Risk Factors Comparison 2025-02-25 to 2024-02-26 Form: 10-K

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The following risk factors and other information included in this Annual Report on Form 10- K should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. You should carefully consider the risks described below, as well as the other information in this Annual Report on Form 10- K, including our financial statements and the related notes and " Management' s Discussion and Analysis of Financial Condition and Results of Operations, " as well as our other filings with the Securities and Exchange Commission, before deciding whether to invest in our common stock. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected **. Moreover, some of the factors, events and contingencies discussed below may have occurred in the past, but the disclosures below are not representations as to whether or not the factors, events or contingencies have occurred in the past and instead reflect our beliefs and opinions as to the factors, events, or contingencies that could materially and adversely affect us in the future** . Risks Related to the Discovery and Development of Our Drug Candidates Our business is highly dependent on the success of our bezuclastinib program and our ability to discover and develop additional product candidates. We may not be successful in our efforts to develop bezuclastinib or expand our pipeline of drug candidates. Our business and future success depend on our ability to develop, obtain regulatory approval for and then successfully commercialize bezuclastinib and any other product candidates that we may discover and develop. We are pursuing clinical development of bezuclastinib to target SM and GIST through our APEX, SUMMIT and PEAK clinical trials. There is no guarantee that any or all of these trials will be successful. Even if our trials are successful, bezuclastinib will require regulatory review and approval, substantial investment, access to sufficient commercial manufacturing capacity and significant marketing efforts before we are able to generate any revenue from product sales, if ever. Through the development of the research team, we are also working to build a pipeline of other product candidates. Researching, developing, obtaining regulatory approval for and commercializing additional product candidates will require substantial additional funding and is prone to the risks of failure inherent in medical product development. Even if we are successful in continuing to build and expand our pipeline, we cannot provide you any assurance that we will be able to successfully advance any of these additional product candidates through the development process, or that any such product candidates will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives. If unacceptable side effects are identified during the development of our drug candidates, we may need to abandon or limit such development. If our drug candidates are associated with unacceptable side effects in preclinical or clinical trials or have characteristics that are unexpected, we may need to abandon their development, limit development to more narrow uses or subpopulations in which the unacceptable side effects or other characteristics are less prevalent, less severe, or more acceptable from a risk- benefit perspective or highlight these risks, side effects, or other characteristics in the approved product label. In pharmaceutical development, many drugs that initially show promise in early- stage testing may later be found to cause side effects that prevent further development of the drug. Currently marketed therapies for the treatment of AdvSM and cancer are generally limited to some extent by their toxicity. In addition, some of our drug candidates would be chronic therapies, for which safety concerns may be particularly important. Use of our drug candidates as monotherapies may also result in adverse events consistent in nature with other marketed therapies. In addition, when used in combination with other therapies, our drug candidates could exacerbate adverse events associated with the other therapy. If unexpected side effects are identified during development, we may be required to develop a Risk Evaluation and Mitigation Strategy (" REMS ") to mitigate those serious safety risks, which could impose significant distribution and / or use restrictions on our products. We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively. The development and commercialization of new pharmaceutical and biotechnology products is highly competitive. We face competition with respect to our current clinical- stage drug candidates and will face competition with respect to any drug candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we are developing our drug candidates. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization. Any product candidates that we successfully develop and commercialize will compete with currently approved therapies and new therapies that may become available in the future from segments of the pharmaceutical, biotechnology and other related markets that pursue precision medicines. Our commercial opportunity could also be reduced or eliminated if our competitors develop and commercialize additional products that are safer, more effective, have superior dosing regimens, have fewer or less severe side effects, are approved for broader indications or patient populations, are approved for specific sub- populations, are more convenient or are less expensive than bezuclastinib or any other products that we may develop. Our competitors also may obtain FDA or other marketing approval for their products more rapidly than any approval we may obtain for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third- party payors seeking to encourage the use of generic products. Many of the companies against which we are competing or against which we may compete in the future have

significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining marketing approvals, and marketing and selling approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. For further information, see " Business- Competition, " which discusses the pharmaceutical and biotechnology companies developing or marketing treatments for cancer and hematologic diseases that are competitive with bezuclastinib and the drug candidates we are developing. If difficulties arise enrolling patients in our clinical trials, clinical development activities could be delayed or otherwise adversely affected. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. The enrollment of patients depends on many factors, including: the patient eligibility criteria defined in the protocol; the size of the patient population required for analysis of the trial' s primary endpoints; and our ability to recruit clinical trial investigators with the appropriate competencies and experience. In addition, our clinical trials compete with approved products as well as other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition reduces the number and types of patients available to us because some patients who might have opted to enroll in our trials may instead opt to take an approved product or otherwise enroll in a trial being conducted by one of our competitors. Any delays in patient enrollment may result in increased costs or may affect the timing or outcome of our ongoing and planned clinical trials, our expected timelines for delivering top- line results across all three of our active studies, and any subsequent regulatory approvals or commercialization activities. The incidence and prevalence for target patient populations of our drug candidates have not been established with precision. If the market opportunities for our drug candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue potential and ability to achieve profitability will be adversely affected. The precise incidence and prevalence for GIST and SM are unknown. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with **bezuclastinib** ~~our drug candidates~~ , are based on estimates, which are inherently uncertain. The total addressable market opportunity for bezuclastinib, and any other drug candidates we may produce will ultimately depend upon, among other things, the diagnosis criteria included in the final label for our future approved drugs for sale for these indications, acceptance by the medical community and patient access, drug pricing, and reimbursement. The number of patients in our targeted commercial markets and elsewhere may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our drug, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business. Clinical trials are expensive, time- consuming, and difficult to design and implement. Human clinical trials are expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. We are unable to predict when or if any of our drug candidates will prove effective or safe in humans or will obtain marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of any drug candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, interim or preliminary results of a clinical trial do not necessarily predict final results, and results for one indication may not be predictive of the success in additional indications. In particular, the small number of patients in our early clinical trials may make the results of these trials less predictive of the outcome of later clinical trials. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy, insufficient durability of efficacy, or unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that commence clinical trials are never approved as products. We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to obtain marketing approval or commercialize our drug or drug candidates. Our product development costs will increase if we experience delays in preclinical studies or clinical trials or in obtaining marketing approvals. We do not know whether any of our planned preclinical studies or clinical trials will begin on a timely basis or at all, will need to be restructured, or will be completed on schedule, or at all. Significant preclinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our drug candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our drug candidates and may harm our business and results of operations. Since the number of patients that we have dosed to date in our clinical trials is small, the results from such clinical trials may be less reliable than results achieved in larger clinical trials. A study design that is considered appropriate for regulatory approval includes a sufficiently large sample size with appropriate statistical power, as well as proper control of bias, to allow a meaningful interpretation of the results. The preliminary results of trials with smaller sample sizes can be disproportionately influenced by the impact the treatment had on a few individuals, which limits the ability to generalize the results across a broader community, thus making the study results less reliable than studies with a larger number of patients. As a result, there may be less certainty that such product candidates would achieve a statistically significant effect in any future clinical trials. In our current and any future clinical trials, we may not achieve a statistically significant result or the same level of statistical significance, if any, that we may have seen in prior clinical trials or preclinical studies. Interim, " top- line " and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available, may be interpreted differently if additional data are disclosed, and are subject to audit and verification procedures that could result in material changes in the final data. From time to time, we publicly disclose preliminary or " top- line " data from our clinical trials, which is based on a preliminary analysis of then- available data in a summary or " top- line " format, and the results and related findings may change as more patient data become available, may be interpreted differently if additional data are disclosed at a later time and are subject to audit and verification

procedures that could result in material changes in the final data. If additional results from our clinical trials are not viewed favorably, our ability to obtain approval for and commercialize our drug candidates, our business, operating results, prospects, or financial condition may be harmed and our stock price may decrease. We may choose not to develop a potential product candidate, or we may suspend, deprioritize or terminate one or more discovery programs or preclinical or clinical product candidates or programs. At any time and for any reason, we may determine that one or more of our discovery programs or preclinical or clinical product candidates or programs does not have sufficient potential to warrant the allocation of resources toward such program or product candidate. Accordingly, we may choose not to develop a potential product candidate or elect to suspend, deprioritize or terminate one or more of our discovery programs or preclinical or clinical product candidates