Risk Factors Comparison 2024-02-27 to 2023-03-01 Form: 10-K

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You should carefully consider the risks and uncertainties described below and the other information in this Annual Report on Form 10- K, including our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10- K and in the section titled " Management' s Discussion and Analysis of Financial Condition and Results of Operations, " before deciding whether to invest in our common stock ~~. Such risks and uncertainties may be amplified by the COVID- 19 pandemic and its potential impact on our business and the global economy~~ . Our business, financial condition, results of operations or prospects could be materially and adversely affected if any of these risks occurs, and as a result, the market price of our common stock could decline and you could lose all or part of your investment. This Annual Report on Form 10- K also contains forward- looking statements that involve risks and uncertainties. See " Cautionary Note Regarding Forward- Looking Statements. " Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. Our actual results could differ materially and adversely from those anticipated in these forward- looking statements as a result of certain important factors, including those set forth below. Risks Related to Our Financial Position and Need for Additional Capital We have a limited operating history and have no products approved for commercial sale, which may make it difficult for you to evaluate our current business and predict our future success and viability. We are a clinical- stage biopharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. We have no products approved for commercial sale and have not generated any revenue from product sales. To date, we have devoted substantially all of our resources and efforts to organizing and staffing our company, business planning, executing partnerships, raising capital, discovering, identifying and developing potential product candidates, securing related intellectual property rights and conducting preclinical studies and clinical trials of our product candidates, including the ongoing clinical trials of azenosertib and ZN- d5. We have not yet demonstrated our ability to obtain marketing approvals, manufacture a product at commercial scale or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. As a result, it may be more difficult for you to accurately predict our future success or viability than it 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 and risks frequently experienced by clinical stage biopharmaceutical companies in rapidly evolving fields. We also may need to transition from a company with a research and development focus to a company capable of supporting commercial activities. If we do not adequately address these risks and difficulties or successfully make such a transition, our business will suffer. We have incurred significant net losses since inception, and we expect to continue to incur significant net losses for the foreseeable future. We have incurred net losses in each reporting period since our inception, we have not generated any revenue from product sales to date, and we have financed our operations principally through private financings, our **initial public offering, or** IPO, and follow- on public offerings of our common stock. We have incurred net losses of $ **292. 3 million and $** 237 ~~. 1 million and $ 166~~ . 1 million for the years ended December 31, **2023 and** 2022 ~~and 2021~~ , respectively. As of December 31, ~~2022~~ **2023** , we had an accumulated deficit of $ ~~596~~ **888** . ~~4~~ **6** million. Our losses have resulted principally from expenses incurred in research and development of our product candidates and from management and administrative costs and other expenses that we have incurred while building our business infrastructure. We expect that it will be several years, if ever, before we have a commercialized product and generate revenue from product sales. Even if we succeed in receiving marketing approval for and commercializing one or more of our product candidates, we expect that we will continue to incur substantial research and development and other expenses as we discover, develop and market additional potential products. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future as we continue our research and development efforts and seek to obtain regulatory approval and commercialization of our product candidates. The net losses we incur may fluctuate significantly from quarter to quarter such that a period- to- period comparison of our results of operations may not be a good indication of our future performance. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our working capital and our ability to achieve and maintain profitability. Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve a number of objectives. Our business depends entirely on the successful discovery, development and commercialization of our product candidates. We currently generate no revenues from sales of any products. We have no products approved for commercial sale and do not anticipate generating any revenue from product sales for the next several years, if ever. Our ability to generate revenue and achieve profitability depends significantly on our ability, or any future collaborator' s ability, to achieve a number of objectives, including: • successful and timely completion of preclinical and clinical development of our product candidates, including azenosertib and ZN- d5 and any other future product candidates, as well as **meeting** the associated costs, including any unforeseen costs we have incurred and may continue to incur as a result of preclinical study or clinical trial delays **including** due to public health emergencies, **U. S. and** ~~including the COVID- 19 pandemic,~~ global economic issues, ~~including~~ **such as** rising inflation and interest rates, or ~~the~~ ongoing military ~~conflict~~ **conflicts** ~~in Ukraine~~ , among other causes; • **if applicable,** the availability or successful development of ~~companion diagnostics~~ **diagnostic tools** for biomarkers associated with our product candidates or any other future product candidates; • establishing and maintaining relationships with ~~contract research organizations, or~~ CROs ~~,~~ and clinical sites for the clinical development, both in the United States and internationally, of our product candidates, including azenosertib and ZN- d5, and any other future product candidates; • timely receipt of marketing approvals from applicable regulatory authorities for any product candidates for which

we successfully complete clinical development; • maintaining marketing approvals, including making any required post-marketing approval commitments to applicable regulatory authorities; • developing an efficient and scalable manufacturing process for our product candidates, including obtaining finished products that are appropriately packaged for sale; • establishing and maintaining commercially viable supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and meet the market demand for product candidates that we develop, if approved; • successful commercial launch following any marketing approval, including the development of a commercial infrastructure, whether in- house or with one or more collaborators; • a continued acceptable safety profile following any marketing approval of our product candidates; • commercial acceptance of our product candidates by patients, the medical community and third- party payors; • identifying, assessing and developing new product candidates; • obtaining, maintaining and expanding our intellectual property rights, including patents, trade secrets and know how, and regulatory exclusivity, both in the United States and internationally; • protecting our rights in our intellectual property portfolio; • defending against third- party interference or infringement claims, if any; • negotiating favorable terms in any collaboration, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize our product candidates; • obtaining adequate pricing, coverage and reimbursement by hospitals, government and third- party payors for product candidates that we develop; • addressing any competing therapies and technological and market developments; and • attracting, hiring and retaining qualified personnel, especially in the current labor market. We may never be successful in achieving our objectives and, even if we do, may never generate revenue that is 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 company and could impair our ability to maintain or further our research and development efforts, raise additional necessary capital, grow our business and continue our operations. We will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and / or eliminate one or more of our research and drug development programs or future commercialization efforts. Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time- consuming, expensive and uncertain process that takes years to complete. Our operations have consumed substantial amounts of cash since inception, and we expect our expenses to increase in connection with our ongoing activities, particularly as we initiate and conduct clinical trials of, and seek marketing approval for, azenosertib, ZN- d5 and **any of** our other product candidates. Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond our expectations if we are required by the FDA, the European Medicines Agency, or the EMA, or other regulatory agencies to perform clinical trials or preclinical studies in addition to those that we currently anticipate. We may also incur costs related to collaborating with certain diagnostic companies for the development, manufacturing and supply of ~~companion~~ diagnostic ~~tests~~ **tools** for biomarkers associated with our product candidates and any future product candidates. Other unanticipated costs may also arise. In addition, if we obtain marketing approval for any of our product candidates, including azenosertib and ZN- d5, we expect to incur significant commercialization expenses related to drug sales, marketing, manufacturing and distribution. Because the design and outcome of our planned and anticipated clinical trials are highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of any product candidate we develop. We have also incurred, and expect to continue to incur ~~additional~~ **,** costs associated with operating as a public company ~~, particularly now that we are no longer an emerging growth company~~ . Accordingly, we will need to obtain substantial additional funding in order to maintain our continuing operations. As of December 31, ~~2022~~ **2023** , we had cash and cash equivalents and marketable securities of $ ~~437~~ **482** . ~~4~~ **9** million. Based on current business plans, we believe that our existing cash, cash equivalents and marketable securities as of December 31, ~~2022~~ **2023** will be sufficient to fund our operating expenses and capital expenditure requirements into ~~the second quarter of 2025~~ **2026** , but will not be sufficient to fund all of the activities that are necessary to complete the development of our product candidates. This estimate is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned **. We maintain the majority of our cash and cash equivalents in accounts with major U. S. and multi- national financial institutions, and our deposits at certain of these institutions exceed insured limits. Market conditions can impact the viability of these institutions. In the event of failure of any of the financial institutions where we maintain our cash and cash equivalents, there can be no assurance that we would be able to access uninsured funds in a timely manner or at all. Any inability to access or delay in accessing these funds could adversely affect our business and financial position** . We will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources, which may dilute our stockholders or restrict our operating activities. We do not have any committed external source of funds. Adequate additional financing may not be available to us on acceptable terms, or at all. Market volatility resulting from public health emergencies ~~such as the COVID- 19 pandemic~~ **, U. S. and global economic issues** , global supply chain disruptions, international political instability, rising inflation and interest rates or other factors could also adversely impact our ability to access capital as and when needed. Our failure to raise capital as and when needed or on acceptable terms would have a negative impact on our financial condition and our ability to pursue our business strategy, and we may have to delay, reduce the scope of, suspend or eliminate one or more of our research- stage programs, clinical trials or future commercialization efforts. Risks Related to the Discovery, Development and Commercialization of Our Product Candidates We are substantially dependent on the success of our lead product candidates, azenosertib and / or ZN- d5, which are currently in clinical trials. If we are unable to complete development of, obtain approval for and commercialize these product candidates in a timely manner, our business will be harmed. Our future success is dependent on our ability to timely complete clinical trials, obtain marketing

approval for and successfully commercialize our lead product candidates. We are investing significant efforts and financial resources in the research and development of our product candidates, which will require additional clinical development, **additional** ~~evaluation of~~ clinical, preclinical and manufacturing activities, marketing approval from government regulators, substantial investment and significant marketing efforts before we can generate any revenues from product sales. We are not permitted to market or promote any other product candidate before we receive marketing approval from the FDA and **/ or** comparable ex- U. S. regulatory authorities, and we may never receive such marketing approvals. The success of our lead product candidates will depend on several factors, including the following: • the successful and timely completion of our ongoing and planned clinical trials; • maintaining and establishing relationships with CROs and clinical sites for the clinical development of our product candidates both in the United States and internationally; • the frequency and severity of AEs observed in clinical trials; • efficacy, safety and tolerability profiles that are satisfactory to the FDA **and /** or any comparable ex- U. S. regulatory authority for marketing approval; • the timely receipt of marketing approvals from applicable regulatory authorities; • the extent of any required post- marketing approval commitments to applicable regulatory authorities; • the maintenance of existing or the establishment of new supply arrangements with third- party drug substance and drug product suppliers and manufacturers for clinical development of our product candidates; • the maintenance of existing, or the establishment of new, scaled production arrangements with third- party manufacturers to obtain finished products that are appropriate for commercial sale of our product candidates if approved, including for supplies of drugs that we are testing in combination with our product candidates; • obtaining and maintaining our intellectual property rights, including patents, trade secrets and know how, and regulatory exclusivity, both in the United States and internationally; • the protection of our rights in our intellectual property portfolio; • the successful launch of commercial sales following any marketing approval; • a continued acceptable safety profile following any marketing approval; • commercial acceptance by patients, the medical community and third- party payors; and • our ability to compete with other therapies. We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights **,** and the manufacturing, marketing, distribution and sales efforts of any future collaborator. If we are not successful with respect to one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. If we do not receive marketing approvals for our product candidates, we may not be able to continue our operations. We have and in the future may enter into collaborations with third parties for the research, development and commercialization of certain of the product candidates we may develop. If any of these collaborations are not successful, we may not be able to capitalize on the market potential of those product candidates. We have and in the future may seek third- party collaborators for the research, development and commercialization of one or more of our product candidates. For example, we are collaborating with Pfizer ~~on development of azenosertib~~, GSK **and** ~~on development of azenosertib,~~ Dana Farber on development of azenosertib, and **we licensed ZPC** ~~Zentera on development of certain of our product candidates, including azenosertib and ZN- d5~~ **21** , ~~in certain Asian jurisdictions including China~~ **our preclinical ROR1 ADC, and our ADC platform technology to Immunome** . Our likely collaborators in any future collaboration arrangements we may enter into include large and mid- size pharmaceutical companies and biotechnology companies. If we were to enter into any collaboration arrangements with third parties, those agreements may limit our control over the amount and timing of resources that our collaborators dedicate to the development and commercialization of any product candidates we may seek to develop with them. We cannot predict the success of any collaboration in which we have entered or may enter. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements. Collaborations involving our research programs, our product candidates and any future research programs or product candidates we may develop pose the following risks to us: • Collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations. • Collaborators may not pursue development and commercialization of any product candidates we may develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator' s strategic focus or market considerations, including as a result of a sale or disposition of a business unit or development function, or available funding or external factors such as an acquisition or business combination that diverts resources or creates competing priorities. If this were to happen, we may need additional capital to pursue further development or commercialization of the applicable product candidates. • Collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, use our product candidates in clinical trials in an unsafe manner, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing. • 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 or can be commercialized under terms that are more economically attractive than ours. • Subject to certain diligence obligations, collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products. • Collaborators may not properly obtain, maintain, enforce or defend our intellectual property or proprietary rights or may use proprietary information in a way that could jeopardize or invalidate our proprietary information or expose us to potential litigation. • Collaborators may own or co- own intellectual property covering our products that results from our collaborating with them, and in cases where that applies, we would not have the exclusive right to commercialize the collaboration intellectual property. • Disputes may arise between our collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources. • We may lose certain rights under circumstances identified in our collaborations, including if we undergo a change of control. • Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates. • Collaboration agreements may not lead to development or

commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished or terminated. • Collaborators may be unable to maintain compliance with applicable laws, regulations and guidance, including good practice quality guidelines and regulations, including GLP, GCP **,** and cGMP, **or similar ex- U. S. requirements** or to secure approval for clinical development plans from the FDA or comparable ex- U. S. regulatory authorities. • We may require certain regulatory, clinical, manufacturing, financial and other information from our collaborators, which, if not provided in a timely manner or at all, could affect our ability to meet our business objectives and / or comply with applicable laws, regulations and guidance. If we do not receive the funding **or other resources** we expect under these agreements, our development of product candidates could be delayed and we may need additional resources to develop our product candidates. In addition, if one of our collaborators terminates its agreement with us, we may find it more difficult to find a suitable replacement collaborator or attract new collaborators and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, marketing approval and commercialization described in this ~~annual~~ report apply to the activities of our collaborators. We may in the future decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of any product candidates we may develop. These and other similar relationships may require us to incur non- recurring and other charges, increase our near- and long- term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators and the negotiation process is time- consuming and complex. Our ability to reach a definitive collaboration agreement 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 several factors. If we license rights to any product candidates we or our collaborators may develop, we may not be able to realize the benefit of those transactions if we are unable to successfully integrate them with our existing operations and company culture. Our long- term prospects depend in part upon discovering, developing and commercializing additional product candidates, which may fail in development or suffer delays that adversely affect their commercial viability. Our future operating results are dependent on our ability to successfully discover, develop, obtain regulatory approval for and commercialize product candidates beyond those we currently have in clinical development. A product candidate can unexpectedly fail at any stage of preclinical and clinical development. The historical failure rate for product candidates is high due to risks relating to safety, efficacy, clinical execution, changing standards of medical care and other unpredictable variables. The results from preclinical testing or early clinical trials of a product candidate may not be predictive of the results that will be obtained in later stage clinical trials of the product candidate. The success of other product candidates we may develop will depend on many factors, including the following: • generating sufficient data to support the initiation or continuation of clinical trials; • obtaining regulatory permission to initiate clinical trials; • contracting with the necessary parties to conduct clinical trials; • successful enrollment of patients in, and the completion of, clinical trials on a timely basis; • the timely manufacture of sufficient quantities of the product candidate for use in clinical trials; and • AEs in the clinical trials. Even if we successfully advance any other product candidates into clinical development, their success will be subject to all of the clinical, regulatory and commercial risks described elsewhere in this " Risk Factors " section. Accordingly, we cannot assure you that we will ever be able to discover, develop, obtain regulatory approval of, commercialize or generate significant revenue from our other product candidates. The regulatory approval processes of the FDA and other comparable ex- U. S. regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be substantially harmed. We are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Ex- U. S. regulatory authorities impose similar requirements. The time required to obtain approval by the FDA and other comparable ex- U. S. regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate' s clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other data. Even if we eventually complete clinical testing and receive approval of any regulatory filing for our product candidates, the FDA and other comparable ex- U. S. regulatory authorities may approve our product candidates for a more limited indication or a narrower patient population than we originally requested. We have not submitted for, or obtained, regulatory approval for any product candidate, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval. Applications for our product candidates could fail to receive regulatory approval for many reasons, including the following: • the FDA or other comparable ex- U. S. regulatory authorities may disagree with the design, implementation or results of our clinical trials; • the FDA or other comparable ex- U. S. regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use; • the population studied in the clinical trial may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval; • the FDA or other comparable ex- U. S. regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials; • the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA **, BLA** or other submission or to obtain regulatory approval in the United States or elsewhere; • we may be unable to demonstrate to the FDA or other comparable ex- U. S. regulatory authorities that a product candidate' s risk- benefit ratio for its proposed

indication is acceptable; • the FDA or other comparable ex- U. S. regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications or facilities of third- party manufacturers with which we contract for clinical and commercial supplies; • if the FDA or comparable **ex- U. S.** regulatory authority requires approval or clearance of a companion diagnostic for a particular product candidate, and the FDA or comparable regulatory authority does not provide such approval or clearance, then the product candidate may not be approved for marketing; and / or • the approval policies or regulations of the FDA or other comparable ex- U. S. regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval. In addition, the policies and practices of the FDA and other **comparable ex- U. S.** regulatory authorities ~~'~~ with respect to clinical trials may change and additional government regulations may be enacted. For example, in recent years the FDA has issued draft guidance and launched programs aiming to reform and modernize the dose optimization procedures used by clinical trial sponsors during the development of oncology drugs. Although these efforts have not yet resulted in any formal changes to the FDA' s regulations or policies, changes in the FDA' s thinking with respect to dose selection and optimization could require us to change the design of our planned or ongoing clinical trials or otherwise conduct additional preclinical, clinical or manufacturing studies beyond those we currently anticipate, which could increase our costs and / or delay the development of our product candidates. ~~The~~ **In April 2022, the** FDA ~~has~~ also issued a draft guidance regarding diversity in clinical trials. The purpose of this **draft** guidance is to provide recommendations to sponsors developing medical products on the approach for developing a Race and Ethnicity Diversity Plan to enroll representative numbers of participants from underrepresented racial and ethnic populations in the United States. If ~~implemented~~ **this guidance is finalized** , the FDA **has stated that it** will evaluate the Race and Ethnicity Diversity Plan as an important part of the sponsor' s development program. This could require us to change the way we **decide to** enroll our planned clinical trials, which could increase our costs and / or delay the development of our product candidates. In addition, the regulatory landscape related to clinical trials in the ~~European Union, or~~ EU ~~,~~ recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the **EU** Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state **in which the clinical trial takes place** , to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application ~~to all member states concerned~~ **for multi- center trials** . The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state' s decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR foresees a three- year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the **EU** Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the **EU** Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials, including those that are ongoing, will become subject to the provisions of the CTR. Compliance with the CTR requirements by us, our collaborators and third- party service providers, such as CROs, may impact our development plans. This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations and prospects. In addition, even if we obtain approval of our product candidates, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may impose significant limitations in the form of narrow indications, warnings **and precautions** , **or** a REMS, or similar risk management measures. Regulatory authorities may not approve the price we intend to charge for products we may develop, may grant approval contingent on the performance of costly post- marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could seriously harm our business. The clinical trials of our product candidates may not demonstrate safety and efficacy to the satisfaction of the FDA or other comparable ex- U. S. regulatory authorities or otherwise produce positive results. Before obtaining marketing approval from the FDA or other comparable ex- U. S. regulatory authorities for the sale of our product candidates, we must complete preclinical development and extensive clinical trials to demonstrate the safety and efficacy of our product candidates. Clinical testing is expensive, difficult to design and implement, can take many years to complete and its ultimate outcome is uncertain. A failure of one or more clinical trials can occur at any stage of the process. The outcome of preclinical studies and early- stage clinical trials may not be predictive of the success of later clinical trials, including that potential biomarkers, even if validated preclinically, may not be functionally validated in clinical trials. ~~The outcome of preclinical studies and early- stage clinical trials may not be predictive of the success of later clinical trials.~~ 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 drugs. We cannot guarantee that the FDA or comparable ex- U. S. regulatory authorities will interpret trial results as we do, and more trials could be required before we are able to submit applications seeking approval of our product candidates, which may require us to expend significant resources that may not be available to us **and / or cause delays in our planned timelines** . Most product candidates that begin clinical trials are never approved by regulatory authorities for commercialization. In addition, we may rely in part on preclinical, clinical and quality data generated by CROs, our collaborators and other third parties for regulatory submissions for our product candidates. While we have or will have agreements governing our relationships with these third parties, we have limited influence over their actual performance. If these third parties do not make data available to us, or, if applicable, make regulatory submissions in a timely manner, in each case pursuant to our agreements with them, our development programs may

be significantly delayed, and we may need to conduct additional studies or collect additional data independently. In either case, our development costs would increase. We do not know whether our future clinical trials will begin on time or enroll patients on time, or whether our ongoing and / or future clinical trials will be completed on schedule or at all. Clinical trials can be delayed for a variety of reasons, including delays related to: • the FDA or comparable ex- U. S. regulatory authorities disagreeing as to the design or implementation of our clinical studies; • obtaining regulatory authorizations to commence a trial or reaching a consensus with regulatory authorities on trial design; • any failure or delay in reaching an agreement with CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites; • obtaining approval from one or more IRBs or ethics committees; • IRBs or ethics committees refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing their approval of the trial; • changes to **the** clinical trial protocol; • clinical sites deviating from **the** trial protocol or dropping out of a trial; • manufacturing sufficient quantities of product candidate or obtaining sufficient quantities of combination therapies for use in clinical trials; • subjects failing to enroll or remain in our trial at the rate we expect, or failing to return for post- treatment follow- up; • subjects choosing an alternative treatment for the indication for which we are developing our product candidates, or participating in competing clinical trials; • lack of adequate funding to continue the clinical trial; • subjects experiencing severe or unexpected drug- related **AEs** ~~adverse effects~~ ; • occurrence of serious AEs in trials of the same class of agents conducted by other companies; • selection of clinical end points that require prolonged periods of clinical observation or analysis of the resulting data; • a facility manufacturing our product candidates or any of their components being ordered by the FDA or comparable ex- U. S. regulatory authorities to temporarily or permanently shut down due to violations of cGMP regulations or similar ex- U. S. requirements or other applicable requirements, or infections or cross- contaminations of product candidates in the manufacturing process; • any changes to our manufacturing process that may be necessary or desired; • third- party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, GCP, or other regulatory requirements; • third- party contractors not performing data collection or analysis in a timely or accurate manner; • third- party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications; and / or • if we are collaborating with a third party on a clinical trial, our collaborator may not devote sufficient resources to or prioritize our clinical trial. ~~In addition, disruptions caused by the COVID- 19 pandemic have caused and may continue to cause difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials.~~ We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by a Data Safety Monitoring Board for such trial or by the FDA or comparable ex- U. S. regulatory authorities. Such ~~authorities may impose such~~ a suspension or termination **may be** due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable ex- U. S. regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs or ethics committees for reexamination, which may impact the costs, timing or successful completion of a clinical trial. Further, conducting clinical trials in ex- U. S. countries, as we may do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in ex- U. S. countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with ex- U. S. regulatory schemes, as well as political and economic risks relevant to such ex- U. S. countries. Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable ex- U. S. regulatory authorities. The FDA or comparable ex- U. S. regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable ex- U. S. regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable ex- U. S. regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates. If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. Moreover, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. Any delays to our clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize our product candidates and our competitors may be able to bring products to market before we do, and the commercial viability of our product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition and prospects significantly. If we are unable to successfully develop ~~companion diagnostics~~ **diagnostic tools** for biomarkers that enable patient selection, or experience significant delays in doing so, we may not realize the full commercial potential of our product candidates. A ~~key~~ component of our strategy **may** ~~includes~~ **include** the use of ~~companion diagnostics~~ **diagnostic tools** to guide patient selection of our product candidates. In some cases, a diagnostic

tool may be commercially available, for example, on a tumor- profiling panel. If not already commercially available, we may be required to seek collaborations with diagnostic companies for the development of diagnostics for biomarkers associated with our product candidates. We may have difficulty in establishing or maintaining such development relationships, and we will face competition from other companies in establishing these collaborations. There are also several risks associated with biomarker identification and validation. We, in collaboration with any diagnostic partners, may not be able to identify predictive biomarkers for one or more of our programs. We may not be able to validate potential biomarkers (e. g., certain genomic mutations) or their functional relevance preclinically in relevant in vitro or in vivo models. Data analytics and information from databases that we rely on for identifying or validating some of our biomarker- target relationships may not accurately reflect potential patient populations or may be based on incorrect methodology. Potential biomarkers, even if validated preclinically, may not be functionally effective or validated in human clinical trials. If we, in collaboration with these parties, are unable to successfully develop **diagnostic tools for our product candidates, or experience delays in doing so, the development of our product candidates may be adversely affected. The development of certain diagnostic tools, such as** companion diagnostics ~~for our product candidates~~, ~~or experience delays in doing so, the development of our product candidates may be adversely affected. The development of companion diagnostic products requires~~ **require** a significant investment of working capital and may not result in any future income. This could require us to raise additional funds, which could dilute our current investors or impact our ability to continue our operations in the future. There are also risks associated with diagnostics that are commercially available, including that we may not have access to reliable supply for such diagnostics, and that ~~we~~ **such diagnostics** may not be ~~able to obtain reimbursement~~ **reimbursed** ~~for its use~~ without obtaining regulatory approval. Interim, initial, " topline **,**" ~~,~~ and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data. From time to time, we may publicly disclose initial, preliminary or topline data from our preclinical studies and clinical trials, which are based on a preliminary analysis of then- available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the initial, topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. ~~Topline~~ **Certain of these** data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, initial, topline and preliminary data should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Adverse differences between interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock. Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the initial, interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition. Even if approved, our product candidates may not achieve adequate market acceptance among physicians, patients, healthcare payors and others in the medical community necessary for commercial success. Even if our product candidates receive regulatory approval, they may not gain adequate market acceptance among physicians, patients, healthcare payors and others in the medical community. The degree of market acceptance of any of our approved product candidates will depend on a number of factors, including: • the efficacy and safety profile as demonstrated in clinical trials compared to alternative treatments; • the timing of market introduction of the product candidate as well as competitive products; • the clinical indications for which the product candidate is approved; • **if applicable,** the availability of ~~companion diagnostics~~ **diagnostic tools** for biomarkers associated with our product candidates or any other future product candidates; • restrictions on the use of our product candidates, such as boxed warnings or contraindications in labeling, or a REMS, or similar risk management measures, if any, which may not be required of alternative treatments and competitor products; • the potential and perceived advantages of product candidates over alternative treatments; • the cost of treatment in relation to alternative treatments; • the availability of coverage and adequate reimbursement, as well as pricing, by third- party payors, including government authorities; • the availability of the approved product candidate for use as a combination therapy; • relative convenience and ease of administration; • the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies; • the effectiveness of sales and marketing efforts; • unfavorable publicity relating to our products or product candidates or similar approved products or product candidates in development by third parties; and • the approval of other new therapies for the same indications. If any of our product candidates is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors and patients, we may not generate or derive sufficient revenue from that product candidate and our financial results could be negatively impacted. If we experience delays or difficulties in the enrollment and / or maintenance of patients in clinical trials, our clinical development activities could be delayed or otherwise adversely affected. Patient enrollment is a significant factor in the timing of clinical trials, and the timing of our clinical trials depends, in part, on the speed at which we can recruit patients to participate in our trials, as well as

