 2023, Signature Bank and Silvergate Capital Corp. were each swept into receivership. While the FDIC has taken steps to make whole all depositors of SVB, there is no assurance that similar guarantees will be made in the event of further bank closures and continued instability in the global banking system. If other banks and financial institutions enter receivership or become insolvent in the future in response to financial conditions affecting the banking system and financial markets, then our ability to obtain financing may be threatened, which could have a material adverse effect on our business and financial condition. Moreover, events such as the closure of SVB, in addition to other global macroeconomic conditions, may cause further turbulence and uncertainty in the capital markets.~~ If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon development plans. There is also a risk that one or more of our current service providers, manufacturers and other partners may not survive these difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget. In addition, regarding the **current ongoing conflict conflicts** in Ukraine **and the Middle East**, we do not have any clinical trial sites or operations in ~~Ukraine or Russia—the respective conflict zones~~. However, if the current conflict in the region continues, there is the potential for trial sites in other eastern European countries to slow or stop enrollment, or to be unable to administer our clinical trials. Changes in tax laws or tax rulings could materially affect our financial position, results of operations and cash flows. The tax regimes we are subject to or operate under, including income and non-income taxes, are unsettled and may be subject to significant change. Changes in tax laws, regulations, or rulings, or changes in interpretations of existing laws and regulations, could materially affect our financial position and results of operations. For example, the **TCJA 2017 Tax Cuts and Jobs Act (the “Tax Act”)** made broad and complex changes to the **U. S. tax code Code**, including changes to U. S. federal tax rates, additional limitations on the deductibility of interest, both positive and negative changes to the utilization of **future net operating loss (“NOL”)** carryforwards, allowing for the expensing of certain capital expenditures, and putting into effect the migration from a “worldwide” system of taxation to a more territorial system. **Under the TCJA, research expenditures incurred by us in taxable years beginning in our taxable year ending April 30, 2023 are subject to capitalization and amortization over five years in the case of domestic research and fifteen years in the case of foreign research.** Future guidance from the IRS with respect to the Tax Act may affect us, and certain aspects of the **TCJA Tax Act** could be repealed or modified in future legislation. ~~The CARES Act has already modified certain provisions of the Tax Act.~~ The IRA, enacted on August 16, 2022, further amended the U. S. tax code, imposing a 15 % minimum tax on “adjusted financial statement income” of certain corporations as well as an excise tax on the repurchase or redemption of stock by certain corporations, beginning in the 2023 tax year. In addition, it is uncertain if and to what extent various states will conform to the **TCJA Tax Act, the CARES Act**, the IRA or any newly enacted federal tax legislation. The issuance of additional regulatory or accounting guidance related to the **TCJA Tax Act** could materially affect our tax obligations and effective tax rate in the period issued. As we continue to expand internationally, we will be subject to other jurisdictions around the world with increasingly complex tax laws, the application of which can be uncertain. The amount of taxes we pay in these jurisdictions could increase substantially as a result of changes in the applicable tax principles, including increased tax rates, new tax laws or revised interpretations of existing tax laws and precedents, which could have an adverse impact on our liquidity and results of operations. In addition, the authorities in several jurisdictions could review our tax returns and impose additional tax, interest and penalties, which could have an impact on us and on our results of operations. In addition, many countries in Europe and a number of other countries and organizations, have recently proposed or recommended changes to existing tax laws or have enacted new laws that could significantly increase our tax obligations in the countries where we do or intend to do business or require us to change the manner in which we operate our business. If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse opinion regarding our stock, our stock price and trading volume could decline. The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If any analysts who cover us issue an adverse report regarding us, our business model, our intellectual property or our stock performance, or if our clinical trials and operating results fail to meet the expectations of analysts, our stock price may decline. If any of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline. We do not currently intend to pay dividends on our common stock, and, consequently, our stockholders’ ability to achieve a return on their investment will depend on appreciation in the price of our common stock. We do not currently intend to pay any cash dividends on our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, our stockholders are not likely to receive any dividends on their common stock for the foreseeable future. Since we do not intend to pay dividends, our stockholders’ ability to receive a return on their investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.