or programs. If we suspend, deprioritize or terminate a program or product candidate in which we have invested significant resources, we will have expended resources on a program or product candidate that will not provide a full return on our investment and may have missed the opportunity to have allocated those resources to potentially more productive uses, including existing or future programs or product candidates. We may form or seek collaborations or strategic alliances or enter into additional licensing arrangements in the future, but we may not realize any resulting benefits. We may form or seek strategic alliances, create joint ventures or collaborations, or enter into additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our product candidates and any future product candidates that we may develop. In particular, we may seek to enter into collaborations with our bezuclastinib program and other collaborations to progress the clinical development of the bezuclastinib program. 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 may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our 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 our product candidates as having the requisite potential to demonstrate safety and efficacy and obtain marketing approval. Further, collaborations involving our product candidates are subject to numerous technical, business, and legal risks. **Collaborative relationships are generally complex and can give rise to disputes regarding the relative rights, including the ownership of intellectual property and associated rights and obligations, especially when the applicable collaborative provisions have not been fully negotiated and documented.** Even if we are successful in entering into a collaboration with respect to the development and / or commercialization of one or more product candidates, there is no guarantee that the collaboration will be successful. We may not be able to file investigational new drug applications (" IND " s) or IND amendments or clinical trial authorization applications (" CTA " s) to commence additional clinical trials on the timelines we expect, and even if we are able to, the FDA or other regulatory authorities may not permit us to proceed. Our timing of filing INDs or CTAs on our product candidates and initiating additional clinical trials is dependent on further research. We cannot be sure that submission of an IND or CTA will result in the FDA or other regulatory authority allowing further clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate such clinical trials. ~~We have limited experience as a company conducting clinical trials. We have limited experience as a company in conducting clinical trials. In part because of this lack of experience, we cannot be certain that our ongoing clinical trials will be completed on time or if the planned clinical trials will begin or be completed on time, if at all.~~ Our updated bezuclastinib formulation is unproven and may not work as intended in clinical trials. In November 2021, we announced an updated formulation of bezuclastinib which is intended to reduce the number of daily tablets required for patients with GIST, thereby potentially improving the overall GIST patient experience. This formulation has now been incorporated into all three of our ongoing clinical trials. The formulation is unproven to date, and there is no guarantee that it will be successful or perform as desired. The commercial success of any future approved drugs, including bezuclastinib, will depend upon the degree of market acceptance by physicians, patients, third- party payors, and others in the medical community. If bezuclastinib and any future approved drugs do not achieve an adequate level of acceptance by physicians, patients, third- party payors, and others in the medical community, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of bezuclastinib and of any current or future drug candidates, if approved for commercial sale, will depend on a number of factors, including the availability, perceived advantages, and relative cost, safety, and efficacy of alternative and competing treatments; and the prevalence and severity of any side effects, adverse reactions, misuse, or any unfavorable publicity in these areas, in particular compared to alternative treatments. Even if a potential drug displays a favorable efficacy and safety profile in preclinical and clinical studies, market acceptance of the drug will not be known until after it is launched. 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 **(either ourselves or through a partner)** and, accordingly, we expect that we **or any future partner** will be subject to additional risks and regulatory requirements related to operating in foreign countries if we **or they** obtain the necessary approvals. Risks associated with ~~our~~ **any** international operations may materially adversely affect our ability to attain or maintain profitable operations. If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates. We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products **. Information obtained from expanded access studies may not reliably predict the efficacy of our future product candidates in company- sponsored clinical trials and may lead to adverse events that could limit approval. We are initiating expanded access programs in the United States for patients with SM and GIST to receive investigational bezuclastinib after meeting certain eligibility criteria. These programs are uncontrolled, carried out by individual physicians and not typically conducted in strict compliance with GCPs, all of which can lead to a treatment effect that may differ from that in placebo- controlled trials. These programs provide only anecdotal evidence of efficacy and contain no control or comparator group for reference. This patient data is not designed to be aggregated or reported as study results. Moreover, expanded access programs provide supportive safety**