completion of required follow- up periods. 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 **each** such trial' s conclusion as required by the FDA or comparable ex- U. S. regulatory authorities. Additionally, certain clinical trials for future product candidates may be focused on indications with relatively small patient populations, which may further limit enrollment of eligible patients or may result in slower enrollment than we anticipate. The eligibility criteria of our clinical trials, once established, may further limit the pool of available trial participants. Patient enrollment may also be affected if our competitors have ongoing clinical trials for product candidates that are under development for the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials instead enroll in clinical trials of our competitors' product candidates. Patient enrollment for any of our clinical trials may be affected by other factors, including: • size and nature of the patient population; • severity of the disease under investigation; • availability and efficacy of approved drugs for the disease under investigation; • patient eligibility criteria for the trial in question as defined in the protocol; • perceived risks and benefits of the product candidate under study; • clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating; • efforts to facilitate timely enrollment in clinical trials; • patient referral practices of physicians; • the ability to monitor patients adequately during and after treatment; • proximity and availability of clinical trial sites for prospective patients; • continued enrollment of prospective patients by clinical trial sites; and • the risk that patients enrolled in clinical trials will drop out of the trials before completion or, because they may be late- stage cancer patients, will not survive the full terms of the clinical trials. Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates and jeopardize our ability to obtain marketing approval for the sale of our product candidates. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining enrollment of such patients in our clinical trials. We are developing our product candidates in combination with other therapies, which exposes us to additional risks. We are developing azenosertib and ZN- d5 in combination with one or more other approved or unapproved therapies to treat cancer or other diseases and may in the future develop additional product candidates in combination with other approved or unapproved therapies **. If we were to experience an unexpected loss of supply of any of those approved or unapproved therapies, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing clinical trials** . Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or comparable ex- U. S. regulatory authorities outside of the United States could revoke approval of the therapy used in combination with our product or that safety, efficacy, manufacturing or supply issues could arise with any of those existing therapies. If the therapies we use in combination with our product candidates are replaced as the standard of care for the indications we choose for any of our product candidates, the FDA or comparable ex- U. S. regulatory authorities may require us to conduct additional clinical trials. The occurrence of any of these risks could result in our own products, if approved, being removed from the market or being less successful commercially. We also may choose to evaluate our product candidates in combination with one or more cancer therapies that have not yet been approved for marketing by the FDA or comparable ex- U. S. regulatory authorities. We will not be able to market and sell any product candidate we develop in combination with an unapproved cancer therapy for a combination indication if that unapproved therapy does not ultimately obtain marketing approval either alone or in combination with our product **candidate** . In addition, unapproved cancer therapies face the same risks described with respect to our product candidates currently in development and clinical trials, including the potential for serious adverse effects, delay in their clinical trials and lack of regulatory approval. If the FDA or comparable ex- U. S. regulatory authorities do not approve these other drugs or revoke their approval of, or if safety, efficacy, quality, manufacturing or supply issues arise with, the drugs we choose to evaluate in combination with our product candidate we develop, we may be unable to obtain approval of or market such combination therapy. If the market opportunity for any product candidate that we or our strategic partners develop is smaller than we believe, our revenue may be adversely affected and our business may suffer. Our projections of addressable patient populations that may benefit from treatment with our product candidates are based on our estimates. These estimates, which have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations and market research, may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these cancers. Additionally, the potentially addressable patient population for our product candidates may not ultimately be amenable to treatment with our product candidates. Our market opportunity may also be limited by future competitor treatments that enter the market. If any of our estimates proves to be inaccurate, the market opportunity for any product candidate that we or our strategic partners develop could be significantly diminished and have an adverse material impact on our business. We face significant competition, and if our competitors develop and market technologies or products more rapidly than we do or that are more effective, safer or less expensive than the product candidates we develop, our commercial opportunities will be negatively impacted. The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary and novel products and product candidates. Our competitors have developed, are developing or may develop products, product candidates and processes competitive with our product candidates. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may attempt to develop product candidates. In addition, our products may need to compete with off- label drugs used by physicians to treat the indications for which we seek approval. This may make it difficult for us to replace existing therapies with our products. In particular, there is intense competition in the fields of oncology we are pursuing. We have competitors both in the United States and internationally, including major

multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies, emerging and start- up companies, universities and other research institutions. We also compete with these organizations to recruit management, scientists and clinical development personnel, which could negatively affect our level of expertise and our ability to execute our business plan. We ~~will~~ also face competition in establishing clinical trial sites, enrolling subjects for clinical trials and in identifying and in- licensing new product candidates. We have chosen to initially address well- validated biochemical targets, and therefore expect to face competition from existing products and products in development for each of our product candidates. There are a large number of companies developing or marketing treatments for cancer, including many major pharmaceutical and biotechnology companies. Many of these current and potential competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources and commercial expertise than we do. Large pharmaceutical and biotechnology companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and manufacturing biotechnology products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in late stages of development, and collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical and biotechnology companies may also invest heavily to accelerate discovery and development of novel compounds or to in- license novel compounds that could make the product candidates that we develop obsolete. Smaller or early- stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result of all of these factors, our competitors may succeed in obtaining approval from the FDA or other comparable ex- U. S. regulatory authorities or in discovering, developing and commercializing products in our field before we do. 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 effects, are more convenient, have a broader label, are marketed more effectively, are reimbursed or are less expensive than any products that we may develop. Our competitors also may obtain marketing approval from the FDA or other comparable ex- U. S. regulatory authorities for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Even if the product candidates we develop achieve marketing approval, they may be priced at a significant premium over competitive products if any have been approved by then, resulting in reduced competitiveness. Technological advances or products developed by our competitors may render our technologies or product candidates obsolete, less competitive or not economical. If we are unable to compete effectively, our opportunity to generate revenue from the sale of our products we may develop, if approved, could be adversely affected. We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success. Because we have limited financial and managerial resources, we focus on research programs, therapeutic platforms and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other therapeutic platforms or product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs, therapeutic platforms and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights. Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay. As product candidates progress through preclinical and clinical trials to marketing approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize yield and manufacturing batch size, minimize costs and achieve consistent quality and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commercialize our product candidates, if approved, and generate revenue. Our business entails a significant risk of product liability and if we are unable to obtain sufficient insurance coverage such inability could have an adverse effect on our business and financial condition. Our business exposes us to significant product liability risks inherent in the development, testing, manufacturing and marketing of therapeutic treatments. Product liability claims could delay or prevent completion of our development programs. If we succeed in marketing products, such claims could result in an FDA or other regulatory authority investigation of the safety and effectiveness of our products, our manufacturing processes and facilities or our marketing programs. FDA or other regulatory authority investigations could potentially lead to a recall of our products or more serious enforcement action, limitations on the approved indications for which they may be used or suspension or withdrawal of approvals. Regardless of the merits or eventual outcome, liability claims may also result in decreased demand for our products, injury to our reputation, costs to defend the related litigation, a diversion of management' s time and our resources and substantial monetary awards to trial participants or patients. We currently have product liability insurance that we believe is appropriate for our stage of development and may need to obtain higher levels prior to marketing any of our product candidates, if approved. Any insurance we have or may obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could have an adverse effect on our business and financial condition. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, ~~will~~ **may**

apply to **diagnostic tools, such as** companion diagnostics **,** that we or our collaborators may develop. Any product candidates we develop may become subject to unfavorable third- party coverage and reimbursement practices, as well as pricing regulations. The availability and extent of coverage and adequate reimbursement by third- party payors, including government health administration authorities, private health coverage insurers, managed care organizations and other third- party payors is essential for most patients to be able to afford expensive treatments. Sales of any of our product candidates that receive marketing approval will depend substantially, both in the United States and internationally, on the extent to which the costs of our product candidates will be covered and reimbursed by 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 an adequate return on our investment. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize any product candidate for which we obtain marketing approval. There is significant uncertainty related to third- party payor coverage and reimbursement of newly approved products. In the United States, for example, principal decisions about reimbursement for new products are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within HHS. CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare, and private third- party payors often follow CMS' s decisions regarding coverage and reimbursement to a substantial degree. However, one third- party payor' s determination to provide coverage for a product candidate does not assure that other payors will also provide coverage for the product candidate. As a result, the coverage determination process is often time- consuming and costly. This process will require us to provide scientific and clinical support for the use of our products to each third- party payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Increasingly, third- party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Further, such payors are increasingly challenging the price, examining the medical necessity and reviewing the cost effectiveness of medical product candidates. There may be especially significant delays in obtaining coverage and reimbursement for newly approved drugs. Third- party payors may limit coverage to specific product candidates on an approved list, known as a formulary, which might not include all FDA- approved drugs for a particular indication. We may need to conduct expensive pharmaco- economic studies to demonstrate the medical necessity and cost effectiveness of our products. Nonetheless, our product candidates may not be considered medically necessary or cost effective. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be. **In August 2022, IRA was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (which first became due by certain manufacturers in 2023, as applicable); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). For more information about the IRA and pricing regulations at the state level, see " Risks Related to Regulatory Approval and Other Legal Compliance Matters – We may face difficulties from changes to current regulations and future legislation. " below.** Outside the United States, 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 therapeutics such as our product candidates. In many countries, particularly the member states of the EU, medical product prices are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after a product receives marketing authorization. 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. In general, product prices under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for products, but monitor and control company profits. Additional ex- U. S. 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 United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits. If we are unable to establish or sustain coverage and adequate reimbursement for any future product candidates from third- party payors, the adoption of those products and sales revenue will be adversely affected, which, in turn, could adversely affect the ability to market or sell those product candidates, if approved. Coverage policies and third- party payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future. Additionally, we or our collaborators may develop **diagnostic tests, including** companion diagnostic tests **,** for use with our product candidates. Companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical products, will apply to companion diagnostics. If coverage and adequate reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize any product candidates that we develop. ~~Risks Related to Regulatory Approval and Other Legal Compliance Matters~~ We may be unable to obtain U. S. or ex- U. S. regulatory approvals and, as a result, may be unable to commercialize our product candidates. Our product candidates are subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, packaging, advertising and promotion, pricing, marketing and distribution of drugs. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process must be successfully completed in

the United States and in many ex- U. S. jurisdictions before a new drug can be marketed. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. We cannot provide any assurance that any product candidate we may develop will progress through required clinical testing and obtain the regulatory approvals necessary for us to begin selling them. We have not conducted, managed or completed large- scale or pivotal clinical trials nor managed the regulatory approval process with the FDA or any other regulatory authority. The time required to obtain approvals from the FDA and other regulatory authorities is unpredictable, and requires successful completion of extensive clinical trials which typically takes many years, depending upon the type, complexity and novelty of the product candidate. The standards that the FDA and its ex- U. S. counterparts use when evaluating clinical trial data can and often ~~changes~~ **change** during drug development, which makes it difficult to predict with any certainty how they will be applied. In addition, the FDA and its ex- U. S. counterparts may require approval or clearance of a companion diagnostic for a particular product candidate and may not approve the product candidate for marketing if such regulatory authority does not approve or clear the companion diagnostic. We may also encounter unexpected delays or increased costs due to new government regulations, including future legislation or administrative action, or changes in FDA or ex- U. S. regulatory authorities policy during the period of drug development, clinical trials and FDA or ex- U. S. regulatory authorities regulatory review. Any delay or failure in seeking or obtaining required approvals would have a material and adverse effect on our ability to generate revenue from the particular product candidate for which we **are** developing and seeking approval. Furthermore, any regulatory approval to market a drug may be subject to significant limitations on the approved uses or indications for which we may market the drug or the labeling or other restrictions. In addition, the FDA has the authority to require a REMS as part of approving a NDA **or BLA**, or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug. Similar requirements may exist in ex- U. S. jurisdictions. These requirements or restrictions might include limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe- use criteria and requiring treated patients to enroll in a registry. These limitations and restrictions may significantly limit the size of the market for the drug and affect reimbursement by third- party payors. We are also subject to numerous ex- U. S. regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third- party reimbursement. The ex- U. S. regulatory approval process varies among countries, and generally includes all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in ex- U. S. jurisdictions. Moreover, the time required to obtain approval in ex- U. S. jurisdictions may differ from that required to obtain FDA approval. Our current or future product candidates may cause significant AEs, toxicities or other undesirable side effects when used alone or in combination with other approved products or investigational new drugs that may result in a safety profile that could inhibit regulatory approval, prevent market acceptance, limit their commercial potential or result in significant negative consequences. As is the case with pharmaceuticals generally, it is likely that there may be side effects and AEs associated with our product candidates' use. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable ex- U. S. regulatory authorities. The drug- related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly. If our product candidates are associated with undesirable side effects or have unexpected characteristics in preclinical studies or clinical trials when used alone or in combination with other approved products or investigational new drugs, 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. Treatment- related side effects could also 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 prevent us from achieving or maintaining market acceptance of the affected product candidate and may harm our business, financial condition and prospects significantly. Patients in our ongoing and planned clinical trials may in the future suffer significant AEs or other side effects not observed in our preclinical studies or previous clinical trials. Some of our product candidates may be used as chronic therapies or be used in pediatric populations, for which safety concerns may be particularly scrutinized by regulatory agencies. In addition, if our product candidates are used in combination with other therapies, our product candidates may exacerbate AEs associated with the therapy. Patients treated with our product candidates may also be undergoing surgical, radiation and chemotherapy treatments, which can cause side effects or AEs that are unrelated to our product candidate, but may still impact the success of our clinical trials. The inclusion of critically ill patients in our clinical trials may result in deaths or other adverse medical events due to other therapies or medications that such patients may be using or due to the gravity of such patients' illnesses. If significant AEs or other side effects are observed in any of our current or future clinical trials, we may have difficulty recruiting patients to the clinical trials, patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of that product candidate altogether. We, the FDA other comparable regulatory authorities or an IRB may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the product candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance due to its tolerability versus other therapies. Any of these developments could materially harm our business, financial condition and prospects. Further, if any of our product candidates obtains marketing approval, toxicities associated with such product candidates ~~and~~ not seen during clinical testing may also develop after such approval and lead to a requirement to conduct additional clinical safety trials, additional contraindications, warnings and precautions being added to the drug label,

significant restrictions on the use of the product or the withdrawal of the product from the market. We cannot predict whether our product candidates will cause toxicities in humans that would preclude or lead to the revocation of regulatory approval based on preclinical studies or early- stage clinical trials. The FDA and other comparable ex- U. S. regulatory authorities may not accept data from trials conducted in locations outside of their jurisdiction. We may choose to conduct international clinical trials in the future. The acceptance of study data by the FDA or other comparable ex- U. S. regulatory authority from clinical trials conducted outside of their respective jurisdictions may be subject to certain conditions. The acceptance of study data from clinical trials conducted outside the U. S. or another jurisdiction by the FDA or comparable ex- U. S. regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from ex- U. S. clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of ex- U. S. data alone unless i) the data are applicable to the U. S. population and U. S. medical practice; ii) the trials were performed by clinical investigators of recognized competence and pursuant to current GCP requirements; and iii) the FDA is able to validate the data through an on- site inspection or other appropriate means. Additionally, the FDA' s clinical trial requirements, including the adequacy of the patient population studied and statistical powering, must be met. Furthermore, even where the ex- U. S. study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well- designed and well- conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many ex- U. S. regulatory authorities have similar approval requirements. In addition, such ex- U. S. trials would be subject to the applicable local laws of the ex- U. S. jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable ex- U. S. regulatory authority will accept data from trials conducted outside of its applicable jurisdiction. If the FDA or any comparable ex- U. S. regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time- consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval for commercialization in the applicable jurisdiction. Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions. 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, comparable regulatory authorities in ex- U. S. jurisdictions must also approve the manufacturing, marketing and promotion and reimbursement of the product candidate in those countries. However, a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the United States, including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval. Obtaining ex- U. S. regulatory approvals and establishing and maintaining compliance with ex- U. S. regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any future collaborator fail to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed. Even if our product candidates receive regulatory approval, they will be subject to significant post- marketing regulatory requirements and oversight. Any regulatory approvals that we may receive for our product candidates will require the submission of reports to regulatory authorities and surveillance to monitor the safety and efficacy of the product candidate, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post- approval study or risk management requirements. For example, the FDA may require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or ex- U. S. regulatory authorities approve our product candidates, the manufacturing processes, labeling, packaging, distribution, AE reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post- marketing information and reports, registration, as well as on- going compliance with cGMPs or similar ex- U. S. requirements and GCP for any clinical trials that we conduct post- approval. In addition, CMOs and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMP regulations or similar ex- U. S. requirements and standards. If we or a regulatory agency discover previously unknown problems with a product, such as **AEs** ~~adverse events~~ of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. In addition, failure to comply with FDA and other comparable ex- U. S. regulatory requirements may subject our company to administrative or judicially imposed sanctions, including: • delays in or the rejection of product approvals; • restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials; • restrictions on the products, manufacturers or manufacturing process; • warning or untitled letters; • civil and criminal penalties; • injunctions; • suspension or withdrawal of regulatory approvals; • product seizures, detentions or import bans; • voluntary or mandatory product recalls and publicity requirements; • total or partial suspension of production; and • imposition of restrictions on operations, including costly new manufacturing requirements. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate

negative publicity. The FDA' s and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off- label uses. If any of our product candidates are approved and we are found to have improperly promoted off- label uses of those products, we may become subject to significant liability. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, such as our product candidates, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product' s approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off- label uses, we may become subject to significant liability. The U. S. federal government has levied large civil and criminal fines against companies for alleged improper promotion of off- label use and has enjoined several companies from engaging in off- label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition ~~. If we pursue development of companion diagnostic tests to identify patients who are likely to benefit from our product candidates, the failure to obtain required regulatory clearances or approvals for such diagnostic tests may prevent or delay approval of the therapeutic product. Moreover, the commercial success of any of our product candidates that require a companion diagnostic may be tied to the regulatory approval, market acceptance and continued availability of such companion diagnostic. A key component of our strategy includes the use of companion diagnostics to guide patient selection of our product candidates. Furthermore, if safe and effective use of any of our product candidates depends on an in vitro companion diagnostic that is not otherwise commercially available, then the FDA generally will require approval or clearance of that companion diagnostic at the same time that the FDA approves our product candidates if at all. According to FDA guidance, if the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic is not also approved or cleared for that indication. If a satisfactory companion diagnostic is not commercially available, we may be required to create or obtain one that would be subject to regulatory approval requirements. The process of obtaining or creating such diagnostic is time consuming and costly. Companion diagnostics are developed in conjunction with clinical programs for the associated product and are subject to regulation as medical devices by the FDA and comparable regulatory authorities, and, to date, the FDA has generally required premarket approval of companion diagnostics for cancer therapies requiring patient selection. The approval of a companion diagnostic as part of the therapeutic product' s labeling limits the use of the therapeutic product to only those patients who express the specific genetic alteration that the companion diagnostic was developed to detect. If the FDA or a comparable regulatory authority requires approval, clearance or certification of, or confirmatory or additional studies with respect to, a companion diagnostic for any of our product candidates, whether before or after it obtains marketing approval, we, and / or future collaborators, may encounter difficulties in developing and obtaining approval for such product candidate. Any delay or failure by us or third- party collaborators to develop, obtain or maintain regulatory approval, clearance or certification of a companion diagnostic could delay or prevent approval or continued marketing of such product candidate. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process for the companion diagnostic or in transferring that process to commercial partners or negotiating insurance reimbursement plans, all of which may prevent us from completing our clinical trials or commercializing our product candidate, if approved, on a timely or profitable basis, if at all. Even if a companion diagnostic is approved, we will rely on the continued ability of any third- party collaborator to make the companion diagnostic commercially available to us on reasonable terms in the relevant geographies. Market acceptance of the companion diagnostic may be low as a result of the cost and complexity of utilizing such companion diagnostic. Additionally, approval, clearance or certification of companion diagnostics may be subject to further legislative or regulatory reforms notably in the EU. On May 25, 2017, the In Vitro Medical Devices Regulation (2017 / 746), or IVDR, entered into force. The IVDR repeals and replaces the EU In Vitro Diagnostic Medical Devices Directive. Unlike directives, which must be implemented into the national laws of the EU member, regulations are directly applicable, i. e., without the need for adoption of EU member states laws implementing them, in all EU member states and are intended to eliminate current differences in the regulation of medical devices among EU member states. The IVDR, among other things, is intended to establish a uniform, transparent, predictable and sustainable regulatory framework across the EU for medical devices and ensure a high level of safety and health while supporting innovation. The IVDR became applicable on May 26, 2022. However, on October 14, 2021, the European Parliament and Council adopted a " progressive " roll- out of the IVDR to prevent disruption in the supply of in vitro diagnostic medical devices, and there is a tiered system extending the grace period for many devices (depending on their risk classification) before they have to be fully compliant with the regulation. The IVDR introduces a new classification system for companion diagnostics which are now specifically defined as diagnostic tests that support the safe and effective use of a specific medicinal product, by identifying patients that are suitable or unsuitable for treatment. Companion diagnostics will have to undergo a conformity assessment by a notified body. Before it can issue an EU certificate, the notified body must seek a scientific opinion from the EMA on the suitability of the companion diagnostic to the medicinal product concerned if the medicinal product falls exclusively within the scope of the centralized procedure for the authorization of medicines, or the medicinal product is already authorized through the centralized procedure, or a marketing authorization application for the medicinal product has been submitted through the centralized procedure. For other substances, the notified body can seek the opinion from a national competent authorities or the EMA. These modifications may make it more difficult and costly for us to obtain regulatory clearances or approvals or certifications for our companion diagnostics or to~~

~~manufacture, market or distribute our products after clearance or approval or certification is obtained~~ . Disruptions at the FDA, the SEC and other government agencies caused by funding shortages or global health concerns could 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 and 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, and statutory, regulatory, and policy changes, and other events that may otherwise affect the FDA' s and ex- U. S. regulatory authorities' ability to perform routine functions. Average review times at the FDA and ex- U. S. regulatory authorities have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies, such as the EMA, following its relocation to Amsterdam and resulting staff changes, may also slow the time necessary for new drugs to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. For example, in recent years, including in 2018 and 2019, the U. S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities. Further, in our operations as a public company, 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. Separately, in response to ~~the~~ COVID- 19 ~~pandemic~~ , the FDA postponed most inspections of domestic and ex- U. S. manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations ~~of domestic facilities where feasible~~ , ~~the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the entities it regulates as it adapts to the evolving COVID- 19 pandemic, and~~ any resurgence of the virus or emergence of new variants may lead to further inspectional **or administrative** delays ~~. Regulatory authorities outside the United States may have adopted similar restrictions and other policy measures in response to the COVID- 19 pandemic~~ . If we are unable to obtain accelerated approval or any other form of expedited development or review from the FDA or comparable ex- U. S. regulatory authorities, we may be required to conduct additional ~~preclinical studies or~~ clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post- marketing requirements, the FDA may seek to withdraw accelerated approval. We may in the future seek ~~an~~ accelerated approval or another form of expedited development or review for ~~our~~ one or more of our product candidates. Under the accelerated approval program, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life- threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor' s agreement to conduct, in a diligent manner, additional confirmatory studies to verity and describe the drug' s clinical benefit. If such confirmatory studies fail to confirm the drug' s clinical benefit, the FDA may withdraw its approval of the drug on an expedited basis. In addition, in December 2022, the President signed ~~an omnibus appropriations bill to fund the U. S. government through fiscal year 2023. Included in the omnibus bill is~~ the Food and Drug Omnibus Reform Act of 2022, which **,** among other things, **provided** ~~introduced reforms intended to expand~~ the FDA ~~' s ability~~ **new statutory authority** to ~~regulate products receiving~~ **mitigate potential risks to patients from continued marketing of ineffective drugs previously granted** accelerated approval, **and additional** ~~including by increasing the FDA' s~~ oversight over ~~the conduct of~~ confirmatory trials **. Under** ~~; however, the ultimate impact of~~ these ~~reforms remains unclear~~ **provisions, the FDA may, among other things, require a sponsor of a product seeking accelerated approval to have a confirmatory trial underway prior to such approval being granted** . In the EU, under the centralized procedure, the EMA' s Committee for Medicinal Products for Human Use may perform an accelerated assessment of a marketing authorization application. Applicants requesting an accelerated assessment procedure must justify that the product candidate is expected to be of major public health interest, particularly from the point of view of therapeutic innovation. Prior to seeking accelerated approval or another form of expedited development or review for any of our product candidates, we intend to seek feedback from the FDA or ex- U. S. regulatory authorities and will otherwise evaluate our ability to seek and receive accelerated approval or another form of expedited development or review. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA for accelerated approval or another form of expedited development, review or approval. Furthermore, if we decide to submit an application for accelerated approval or another form of expedited development, review or approval for our product candidates, there can be no assurance that such submission or application will be accepted or that any such expedited development, review or approval will be granted on a timely basis, or at all. The FDA or other comparable ex- U. S. regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidate would result in a longer time period to commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace. ~~We may face difficulties from changes to current regulations and future legislation.~~

Existing regulatory policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates **and affect our ability to profitably sell our products for which we receive approval** . We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability. For example, in March 2010, the ACA was passed, which substantially changes the way healthcare is financed by both the government and private insurers, and significantly impacts the U. S. pharmaceutical industry. Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U. S. Supreme Court dismissed the most recent judicial challenge to the ACA without specifically ruling on the constitutionality of the ACA. **Thus** ~~Prior to the Supreme Court' s decision~~ , ~~President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through~~ the ACA **will remain in effect in its current form** ~~marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA~~ . It is unclear how other healthcare reform measures will impact our business. ~~We are continuing to monitor any changes to the ACA that, in turn, may potentially impact our business in the future.~~ In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. These changes include the American Rescue Plan Act of 2021, which ~~eliminates~~ **eliminated** the statutory Medicaid drug rebate cap, ~~currently set~~ **beginning January 1, 2024. The rebate was previously capped** at 100 % of a drug ~~'~~ **'** s average manufacturer price ~~, beginning January 1, 2024~~ . Moreover, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several U. S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. Most recently, on August 16, 2022, the IRA was signed into law. **This statute marks the most significant action by Congress with respect to the pharmaceutical industry since adoption of the ACA in 2010.** Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (**which** first **became** due **by certain manufacturers** in 2023 **, as applicable**); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. ~~For~~ **On August 29, 2023, HHS announced the list of the first ten drugs** that **will be subject to price negotiations. HHS has issued** and **will continue to issue guidance implementing** ~~other~~ -- **the** ~~reasons~~ **IRA, although the Medicare drug price negotiation program is currently subject to legal challenges. While the impact of the IRA on the pharmaceutical industry cannot yet be fully determined** , it is **likely to** ~~currently unclear how the IRA will~~ be ~~effectuated~~ **significant** . At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. 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. 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 product candidates. Legislative and regulatory proposals have been made to expand post- approval requirements and restrict sales and promotional activities for biotechnology products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA or ex- U. S. 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 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. Our relationships with healthcare professionals, clinical investigators, CROs and third party payors in connection with our current and future business activities may be subject to fraud and abuse laws and other healthcare laws and regulations. Healthcare providers and third- party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, clinical investigators, CROs, third- party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal, state and ex- U. S. healthcare laws and regulations include the following: • the federal Anti- Kickback Statute prohibits, among other things, persons 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 healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti- Kickback Statute or specific intent to violate it in order to have committed a violation; • the federal false claims laws, including the civil False Claims Act, which can be enforced by private citizens through civil whistleblower or qui tam actions, prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or

fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items or services resulting from a violation of the U. S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act; • the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, prohibits, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. 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; • the federal **Open Payments Act (formerly known as the** Physician Payments Sunshine ~~Act (renamed the Open Payments~~ Act) requires applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children' s Health Insurance Program, with specific exceptions, to annually report to CMS information regarding payments and other transfers of value to physicians, as defined by such law, certain non- physician practitioners including physician assistants and nurse practitioners, and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members. The information reported is publicly available on a searchable website, with disclosure required annually; and • analogous state and ex- U. S. laws and regulations, such as state anti- kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non- governmental third-party payors, including private insurers. Some state laws require biotechnology companies to comply with the biotechnology industry' s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. Some state laws require biotechnology companies to report information on the pricing of certain drug products. Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition. The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and ex- U. S. laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal information, such as information that we may collect in connection with clinical trials. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or ex- U. S. laws or regulations, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our business, results of operation, and financial condition. In the United States, HIPAA imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. We do not believe that we are currently acting as a covered entity or business associate under HIPAA and thus are not directly subject to its requirements or penalties, but we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA. Depending on the facts and circumstances, we could be subject to significant penalties if we violate HIPAA. ~~Certain states have also adopted comparable privacy and security laws and regulations governing the privacy, processing and protection of personal information.~~ For example, ~~the State of California enacted~~ the California Consumer Privacy Act, ~~or CCPA, which went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations,~~ as **amended by** ~~well as a private right of action for data breaches that has increased the likelihood of, and risks associated with, data breach litigation. Further,~~ the California Privacy Rights Act, or ~~CPRA~~ **collectively** , ~~generally went into effect on January 1, 2023, and significantly amends~~ the CCPA **, requires** ~~. The CPRA imposes additional data protection obligations on~~ covered businesses **that** ~~, including additional consumer rights processes~~ -- **process the personal information of California residents to** , ~~limitations~~ **among other things: provide certain disclosures to California residents regarding the business' s collection, use, and disclosure of their personal information; receive and respond to requests from California residents to access, delete, and correct their personal information, or to opt out of certain disclosures of their personal information, and enter into specific contractual provisions with service providers that process California resident personal information** on **the** ~~data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also creates a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. Additional compliance investment and potential~~ business **' s behalf** ~~process changes may be required~~ . Similar laws have passed in ~~Virginia, Connecticut, Utah and Colorado, and have been proposed in~~ other states **,** and **are continuing to be proposed** at the **state and** federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA ~~, the CPRA~~ or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition. Our operations abroad may also be subject to increased scrutiny or attention from data protection authorities. For instance, the EU General Data Protection Regulation, or GDPR, went into effect in May 2018 and imposes strict requirements for processing the personal data of individuals within the **European Economic Area, or the** EEA **, or in the context of our activities in the EEA. In addition, some of the personal data we process in respect of clinical trial participants is special category or sensitive personal data under the GDPR, and subject to additional compliance obligations and to local law**

derogations . Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements, administrative penalties and potential fines for noncompliance of up to € 20 million or 4 % of the annual global revenues of the noncompliant company, whichever is greater **. In addition to fines, a breach of the GDPR may result in regulatory investigations, reputational damage, orders to cease / change our data processing activities, enforcement notices, assessment notices (for a compulsory audit) and / or civil claims (including class actions)** . Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States ~~. In July 2020~~ , **and** the ~~Court~~ **efficacy and longevity** of **current** ~~Justice of the EU, or CJEU, limited how organizations could lawfully~~ transfer **mechanisms between** ~~personal data from~~ the EEA ~~to~~ **and** the United States **remains uncertain** ~~by invalidating the Privacy Shield for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses, or SCCs~~ . ~~In March~~ **On July 10,** ~~2022~~ **2023** , the **European Commission adopted its Adequacy Decision in** ~~US and EU announced a new regulatory regime intended to replace the invalidated regulations~~ --- **relation to the** ~~; however, this~~ new EU- US Data Privacy Framework **, or the DPF, rendering the DPF effective** ~~has~~ - **as** ~~not been implemented beyond an executive order signed~~ **a GDPR transfer mechanism to U. S. entities self- certified under the DPF. We currently rely** on ~~October 7, 2022 on Enhancing Safeguards for Untied States Signals Intelligence Activities. The European Commission issued revised SCCs on June 4, 2021 to account for~~ the **EU** ~~decision of the CJEU and recommendations made by the European Data Protection Board. The revised SCCs have been required for relevant new data transfers since September 27, 2021; existing~~ standard contractual clauses **,** ~~arrangements had to be migrated to~~ the ~~revised~~ **UK Addendum to the EU standard contractual** clauses **and** ~~by December 27, 2022. The new SCCs apply only to~~ the **UK International Data Transfer Agreement, as relevant, to** transfer ~~of~~ personal data outside ~~of~~ the EEA and ~~not~~ the UK **, including to the United States, with respect to both intragroup and third party** ~~. The UK' s Information Commissioner' s Office has published new data transfer standard contracts for~~ transfers ~~from the United Kingdom under the UK GDPR~~ . **We may also rely** ~~This new documentation has been mandatory for relevant data transfers since September 21, 2022; existing SCCs arrangements must be migrated to the new documentation by March 21, 2024. European court and regulatory decisions subsequent to the CJEU decision of July 16, 2020 have taken a restrictive approach to international data transfers. As supervisory authorities issue further guidance~~ on **individual consent** ~~personal data export mechanisms, including circumstances where the SCCs cannot be used, and / or start taking enforcement action, we could suffer additional costs, complaints and / or regulatory investigations or fines, and / or if we are otherwise unable~~ to transfer personal data ~~between and among countries and regions~~ in ~~which we operate~~ **certain circumstances. We expect the existing legal complexity and uncertainty regarding international personal data transfers to continue. In particular** , ~~it could affect~~ **we expect the DPF Adequacy Decision to be challenged and international transfers to the United States and to** ~~the~~ **other** ~~manner in which we provide our services~~ **jurisdictions more generally to continue to be subject to enhanced scrutiny by regulators. As a result** , **we may have to make certain operational changes and we will have to implement revised standard contractual clauses and** ~~the~~ **other** ~~geographical location or segregation of our~~ relevant **documentation for existing data transfers within required time frames** ~~systems and operations, and could adversely affect our financial results~~ . Further, from January 1, 2021, we have had to comply with both the GDPR and also the UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in United Kingdom national law. The UK GDPR mirrors the fines under the GDPR, i. e., fines up to the greater of £ 17. 5 million or 4 % of global turnover **. On October 12, 2023, the UK Extension to the DPF came into effect (as approved by the UK Government), as a data transfer mechanism to from the UK to U. S. entities self- certified under the DPF** . As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business. Our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, CMOs, suppliers and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements. We are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, CMOs, suppliers and vendors may engage in misconduct or other improper activities. Misconduct by these parties could include failures to comply with FDA and other ex- U. S. authorities regulations, provide accurate information to the FDA or ex- U. S. regulatory authorities, comply with federal, state and ex- U. S. health care fraud and abuse laws and regulations, accurately report financial information or data or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, 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. Misconduct by these parties 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 misconduct by these parties, 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 comply with these 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 significant impact on our business, including the imposition of significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations. 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 have a material adverse effect on 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 our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. 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 our storage or disposal of hazardous and flammable materials, including chemicals and biological 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 research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions. Our research and development activities could be affected or delayed as a result of possible restrictions on animal testing. Certain laws and regulations require us to test our product candidates on animals before initiating clinical trials involving humans. Animal testing activities have been the subject of controversy and adverse publicity. Animal rights groups and other organizations and individuals have attempted to stop animal testing activities by pressing for legislation and regulation in these areas and by disrupting these activities through protests and other means. To the extent the activities of these groups are successful, our research and development activities may be interrupted, delayed or become more expensive. Our business activities may be subject to the U. S. Foreign Corrupt Practices Act, or the FCPA, and similar anti- bribery and anti- corruption laws of other countries in which we operate, as well as U. S. and certain ex- U. S. export controls, trade sanctions, and import laws and regulations. Compliance with these legal requirements could limit our ability to compete in ex- U. S. markets and subject us to liability if we violate them. If we further expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. Our business activities may be subject to the FCPA and similar anti-bribery or anti- corruption laws, regulations or rules of other countries in which we operate. The FCPA generally prohibits companies and their employees and third party intermediaries from offering, promising, giving or authorizing the provision of anything of value, either directly or indirectly, to a non- U. S. government official in order to influence official action or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non- U. S. governments. Additionally, in many other countries, hospitals owned and operated by the government, and doctors and other hospital employees would be considered ex- U. S. officials under the FCPA. Recently the SEC and the U. S. Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents or contractors, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers or our employees, disgorgement, and other sanctions and remedial measures, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries and could materially damage our reputation, our brand, our international activities, our ability to attract and retain employees and our business, prospects, operating results and financial condition. In addition, our products and activities may be subject to U. S. and ex- U. S. export controls, trade sanctions and import laws and regulations. Governmental regulation of the import or export of our products, or our failure to obtain any required import or export authorization for our products, when applicable, could harm our international sales and adversely affect our revenue. Compliance with applicable regulatory requirements regarding the export of our products may create delays in the introduction of our products in international markets or, in some cases, prevent the export of our products to some countries altogether. Furthermore, U. S. export control laws and economic sanctions prohibit the shipment of certain products and services to countries, governments, and persons targeted by U. S. sanctions. If we fail to comply with export and import regulations and such economic sanctions, penalties could be imposed, including fines and / or denial of certain export privileges. Moreover, any new export or import restrictions, new legislation or shifting approaches in the enforcement or scope of existing regulations, or in the countries, persons, or products targeted by such regulations, could result in decreased use of our products by, or in our decreased ability to export our products to existing or potential customers with international operations. Any decreased use of our products or limitation on our ability to export or sell access to our products would likely adversely affect our business. Risks Related to Employee Matters, Managing Our Growth and Other Risks Related to Our Business ~~The COVID-19 pandemic has adversely impacted, and we expect will continue to adversely impact, our business, including our preclinical studies and clinical trials. In 2020, a strain of the novel coronavirus disease, COVID- 19, was declared a pandemic and spread across the world, including throughout the United States, Europe and Asia. The pandemic and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. Our employees are working based on a hybrid work model, in which they work both from our offices and remotely. As a result of the COVID- 19 pandemic, we have experienced and we may continue to experience disruptions that could severely impact our business, preclinical studies and clinical trials, including: • delays or difficulties in enrolling patients in our clinical trials; • delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff; • delays in receiving authorizations from regulatory authorities to initiate our planned clinical trials; • diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and~~

~~hospital staff supporting the conduct of our clinical trials; • interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state or ex- U. S. governments, employers and others or interruption of clinical trial subject visits and study procedures (such as endoscopies that are deemed non-essential), which may impact the integrity of subject data and clinical study endpoints; • risk that participants enrolled in our clinical trials will contract COVID- 19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed AEs; • risk that we are unable to enroll participants in our clinical trials in adequate numbers; • interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines; • interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems; • interruptions in preclinical studies due to restricted or limited operations at our laboratory facility; • delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees; • changes in local regulations as part of a response to the COVID- 19 pandemic, which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue such clinical trials altogether; • limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people; • interruption or delays to our sourced discovery and clinical activities; and • refusal of the FDA to accept data from clinical trials in affected geographies outside the United States. The COVID- 19 pandemic continues to evolve. The extent to which the pandemic impacts our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the pandemic, the impact of variants, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the adoption, the prolonged efficacy of available vaccines and effectiveness of vaccination efforts and other actions taken in the United States and other countries to contain and treat the disease.~~ Our success is highly dependent on our ability to attract and retain highly skilled executive officers and employees. To succeed, we must recruit, retain, manage and motivate qualified clinical, scientific, technical and management personnel, and we face significant competition for experienced personnel. We are highly dependent on the principal members of our management and scientific and medical staff. If we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could adversely affect our ability to execute our business plan and harm our operating results. In particular, the loss of one or more of our executive officers could be detrimental to us if we cannot recruit suitable replacements in a timely manner. The competition for qualified personnel in the biotechnology field is intense and as a result, we may be unable to continue to attract and retain qualified personnel necessary for the future success of our business. We could in the future have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts. Many of the other biotechnology companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better prospects for career advancement. Some of these characteristics may be more appealing to high- quality candidates than what we have to offer. If we are unable to continue to attract and retain high- quality personnel, the rate and success at which we can discover, develop and commercialize our product candidates will be limited and the potential for successfully growing our business will be harmed. If we are unable to establish effective sales or marketing capabilities or enter into agreements with third parties to sell or market our product candidates, we may not be able to successfully sell or market our product candidates that obtain regulatory approval. We have never commercialized a product candidate. In order to commercialize any product candidates, if approved, for which we retain commercialization rights, we must build marketing, sales, distribution, **market access,** managerial and other non- technical capabilities or make arrangements with third parties to perform these services for each of the territories in which we may have approval to sell or market our product candidates. We may not be successful in accomplishing these required tasks. In addition, for product candidates for which we do not retain commercialization rights, we will rely on the assistance of collaborators to successfully commercialize any product candidates that are approved. Establishing ~~an~~ internal sales ~~or~~ **,** marketing **and market access** ~~team~~ **teams** with technical expertise and supporting distribution capabilities to commercialize our product candidates will be expensive and time- consuming, and will require significant attention of our executives to manage. Factors that may affect our ability to commercialize our product candidates on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, obtaining access to or persuading adequate numbers of physicians to prescribe our product candidates and other unforeseen costs associated with creating an independent sales and marketing organization. Any failure or delay in the development of our internal sales, marketing **, market access** and distribution capabilities could adversely impact the commercialization of any of our product candidates that we obtain approval to market, especially if we also do not have arrangements in place with third parties to provide such services on our behalf. Alternatively, if we choose to collaborate, either globally or on a territory- by- territory basis, with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems, we will be required to negotiate and enter into arrangements with such third parties relating to the proposed collaboration. 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 unable to successfully commercialize our approved 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. In order to successfully implement our plans and strategies, we will need to grow the size of our organization, and we may experience difficulties in managing this growth. In order to successfully implement our development and commercialization plans and strategies, and as we continue to operate as a public company, we expect to need additional

managerial, operational, sales, marketing, financial, legal, compliance and other personnel. Future growth would impose significant added responsibilities on members of management, including: • identifying, recruiting, integrating, maintaining and motivating additional employees; • managing our internal development efforts effectively, including the clinical, FDA and other comparable ex- U. S. regulatory agencies' review process for our product candidates, while complying with any contractual obligations to contractors and other third parties we may have; and • improving our operational, financial and management controls, reporting systems and procedures. Our future financial performance and our ability to successfully develop and, if approved, commercialize, our product candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day- to- day activities in order to devote a substantial amount of time to managing these growth activities ~~. Furthermore, certain of our employees, including members of our management team perform services on behalf of Kalyra Pharmaceuticals, Inc., and Zentera Therapeutics, pursuant to intercompany and collaborative agreements, respectively. As a result, such individuals do not allocate all of their time and resources to us and our other subsidiaries which, coupled with the need to manage growth activities, could further limit their ability to devote a sufficient amount of attention to day- to- day activities of our business~~ . We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including key aspects of clinical development and manufacturing. We cannot assure you that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by third party service providers is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain marketing approval of our product candidates or otherwise advance our business. We cannot assure you that we will be able to manage our existing third party service providers or find other competent outside contractors and consultants on economically reasonable terms, or at all. If we are not able to effectively expand our organization by hiring new employees and / or engaging additional third party service providers, we may not be able to successfully implement the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals. Our business and operations may suffer in the event of information technology system failures, cyberattacks or deficiencies in our cybersecurity. **We collect and maintain information in digital form that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business, including our mobile and web- based applications. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information, clinical trial data, and personal information, or collectively, Confidential Information, of customers and our employees and contractors.** Despite the implementation of security measures, our information systems and those of our current and any future **contract research organizations, or** CROs, CMOs and other contractors, consultants, collaborators and third- party service providers, are vulnerable to attack, damage and interruption from computer viruses and malware (e. g., ransomware), malicious code **, misconfigurations, " bugs " or other vulnerabilities** , natural disasters, terrorism, war, telecommunication and electrical failure, hacking, cyberattacks, phishing attacks and other social engineering schemes, employee theft or misuse, human error, fraud, denial or degradation of service attacks, sophisticated nation- state and nation- state- supported actors or unauthorized access or use by persons inside our organization, or persons with access to systems inside our organization. Attacks upon information technology systems are also increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. As a result of the ~~COVID- 19 pandemic~~ **continued hybrid working environment** , we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. **There can be no assurance that our and our current and any future CROs', CMOs' and other contractors', consultants', collaborators' and third- party service provider' s cybersecurity risk management program and processes, including policies, controls or procedures, will be fully implemented, complied with or effective in protecting our systems, networks and Confidential Information.** We and certain of our service providers are from time to time subject to cyberattacks and security incidents. If such an event were to occur and cause interruptions in our operations or result in the unauthorized acquisition of or access to our **Confidential** ~~trade secrets, personal information~~ **Information** ~~or other proprietary or sensitive information~~ , it could result in a material disruption of our drug discovery and development programs. Some federal, state and ex- U. S. government requirements include obligations of companies to notify individuals of security breaches involving particular personally identifiable information, which could result from breaches experienced by us or by our vendors, contractors, or organizations with which we have formed strategic relationships. Notifications and follow- up actions related to a security breach could impact our reputation, cause us to incur significant costs, including legal expenses and remediation costs. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the lost data. We also rely on third parties to manufacture our product candidates, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data, or inappropriate disclosure of ~~confidential~~ **Confidential** ~~or proprietary information~~ **Information** , we could be exposed to litigation and governmental investigations, the further

development and commercialization of our product candidates could be delayed, and we could be subject to significant fines or penalties for any noncompliance with certain state, federal and / or international privacy and security laws. Our insurance policies may not be adequate to compensate us for the potential losses arising from any such disruption, failure or security breach. In addition, such insurance may not be available to us in the future on economically reasonable terms, or at all. Further, our insurance may not cover all claims made against us and could have high deductibles in any event, and defending a suit, regardless of its merit, could be costly and divert management attention. EU pricing, drug marketing and reimbursement regulations may materially affect our ability to market and receive coverage for our products in the European member states. We intend to seek approval to market our product candidates in both the United States and in selected ex- U. S. jurisdictions. If we obtain approval in one or more ex- U. S. jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. In some ex- U. S. countries, particularly those in the EU, the pricing of drugs is subject to governmental control and other market regulations which could put pressure on the pricing and usage of our product candidates. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a product candidate. In addition, market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third- party payors for our product candidates and may be affected by existing and future healthcare reform measures. Much like the federal Anti- Kickback Statute prohibition in the United States, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to physicians is governed by the national laws of EU member states, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain EU member states must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and / or approval by the physician' s employer, his or her competent professional organization and / or the regulatory authorities of the individual EU member states. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low- priced and high- priced member states, can further reduce prices. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. In some countries, we may be required to conduct a clinical study or other studies that compare the cost- effectiveness of any of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for biopharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the United States and generally prices tend to be significantly lower. Publication of discounts by third- party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales and the potential profitability of any of our product candidates in those countries would be negatively affected. Unfavorable **U. S.,** global, political or economic conditions could adversely affect our business, financial condition or results of operations. Our results of operations could be adversely affected by general conditions in the **U. S. and** global economy and in the **U. S. and** global financial markets. For example, the recent global economic downturn has caused rising inflation and interest rates and has led to extreme volatility and disruptions in the capital and credit markets. A worsening or prolonged economic downturn or recession could result in a variety of risks to our business, including our ability to raise additional capital when needed on acceptable terms, if at all. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, and cause the prices of our supplies to increase or cause our customers to delay making payments for our services. In addition, ~~the~~ current military ~~conflict~~ **conflicts** ~~between Russia and Ukraine~~ could disrupt or otherwise adversely impact our operations and those of third parties upon which we rely. Related sanctions, export controls or other actions have and may in the future be initiated by nations including the U. S., the EU or Russia (e. g., potential cyberattacks, disruption of energy flows, etc.), which could adversely affect our business and / or our supply chain, our CROs, CMOs and other third parties with which we conduct business. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business. **Business interruptions could adversely affect our operations.** Our operations are vulnerable to interruption by fire, severe weather conditions, power loss, telecommunications failure, terrorist activity **, public health crisis and pandemic diseases** and other **natural and man- made disasters or** events beyond our control ~~, which could harm our business~~. Our facilities are located in regions that experience severe weather from time to time. We have not undertaken a systematic analysis of the potential consequences to our business and financial results from a major tornado, flood, fire, earthquake, power loss, terrorist activity **, public health crisis, pandemic diseases** or other disasters and do not have a recovery plan for such disasters. In addition, we do not carry sufficient insurance to compensate us for actual losses from interruption of our business that may occur, and any losses or damages incurred by us could harm our business. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited. As of December 31, ~~2022~~ **2023**, we had ~~available~~ **U. S.** federal and state net operating loss **, or NOL,** carryforwards ~~, or NOLs,~~ of approximately $ ~~390~~ **396**. ~~3~~ **1** million and $ ~~192~~ **193**. ~~4~~ **0** million, respectively. $ ~~369~~ **375**. ~~4~~ **2** million of our **U. S.** federal

NOLs were generated in taxable years beginning after December 31, 2017 and **some** can be carried forward indefinitely, but may only be used to offset up to 80 % of our taxable income in future periods. This limitation may require us to pay U. S. federal income taxes in future years despite generating **U. S.** federal NOLs in prior years. Our **U. S.** federal NOLs generated in tax years beginning prior to January 1, 2018 are not subject to this limitation, but are only permitted to be carried forward for 20 taxable years under applicable U. S. federal tax law, and will start to expire in 2033 if not utilized. Our state NOLs begin to expire in 2033. In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an " ownership change " (generally defined as a cumulative change in its ownership by one or more " 5- percent shareholders " that exceeds 50 percentage points over a rolling three- year period), the corporation' s ability to use its pre-ownership change federal NOLs and certain other pre- change tax attributes **, including tax credits,** to offset its post- change taxable income and income tax liabilities may be limited. Similar rules may apply under state tax laws. We may have experienced such ownership changes in the past and we may experience ownership changes in the future as a result of shifts in our stock ownership, some of which are outside our control. We have ~~not conducted any studies to determine whether any such~~ **completed a Code Section 382 analysis through June 30, 2023 regarding the limitation of NOL carryforwards and other tax attributes. Under the Section 382 rules, we experienced** ownership changes ~~have occurred~~ **in 2015, 2019 and 2022. Additionally, several of** ~~or~~ **our subsidiaries experienced an ownership change in 2020 based on** the **Section 382 rules for the time period prior to when we were a consolidated group for tax purposes. Our attributes are subject to** annual limitations, ~~if any,~~ **and some could expire unused prior to expiration. There is a risk** that **additional** ~~could result from such~~ ownership changes **may** ~~. Our ability to utilize our~~ **occur in the future. If a future change in ownership occurs, our** ~~NOLs~~ **NOL carryforwards** and ~~certain~~ other tax attributes could be limited ~~by an ownership change as described above and~~ **or restricted. Additionally, our NOLs prior to the tax consolidation are also subject to the separate return loss year, or SRLY, rules. The SRLY rules may limit one member from offsetting taxable income with losses generated from another member prior to joining the consolidated group.** ~~consequently~~ **Consequently , even if we attain profitability in the future** , we may not be able to utilize a material portion of our NOLs and certain other tax attributes, which could have a material adverse effect on our cash flows and results of operations. A variety of risks associated with marketing our product candidates internationally could materially adversely affect our business. We plan to seek regulatory approval of our product candidates outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating in ex- U. S. countries if we obtain the necessary approvals, including: • differing regulatory requirements and reimbursement regimes in ex- U. S. countries; • unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements; • economic weakness, including inflation, or political instability in particular ex- U. S. economies and markets; • compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; • ex- U. S. taxes, including withholding of payroll taxes; • ex- U. S. currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; • difficulties staffing and managing ex- U. S. operations; • workforce uncertainty in countries where labor unrest is more common than in the United States; • potential liability under the FCPA or comparable ex- U. S. regulations; • challenges enforcing our contractual and intellectual property rights, especially in those ex- U. S. countries that do not respect and protect intellectual property rights to the same extent as the United States; • production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and • business interruptions resulting from ~~geo- political~~ **geopolitical** actions, including war and terrorism. These and other risks associated with our international operations may materially adversely affect our ability to attain or maintain profitable operations. If we engage in future acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks. From time to time, we may evaluate various acquisition opportunities and strategic partnerships, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including: • increased operating expenses and cash requirements; • the assumption of additional indebtedness or contingent liabilities; • the issuance of our equity securities; • assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel; • the diversion of our management' s attention from our existing programs and initiatives in pursuing such a strategic merger or acquisition; • retention of key employees, the loss of key personnel and uncertainties in our ability to maintain key business relationships; • risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and marketing approvals; and • our inability to generate revenue from acquired technology and / or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs. In addition, if we undertake acquisitions or pursue partnerships in the future, we may issue dilutive securities, assume or incur debt obligations, incur large one- time expenses and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities, and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business. The requirements of being a public company may strain our resources, result in more litigation and divert management' s attention. As a public company, we are and will continue to be subject to the reporting requirements of the Exchange Act, the Sarbanes- Oxley Act, the Dodd- Frank Wall Street Reform and Consumer Protection Act, ~~or the Dodd- Frank Act,~~ the listing requirements of Nasdaq and other applicable securities rules and regulations. Complying with these rules and regulations has increased and will increase our legal and financial compliance costs, make some activities more difficult, time consuming or costly and increase demand on our systems and resources. The Exchange Act requires, among other things, that we file annual, quarterly and current reports with respect to our business and operating results. The Sarbanes- Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. We are required to disclose changes made in our internal control over financial reporting on a quarterly basis. In order

to maintain and, if required, improve our disclosure controls and procedures and internal control over financial reporting to meet this standard, significant resources and management oversight may be required. As a result, management' s attention may be diverted from other business concerns, which could adversely affect our business and operating results. We may also need to hire additional employees or engage outside consultants to comply with these requirements, which will increase our costs and expenses. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure **, including new disclosure requirements surrounding cybersecurity risk and governance,** are creating uncertainty for public companies, increasing legal and financial compliance costs and making some activities more time consuming. These laws, regulations and standards are subject to varying interpretations, in many cases due to their lack of specificity and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We have invested and intend to continue to invest in resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management' s time and attention from revenue- generating activities to compliance activities. If our efforts to comply with new laws, regulations and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to their application and practice, regulatory authorities may initiate legal proceedings against us and our business may be adversely affected. These new rules and regulations may make it more expensive for us to obtain director and officer liability insurance and, in the future, we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These factors could also make it more difficult for us to attract and retain qualified members of our Board of Directors, particularly to serve on our Audit Committee and Compensation Committee, and qualified executive officers. By disclosing information in filings required of us as a public company, our business and financial condition will continue to become more visible, which we believe may result in threatened or actual litigation, including by competitors and other third parties. If those claims are successful, our business could be seriously harmed. Even if the claims do not result in litigation or are resolved in our favor, the time and resources needed to resolve them could divert our management' s resources and seriously harm our business. A portion of our manufacturing of our lead product candidates takes place in ex- U. S. countries, including China, through third- party manufacturers. A significant disruption in the operation of those manufacturers, a trade war or political unrest in such ex- U. S. countries, including China, could materially adversely affect our business, financial condition and results of operations. We currently contract manufacturing operations to third parties, and clinical quantities of our lead product candidates are manufactured by certain of these third parties outside the United States, including in China, and we expect to continue to use such third- party manufacturers for such product candidates. Any disruption in production or inability of our manufacturers in such ex- U. S. countries, including in China, to produce adequate quantities to meet our needs, whether as a result of a natural disaster or other causes, could impair our ability to operate our business on a day- to- day basis and to continue our development of our product candidates. Furthermore, since these manufacturers are located outside the United States, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the policies of the United States or ex- U. S. governments, political unrest or unstable economic conditions in such ex- U. S. countries, including in China. For example, a trade war could lead to tariffs on the chemical intermediates we use that are manufactured in China. Any of these matters could materially and adversely affect our business and results of operations. ~~Any recall of the manufacturing lots or similar action regarding our product candidates used in clinical trials could delay the trials or detract from the integrity of the trial data and its potential use in future regulatory filings.~~ In addition, manufacturing interruptions or failure to comply with regulatory requirements by any of these manufacturers could significantly delay clinical development of potential products and reduce third- party or clinical researcher interest and support of proposed trials. These interruptions or failures could also impede commercialization of our product candidates and impair our competitive position. Further, we may be exposed to fluctuations in the value of the local currency in the ex- U. S. countries. Future appreciation of the local currency could increase our costs. In addition, our labor costs could continue to rise as wage rates increase due to increased demand for skilled laborers and the availability of skilled labor declines in the ex- U. S. countries, including in China. Risks Related to Our Intellectual Property Our success depends on our ability to protect our intellectual property and our proprietary platform. Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies and their uses, our and our licensors' **or licensees'** ability to operate without infringing the proprietary rights of others, and our and our licensors' **or licensees'** ability to successfully defend our patents, including those that we have in **- licensed or out** - licensed, against third- party challenges. If we or our licensors **or licensees** are unable to protect our intellectual property rights or if our intellectual property rights are inadequate for our technology or our product candidates, our competitive position could be harmed. We and our licensors **or licensees** generally seek to protect our proprietary position by filing patent applications in the United States and outside of the United States related to our product candidates, proprietary technologies and their uses that are important to our business. Our patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology. There can be no assurance that our patent applications will result in patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents, if issued, will be infringed or will not be designed around ~~, invalidated or rendered unenforceable~~ by third parties. Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our and our licensors' **or licensees'** proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our or our licensors' **or licensees'** rights or permit us or our licensors **or licensees** to gain or keep any competitive advantage. These uncertainties and / or limitations in our and our licensors' **or licensees'** ability to properly protect the intellectual property rights relating to our product candidates could have a material adverse effect on our financial condition

and results of operations. Although we license issued patents in the United States and ex- U. S. countries, we cannot be certain that the claims in our other U. S. pending patent applications, corresponding international patent applications and patent applications in certain ex- U. S. countries will be considered patentable by the ~~United States Patent and Trademark Office, or~~ USPTO, courts in the United States or by the patent offices and courts in ex- U. S. countries, nor can we be certain that the claims in our issued patents will not be found invalid or unenforceable if challenged. The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or our licensors **or licensees** or any of our potential future collaborators will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include the following: • the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant ~~jurisdiction~~ **jurisdictions** ; • patent applications may not result in any patents being issued; • patents may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage; • our competitors, many of whom have substantially greater resources than we or our licensors **or licensees** do and many of whom have made significant investments in competing technologies, may seek, may have filed patent applications, or may have already obtained patents that will limit, interfere with or block our ability to make, use and sell our product candidates; • there may be significant pressure on the U. S. **and ex- U. S.** ~~government~~ **governments** and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and • countries other than the United States may have patent laws less favorable to patentees than those upheld by U. S. courts, allowing ex- U. S. competitors a better opportunity to create, develop and market competing products. The patent prosecution process is also expensive and time- consuming, and we or our licensors **or licensees** may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. It is also possible that we or our licensors **or licensees** may not identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we ~~do~~ **may** not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, directed to technology that we **out- license or in-** license, including those **which we out- license to our licensees and those which we in- license** from our licensors and from third parties. We also may require the cooperation of our licensors **or licensees** in order to enforce the licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. We cannot be certain that patent prosecution and maintenance activities by our licensors **or licensees** have been or will be conducted in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such applications. If they fail to do so, this could cause us to lose rights in any applicable intellectual property that we in- license **or out- license** , and as a result our **and our licensees'** ability to develop and commercialize products or product candidates may be adversely affected and we **and our licensees** may be unable to prevent competitors from making, using and selling competing products. In addition, although we enter into non- disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, outside scientific collaborators, CROs, CMOs, consultants, advisors, licensors, **licensees,** and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. If we fail to comply with our obligations in the agreements under which we license intellectual property rights from our licensors and third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business. We are a party to ~~a number of~~ license agreements under which we are granted rights to intellectual property that are important to our business and we may enter into additional license agreements in the future. For example, our wholly owned subsidiary, ZMI, is party to a license agreement with Recurium IP under which we have an exclusive license to certain intellectual property rights, including certain intellectual property covering azenosertib ~~,~~ **and** ZN- d5 ~~, and our BCL- xL product candidate~~ . This and our other existing license agreements impose on us, and we expect that any future license agreements where we in- license intellectual property will impose on us, various development, regulatory and / or commercial diligence obligations, payment of milestones and / or royalties and other obligations. If we fail to comply with our obligations under these agreements, or we are subject to bankruptcy- related proceedings, the licensors may have the right to terminate the licenses, in which event we would not be able to market products covered by the licenses. We may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we cannot provide any assurances that third- party patents do not exist that might be enforced against our product candidates in the absence of such a license. We may fail to obtain any of these licenses on commercially reasonable terms, if at all. Even if we are able to obtain a license, it may be non- exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and / or other forms of compensation. Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including: • the scope of rights granted under the license agreement and other interpretation- related issues; • whether and the extent to which our technology and processes infringe intellectual property of the licensor that is not subject to the licensing agreement; • our right to sublicense patents and other rights to third parties; • our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations; • our right

to transfer or assign the license; and • the ownership of inventions and know- how resulting from the joint creation or use of intellectual property by our licensors and ~~its~~ **their** affiliates and sublicensees and by us and our partners and sublicensees. If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may not be able to successfully develop and commercialize the affected product candidates, which would have a material adverse effect on our business. In addition, certain of our agreements may limit or delay our ability to consummate certain transactions, may impact the value of those transactions, or may limit our ability to pursue certain activities. For example, if we choose to sublicense or assign to any third parties certain patent rights exclusively in- licensed under the Recurium Agreement, we may be required to pay to Recurium a specified percentage of certain sublicensing income to be received in connection with such transaction. If the scope of any patent protection our licensors **or licensees** obtain is not sufficiently broad, or if our licensors **or licensees** lose any of the patent protection we license, our ability to prevent our competitors from commercializing similar or identical product candidates would be adversely affected. The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the existence, 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 that protect our product candidates or that effectively prevent others from commercializing competitive product candidates. Moreover, the scope of claims in a patent application can be significantly reduced before any claims in a patent issue, and claim scope can be reinterpreted after issuance. Even if patent applications we license currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we license may be challenged or circumvented by third parties or may be narrowed or invalidated as a result of challenges by third parties. Consequently, we do not know whether our product candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non- infringing manner, which could materially adversely affect our business, financial condition, results of operations and prospects. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our in- licensed patents may not cover our product candidates or may be challenged in the courts or patent offices in the United States and abroad. We may be subject to a third party pre- issuance submission of prior art to the USPTO, or become involved in opposition, derivation, revocation, reexamination, post- grant review, or PGR, and inter partes review, or IPR, or other similar proceedings in the USPTO or ex- U. S. patent offices challenging our patent rights. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity of our patents, for example, we cannot be certain that there is no invalidating prior art, of which we or our licensors **or licensees** and the patent examiner were unaware during prosecution. There is no assurance that all potentially relevant prior art relating to our patents and patent applications or those of our licensors **or licensees** has been found. There is also no assurance that there is not prior art of which we or licensors **or licensees** were or are aware of, but which we do not believe affects the validity or enforceability of a claim in our patents and patent applications or those of our licensors **or licensees** , which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our patent rights, allow third parties to commercialize our product candidates and compete directly with us, without payment to us. Such loss of in- licensed patent rights, loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable 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 product candidates. Such proceedings also may result in substantial ~~cost~~ **costs** and require significant time from our scientists and management, even if the eventual outcome is favorable to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. The patent protection and patent prosecution for some of our product candidates may be dependent on our licensors **or licensees** and third parties. We or our licensors **or licensees** may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to strengthen our patent position. It is possible that defects as to form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, **written descriptions,** claim scope, or requests for patent term adjustments **, patent term extensions or any foreign equivalents thereof** . If we or our licensors **or licensees** , whether current or future, fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our licensors **or licensees** are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our ~~in-~~ licensed patents or patent applications, such patents may be invalid and / or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business. As a licensee **or licensor** , we **may** rely on third parties to file and prosecute patent applications and maintain patents and otherwise protect the licensed intellectual property under some of our license agreements. We **may** ~~have not had and do~~ not have primary control over these activities for certain of our patents or patent applications and other intellectual property rights. We cannot be certain that such activities by third parties have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents or other intellectual property rights. Pursuant to the terms of the license agreements with some of our licensors **or licensees** , the licensors **or licensees** may have the right to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents and even if we are permitted to pursue such enforcement or defense, we will require the cooperation of our licensors **or licensees** . We cannot be certain that our licensors **or licensees** will

allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. Even if we are not a party to these legal actions, an adverse outcome could harm our business because it might prevent us from continuing to license intellectual property that we may need to operate our business. If any of our licensors or **licensees or** any of our future licensors **or licensees** or future collaborators fails to appropriately prosecute and maintain patent protection for patents covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications we have acquired or licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensors **or licensees** and their counsel that took place prior to us assuming control over patent prosecution. Our technology acquired or licensed from various third parties, including our licensors, may be subject to retained rights. Our licensors often retain certain rights under their agreements with us, including the right to use the underlying technology for use in fields other than the fields licensed to us or for use in noncommercial academic and research use, to publish general scientific findings from research related to the technology, and to make customary scientific and scholarly disclosures of information relating to the technology. It is difficult to monitor whether our licensors limit their use of the technology to these uses, and we could incur substantial expenses to enforce our rights to our licensed technology in the event of misuse. If we are limited in our ability to utilize acquired or licensed technologies, or if we lose our rights to critical licensed technology, we may be unable to successfully develop, out- license, market and sell our products, which could prevent or delay new product introductions. Our business strategy depends on the successful development of licensed and acquired technologies into commercial products. Therefore, any limitations on our ability to utilize these technologies may impair our ability to develop, out- license or market and sell our product candidate. Some of our intellectual property may be subject to federal regulations such as " march- in " rights, certain reporting requirements and a preference for U. S.- based companies if it is determined that our intellectual property has been discovered through government- funded programs. Compliance with such regulations may limit our exclusive rights, and limit our ability to contract with non- U. S. manufacturers. Some of the intellectual property rights we have acquired or licensed or may acquire or license in the future may have been generated through the use of U. S. government funding and may therefore be subject to certain federal regulations. These U. S. government rights include a non- exclusive, non- transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U. S. government has the right, under certain limited circumstances, to require us to grant exclusive, partially exclusive, or non- exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as " march- in rights "). The U. S. government also has the right to take title to these inventions if the grant recipient fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the U. S. government requires that any products embodying any of these inventions or produced through the use of any of these inventions be manufactured substantially in the United States. This preference for U. S. industry may be waived by the federal agency that provided the funding if the owner or assignee of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U. S. industry may limit our ability to contract with non- U. S. product manufacturers for products relating to such intellectual property. To the extent any of our future intellectual property is also generated through the use of U. S. government funding, the provisions of the Bayh- Dole Act may similarly apply. Intellectual property rights do not necessarily address all potential threats to our competitive advantage. The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. For example: • others may be able to develop products that are similar to our product candidates but that are not covered by the claims of the patents that we own or license; • we or our licensors might not have been the first to make the inventions covered by the issued patents or patent application that we own or license; • we or our licensors **or licensees** might not have been the first to file patent applications covering certain of our inventions; • others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights; • it is possible that our licensors' **or licensees'** pending patent applications will not lead to issued patents; • issued patents that we own or license may be held invalid or unenforceable, as a result of legal challenges by our competitors; • our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; • we may not develop additional proprietary technologies that are patentable; and • the patents of others may have an adverse effect on our business. • Should any of these events occur, it could significantly harm our business, results of operations and prospects. Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts. Our commercial success depends in part on avoiding infringement of the patents and proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Other entities may have or obtain patents or proprietary rights that could limit **, interfere or block** our ability to make, use, sell, offer for sale or import our product candidates and products that may be approved in the future, or impair our competitive position. There is a substantial amount of litigation and administrative proceedings, both within and outside the United States, involving patent and other intellectual property rights in

the biopharmaceutical industry, including patent invalidity and infringement lawsuits, oppositions, reexaminations, IPR proceedings and PGR proceedings before the USPTO, ex- U. S. patent offices and / or in a court of law. Numerous third- party U. S. and ex- U. S. issued patents and pending patent applications exist in the fields in which we are developing product candidates. There may be third- party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. As the biopharmaceutical industry expands and more patents issue, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained as confidential for a certain period of time, until the relevant application is published we may be unaware of third- party patents that may be infringed by commercialization of any of our product candidates, and we cannot be certain that we were the first to file a patent application related to a product candidate or technology. Moreover, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, identification of third- party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes these patents. Any claims of patent infringement asserted by third parties would be time consuming and could: • result in costly litigation that may cause negative publicity; • divert the time and attention of our technical personnel and management; • cause development delays; • prevent us from commercializing any of our product candidates until the asserted patent expires or is held finally invalid or unenforceable or not infringed in a court of law; • require us to develop non- infringing technology, which may not be possible on a cost- effective basis; • subject us to significant liability to third parties; or • require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all, or which might be non- exclusive, which could result in our competitors gaining access to the same technology. Although no third party has asserted a claim of patent infringement against us as of the date of this periodic report, others may hold proprietary rights that could prevent our product candidates from being marketed. Any patent- related legal action against us claiming damages and seeking to enjoin activities relating to our product candidates or processes could subject us to potential liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or develop our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and employee resources from our business. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Moreover, even if we or our future strategic partners were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. In addition, we cannot be certain that we could redesign our product candidates or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing our product candidates, which could harm our business, financial condition and operating results. Parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time- consuming and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court. Competitors may infringe our intellectual property rights or those of our licensors. To prevent infringement or unauthorized use, we and / or our licensors **or licensees** may be required to file infringement claims, which can be expensive and time- consuming. Further, our licensors **or licensees** may need to file infringement claims, but they may elect not file such claims. In addition, in a patent infringement proceeding, a court may decide that a patent we own or license is not valid, is unenforceable and / or is not infringed. If we or any of our licensors or **licensees or** potential future collaborators were to initiate legal proceedings against a third party to enforce a patent directed at one of our product candidates, the defendant could assert that our patent is invalid **, not infringed** and / or unenforceable in whole or in part. In patent litigation, defendant allegations of invalidity and / or unenforceability of asserted patents are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including **patent- ineligible subject matter,** lack of **utility, lack of** novelty **, obviousness** or **lack of** written description, ~~obviousness~~ or non- enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent intentionally withheld material information from the USPTO or **an ex- U. S. patent office or** made a misleading statement during prosecution. If a defendant were to prevail on a legal assertion of invalidity and / or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. In addition, if the breadth or strength of protection provided by our patents and patent applications or those of our licensors is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Such a loss of patent protection would have a material adverse impact on our business. Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation

of patent litigation or other proceedings could compromise our ability to compete in the marketplace. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other legal proceedings relating to our intellectual property rights, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings. Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our common shares to decline. During the course of any intellectual property litigation, there could be public announcements of the initiation of the litigation as well as results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our existing products, programs or intellectual property could be diminished. Accordingly, the market price of shares of our common stock may decline. Such announcements could also harm our reputation or the market for our future products, which could have a material adverse effect on our business. Derivation or interference proceedings may be necessary to determine priority of inventions, and an unfavorable outcome may require us to cease using the related technology or to attempt to license rights from the prevailing party. Derivation or interference proceedings provoked by third parties or brought by us or our licensors **or licensees** , or declared by the USPTO or similar proceedings in ex- U. S. patent offices may be necessary to determine the priority of inventions with respect to our or our licensors' **or licensees'** patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our or our licensors' **or licensees'** defense of such proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with such proceedings could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our product candidates to market. Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. In September 2011, the Leahy- Smith America Invents Act, or Leahy- Smith Act, was signed into law. The Leahy- Smith Act includes a number of significant changes to U. S. patent law. These include provisions that affect the way patent applications are prosecuted and also affect patent litigation. In particular, under the Leahy- Smith Act, the United States transitioned in March 2013 to a " first inventor to file " system in which, assuming that other requirements of patentability are met, the first inventor to file a patent application will be entitled to the patent regardless of whether a third party was first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013 but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Furthermore, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our technology and the prior art allow our technology to be patentable over the prior art. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we were the first to either (1) file any patent application related to our product candidates or (2) invent any of the inventions claimed in our patents or patent applications. The Leahy- Smith Act also includes a number of significant changes that affect the way patent applications are prosecuted and also affect patent litigation. These include allowing third- party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post- grant proceedings, including PGR, IPR, and derivation proceedings. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Thus, the Leahy- Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Changes in U. S. patent law, or laws in other countries, could diminish the value of patents in general, thereby impairing our ability to protect our product candidates. As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry ~~involve~~ **involves** a high degree of technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time- consuming and inherently uncertain. Changes in either the patent laws or in the interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property and may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. We cannot predict the breadth of claims that may be allowed or enforced in our patents or in third- party patents. In addition, Congress or other ex- U. S. legislative bodies may pass patent reform legislation that is unfavorable to us. For example, the U. S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our or our licensors' **or licensees** ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U. S. Congress, the U. S. federal courts, the USPTO, or similar authorities in ex- U. S. jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our or our licensors' **or licensees'** ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future. We or our licensors **or licensees** may be subject to claims challenging the inventorship or ownership of ~~our or~~ our patents and other intellectual

property. We or our licensors **or licensees** may be subject to claims that former employees or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we or our licensors **or licensees** fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Such an outcome could have a material adverse effect on our business. Even if we or our licensors **or licensees** are successful in defending against such claims, litigation could result in substantial costs and distraction to management and other employees. Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time. Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U. S. non-provisional filing date. Various extensions may be available, but the term of a patent, and the protection it affords, is limited. Even if patents directed to our product candidates are obtained, once the patent term has expired, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of product candidates, patents directed to our product candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. If we or our licensors **or licensees** do not obtain patent term extension for our product candidates, our business may be materially harmed. Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of our U. S. patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch- Waxman Amendments. The Hatch- Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. A maximum of one patent may be extended per FDA- approved product as compensation for the patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it **for an FDA- approved indication** or a method for manufacturing it may be extended. Patent term extension **or equivalents thereof** may also be available in certain ex- U. S. countries upon regulatory approval of our product candidates. However, we or our licensors **or licensees** may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we or our licensors **or licensees** are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. We may not be able to protect our intellectual property rights throughout the world. Although we have issued patents and pending patent applications in the United States and certain other countries, filing, prosecuting and defending patents in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some ex- U. S. countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we or our licensors **or licensees** have patent protection but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our or our licensors' **or licensees'** patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in ex- U. S. jurisdictions. The legal systems of many ex- U. S. countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our or our licensors' **or licensees' or licensees'** patents or marketing of competing products in violation of our proprietary rights. Proceedings to enforce our or our licensors' **or licensees'** patent rights in ex- U. S. jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our or our licensors' **or licensees'** patents at risk of being invalidated or interpreted narrowly and our or our licensors' **or licensees'** patent applications at risk of not issuing and could provoke third parties to assert claims against us. We or our licensors **or licensees** may not prevail in any lawsuits that we or our licensors **or licensees** initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our or our licensors' **or licensees'** efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or our licensors **or licensees** are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected. Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by regulations and governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and / or applications will be due to the USPTO and various ex- U. S. patent offices at various points over the lifetime of our patents and / or applications. We have systems in place to remind us to pay these fees, and we rely on third parties to pay these fees when due. Additionally, the USPTO and various ex- U. S. patent offices 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 rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, it could have a material adverse effect 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, we rely on the protection of our trade secrets, including unpatented know- how, technology and other proprietary information to maintain our competitive position. Although we have taken steps to protect our trade secrets and unpatented know- how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants, licensors **, licensees** and advisors, we cannot provide any assurances that all such agreements have been duly executed, and 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 United States are less willing or unwilling to protect trade secrets. Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position would be harmed. If we or our licensors **or licensees** do not apply for patent protection prior to ~~such publication~~ **public disclosure** or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized. We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers. As is common in the biopharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other biopharmaceutical companies including our competitors or potential competitors. We may become subject to claims that we, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees. Risks Related to Our Dependence on Third Parties We rely, and expect to continue to rely, on third parties, including independent clinical investigators and CROs, to conduct certain aspects of our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties, comply with applicable regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed. We have relied upon and plan to continue to rely upon third parties, including independent clinical investigators and third- party CROs, to conduct certain aspects of our preclinical studies and clinical trials and to monitor and manage data for our ongoing preclinical and clinical programs. We rely on these parties for execution of our preclinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third- party contractors, including CROs, are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable ex- U. S. regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable ex- U. S. regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations and similar ex- U. S. requirements. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be adversely affected if any of these third parties violates federal, state or ex- U. S. fraud and abuse or false claims laws and regulations or healthcare privacy and security laws. Further, these investigators ~~and ,~~ CROs **and other third parties** are not our employees and we will not be able to control, other than by contract, the amount of resources, including time, which they devote to our product candidates and clinical trials. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If independent investigators or CROs fail to devote sufficient resources to the development of our product candidates, or if CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed or precluded entirely. Our CROs have the right to terminate their agreements with us in the event of an uncured material breach. In addition, some of our CROs have an ability to terminate their respective agreements with us if it

can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination, if we make a general assignment for the benefit of our creditors or if we are liquidated ~~. The COVID- 19 pandemic and government measures taken in response have also had a significant impact on our CROs, and we expect that they will face further disruption which may affect our ability to initiate and complete our preclinical studies and clinical trials~~ . If any of our relationships with these third- party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Additionally, CROs may lack the capacity to absorb higher workloads or take on additional capacity to support our needs. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects. We contract with third parties for the manufacture of our product candidates for preclinical studies and our ongoing clinical trials, and expect to continue to do so for additional clinical trials and ultimately for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts. We do not currently have the infrastructure or internal capability to manufacture supplies of our product candidates for use in development and commercialization. We rely, and expect to continue to rely, on third- party manufacturers for the production of our product candidates for preclinical studies and clinical trials under the guidance of members of our organization. We do not have long- term supply agreements, and we purchase our required supply on a purchase order basis. Furthermore, the raw materials for our product candidates are sourced, in some cases, from a single- source supplier. We currently mitigate potential supply risks for azenosertib and ZN- d5, if any, through inventory management. If we were to experience an unexpected loss of supply of any of our product candidates or any of our future product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing clinical trials. We expect to continue to rely on third- party manufacturers for the commercial supply of any of our product candidates for which we obtain marketing approval. We may be unable to maintain or establish required 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: • the failure of the third- party manufacturers to manufacture our product candidates according to our schedule, or at all, including if our third- party manufacturers give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them; • the reduction or termination of production or deliveries by suppliers, or the raising of prices or renegotiation of terms; • the termination or nonrenewal of arrangements or agreements by our third- party manufacturers at a time that is costly or inconvenient for us; • the breach by the third- party manufacturers of our agreements with them; • the failure of third- party manufacturers to comply with applicable regulatory requirements; • the failure of the third- party manufacturers to manufacture our product candidates according to our specifications; • the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified; • clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and • the misappropriation of our proprietary information, including our trade secrets and know- how. We do not have complete control over all aspects of the manufacturing process of, and are dependent on, our third- party contract manufacturing partners for compliance with cGMP regulations or similar ex- U. S. requirements for manufacturing both active drug substances and finished drug products. Third- party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. If our third- party contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and / or maintain marketing approval for **the use of** their manufacturing facilities **for the manufacture of our product candidates** . In addition, we do not have control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable ex- U. S. regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our product candidates, if approved. Our failure, or the failure of our third- party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates or drugs and harm our business and results of operations. Our current and anticipated future dependence upon others for the manufacture of our product candidates or drugs may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis. The manufacture of drugs is complex and our third- party manufacturers may encounter difficulties in production. If any of our third- party manufacturers encounter such difficulties, our ability to provide adequate supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or prevented. Manufacturing drugs, especially in large quantities, is complex and may require the use of innovative technologies. Each lot of an approved drug product must undergo thorough testing for identity, strength, quality, purity and potency. Manufacturing drugs requires facilities specifically designed for and validated for this purpose, and sophisticated quality assurance and quality control procedures are necessary. Slight deviations anywhere in the manufacturing process, including filling, labeling, packaging, storage and shipping and quality control and testing, may result in lot failures, ~~product recalls~~ **stock recovery** or spoilage **. Any stock recovery of the manufacturing lots or similar action regarding our product candidates**

used in clinical trials could delay the trials or detract from the integrity of the trial data and its potential use in future regulatory filings . When changes are made to the manufacturing process, we may be required to provide preclinical and clinical data showing the comparable identity, strength, quality, purity or potency of the products before and after such changes. If microbial, viral or other contaminations are discovered at the facilities of our manufacturer, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely harm our business. The use of biologically derived ingredients can also lead to allegations of harm, including infections or allergic reactions, or closure of product facilities due to possible contamination. If our manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization as a result of these challenges, or otherwise, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects. If we decide to establish collaborations in the future, but are not able to establish those collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans. Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. We may continue to seek to selectively form collaborations to expand our capabilities, potentially accelerate research and development activities and provide for commercialization activities by third parties. Any of these relationships may require us to incur non- recurring and other charges, increase our near and long- term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business. We would face significant competition in seeking appropriate collaborators and the negotiation process is time- consuming and complex. Whether we reach a definitive agreement for a 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. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or comparable ex- U. S. regulatory authorities, 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 drugs, the existence of uncertainty with respect to our ownership of intellectual property and industry and market conditions generally. The potential collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such collaboration could be more attractive than the one with us for our product candidate. Further, we may not be successful in our efforts to establish a collaboration or other alternative arrangements for future product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view them as having the requisite potential to demonstrate safety and efficacy. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. Even if we are successful in entering into a collaboration, the terms and conditions of that collaboration may restrict us from entering into future agreements on certain terms with potential collaborators. If and when we seek to enter into collaborations, we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue. Risks Related to Ownership of Our Common Stock The price of our stock may be volatile, and you could lose all or part of your investment. The trading price of our common stock is likely to be highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. The stock market in general, and pharmaceutical and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In addition to the factors discussed in this " Risk Factors " section these factors include: • the timing and results of preclinical studies and clinical trials of our product candidates or those of our competitors; • the success of competitive products or announcements by potential competitors of their product development efforts; • regulatory actions with respect to our products or our competitors' products; • actual or anticipated changes in our growth rate relative to our competitors; • regulatory or legal developments in the United States and other countries; • developments or disputes concerning patent applications, issued patents or other proprietary rights; • the recruitment or departure of key personnel; • announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures, collaborations or capital commitments; • actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts; • fluctuations in the valuation of companies perceived by investors to be comparable to us; • market conditions in the pharmaceutical and biotechnology sector; • changes in the structure of healthcare payment systems; • speculative trading in and short sales of our common stock, as well as trading phenomena such as the" short squeeze"; • share price and volume fluctuations attributable to inconsistent trading volume levels of our shares; • announcement or expectation of additional financing efforts; • sales of our common stock by us, our insiders or our other stockholders; • expiration of market stand- off or lock- up agreements; and • general economic, industry and market conditions. In addition, the trading prices for common stock of other biopharmaceutical companies have been highly volatile as a result of **U** ~~the COVID- 19 pandemic~~ . **S.** ~~The COVID- 19 pandemic continues to evolve~~ and **global economic conditions** ~~the duration of its impact remains uncertain~~ . The extent to which ~~the~~ **these** ~~pandemic~~ **events** may impact our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence. The realization of any of the above risks or any of a broad range of other risks, including those described in this " Risk Factors " section, could have a dramatic and adverse impact on the market price of our common stock. Our quarterly operating results may fluctuate

significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline. We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including: • variations in the level of expense related to the ongoing development of our product candidates or future development programs; • results of clinical trials, or the addition or termination of clinical trials or funding support by us or potential future partners; • our execution of any collaboration, licensing or similar arrangements, and the timing of payments we may make or receive under potential future arrangements or the termination or modification of any such potential future arrangements; • any intellectual property infringement, misappropriation or violation lawsuit or opposition, interference or cancellation proceeding in which we may become involved; • additions and departures of key personnel; • strategic decisions by us or our competitors, such as acquisitions, divestitures, spin- offs, joint ventures, strategic investments or changes in business strategy; • if any of our product candidates receives regulatory approval, the terms of such approval and market acceptance and demand for such product candidates; • regulatory developments affecting our product candidates or those of our competitors; and • changes in general market and economic conditions. If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance. Our principal stockholders and management own a significant percentage of our stock and are able to exert significant influence over matters subject to stockholder approval. As of December 31, ~~2022~~ **2023**, our executive officers and directors, combined with our stockholders who owned more than 5 % of our common stock, together with their respective affiliates, owned a significant percentage of our outstanding common stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as matters related to our management and affairs. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock. Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall. Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. Outstanding shares of our common stock may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act, or to the extent that such shares have already been registered under the Securities Act and are held by non- affiliates of ours. ~~Moreover, holders of a substantial number of shares of our common stock have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders.~~ We also register all shares of common stock that we may issue under our equity compensation plans or that are issuable upon exercise of outstanding options. These shares can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline. Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our product candidates on unfavorable terms to us. We may seek additional capital through a variety of means, including through public or private equity, debt financings or other sources, including up- front payments and milestone payments from strategic collaborations. For example, in August 2020, July 2021 ~~and~~ **,** May 2022 **and June 2023**, we completed underwritten public offerings of our common stock and in April 2022, we completed a direct offering of our common stock. To the extent that we raise additional capital through the sale of equity or convertible debt or equity securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. Such financing may result in dilution to stockholders, imposition of debt covenants, increased fixed payment obligations or other restrictions that may affect our business. If we raise additional funds through up- front payments or milestone payments pursuant to strategic collaborations with third parties, we may have to relinquish valuable rights to our product candidates, or grant licenses on terms that are not favorable to us. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. If securities or industry analysts do not publish research or reports, or if they publish adverse or misleading research or reports, regarding us, our business or our market, our stock price and trading volume could decline. The trading market for our common stock will be influenced by the research and reports that securities or industry analysts publish about us, our business or our market. If any of the analysts who cover us issue adverse or misleading research or reports regarding us, our business model, our intellectual property, our stock performance or our market, or if our operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more 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. Provisions in our certificate of incorporation and bylaws and Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the market price of our common stock. Our certificate of incorporation and bylaws contain provisions that could depress the market price of our common stock by acting to discourage, delay or prevent a change in control of our company or changes in our management that the stockholders of our company may deem advantageous. These provisions, among other things: • establish a classified Board of Directors so that not all members of our Board of Directors are elected at one time; • permit only the Board of Directors to establish the number of directors and fill vacancies on the Board of Directors; • provide that directors

may only be removed " for cause " and only with the approval of two- thirds of our stockholders; • authorize the issuance of " blank check " preferred stock that our Board of Directors could use to implement a stockholder rights plan (also known as a " poison pill "); • eliminate the ability of our stockholders to call special meetings of stockholders; • prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders; • prohibit cumulative voting; • authorize our Board of Directors to amend the bylaws; • establish advance notice requirements for nominations for election to our Board of Directors or for proposing matters that can be acted upon by stockholders at annual stockholder meetings; and • require a super- majority vote of stockholders to amend some provisions described above. In addition, Section 203 of the General Corporation Law of the State of Delaware, or the DGCL, prohibits a publicly- held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15 % of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. Any provision of our certificate of incorporation, bylaws or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock. Our certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees. Our certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for: • any derivative action or proceeding brought on our behalf; • any action asserting a claim of breach of fiduciary duty; • any action asserting a claim against us arising under the DGCL, our certificate of incorporation or our bylaws; and • any action asserting a claim against us that is governed by the internal- affairs doctrine. This exclusive- forum provision may limit a stockholder' s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage lawsuits against us and our directors, officers and other employees. Any person or entity purchasing or otherwise acquiring any interest in any of our securities shall be deemed to have notice of and consented to this provision. If a court were to find this exclusive- forum provision in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business. Nothing in our certificate of incorporation precludes stockholders that assert claims under the Securities Act or the Exchange Act from bringing such claims in state or federal court, subject to applicable law. We do not currently intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on appreciation of the value of our common stock. We have never declared or paid any cash dividends on our equity securities. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to any appreciation in the value of our common stock, which is not certain. If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock. Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock. We are required to disclose changes made in our internal controls and procedures on a quarterly basis and our management is required to assess the effectiveness of these controls annually. **Our** ~~Now that we are no longer an emerging growth company, our~~ independent registered public accounting firm is required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. An independent assessment of the effectiveness of our internal controls over financial reporting could detect problems that our management' s assessment might not. Undetected material weaknesses in our internal controls over financial reporting could lead to restatements of our financial statements and require us to incur the expense of remediation. We may be subject to securities litigation, which is expensive and could divert management attention. The market price of our common stock may be volatile and, in the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management' s attention from other business concerns, which could seriously harm our business.