information for regulatory review, and many of the patients in our programs will have life- threatening illnesses where the risk for serious adverse events is high. If serious adverse events in these programs are determined to be bezuclastinib- related, they could have a negative impact on the safety profile of bezuclastinib, which could cause significant delays or an inability to successfully obtain regulatory approval with labeling that we consider desirable, if at all. In addition, our supply capabilities may limit the number of patients who are able to enroll in the programs, which could prompt adverse publicity or other disruptions related to current or potential participants in these programs . Risks Related to Our Reliance on Third Parties We currently rely and for the foreseeable future will continue to rely on third parties to conduct our clinical trials and to assist with various research, discovery, manufacturing and supply activities. If these third parties do not properly and successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval of or commercialize our product candidates or discover new product candidates on our intended timelines, if at all. We depend and will depend upon independent investigators and collaborators, such as medical institutions, contract research organizations (" CROs "), contract manufacturing organizations (" CMO " s) and strategic partners to conduct our preclinical studies and clinical trials under agreements with us. We rely heavily on these third parties over the course of our clinical trials, and we control only certain aspects of their activities. As a result, we have less direct control over the conduct, timing and completion of these clinical trials and the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. We and these third parties are required to comply with good clinical practices (" GCP " s), which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. If we or any of these third parties fail to comply with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, failure or any failure by these third parties to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws. 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 drug development activities, which could affect their performance on our behalf. If any CMO with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different CMO, which we may not be able to do on reasonable terms, if at all. In either scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or product candidates may be unique or proprietary to the original CMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back- up or alternate supplier, or we may be unable to transfer such skills at all. Furthermore, a CMO may possess technology related to the manufacture of our product candidate that such CMO owns independently. This would increase our reliance on such CMO or require us to obtain a license from such CMO in order to have another CMO manufacture our product candidates. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials. We also rely on third - party vendors and collaborators to support our research and discovery efforts and to help expand our drug candidate pipeline, including certain third parties located in China, and we expect to continue to use such third parties. A natural disaster, epidemic or pandemic disease outbreaks, trade war, political unrest or other local events could disrupt the business or operations of these third parties and thus negatively impact our research and discovery capabilities and timelines. We contract with third parties for the manufacture of our drug candidates for preclinical development and clinical trials. This reliance on third parties increases the risk that we will not have sufficient quantities of our drug candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts. We do not currently own or operate any manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of our drug candidates for preclinical development and clinical testing, as well as for the commercial manufacture of our current and future drugs. This reliance on third parties increases the risk that we will not have sufficient quantities of our drug candidates or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. We do not have long- term supply agreements with our contract manufacturers, and purchase our required drug supply, including the API and drug product used in our drug candidates, on a purchase order basis with certain contract manufacturers. In addition, we may be unable to establish or maintain any agreements with third- party manufacturers or to do so on acceptable terms. Even if we are able to establish and maintain agreements with third- party manufacturers, reliance on third- party manufacturers entails additional risks. In addition, our drug candidates may compete with other drug candidates for access to manufacturing facilities. As a result, we may not obtain access to these facilities on a priority basis or at all. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. If any of our product candidates receive regulatory approval and we are not able to negotiate commercial supply terms with any third- party manufacturers, we may be unable to commercialize our products, and our business and financial condition would be materially harmed. If we are forced to accept unfavorable terms for our relationships with any such third- party manufacturer, our business and financial condition would be materially harmed. Third- party manufacturers may not be able to comply with the FDA' s cGMP regulations or similar regulatory requirements outside of the U. S. Our failure, or the failure of our third- party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, seizures or voluntary recalls of drug candidates or products, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. Third- party manufacturers' failure to achieve and

maintain high manufacturing standards, in accordance with applicable regulatory requirements, or the incidence of manufacturing errors, also could result in patient injury or death, product shortages, delays or failures in product testing or delivery, cost overruns, or other problems that could seriously harm our business. Third- party manufacturers often encounter difficulties involving production yields, quality control, and quality assurance, as well as shortages of qualified personnel. The third parties upon whom we rely for the supply of the API and drug product used in bezuclastinib are our sole source of supply, and the loss of any of these suppliers could significantly harm our business. The API and drug product used in bezuclastinib are currently supplied to us from single- source suppliers. Our ability to successfully develop our drug candidates and supply our drug candidates for clinical trials, depends in part on our ability to obtain the API and drug product for these drugs in accordance with regulatory requirements and in sufficient quantities and on sufficient timelines for clinical testing. We will need to enter into arrangements to establish redundant or second- source supply of some of the API and drug product. If any of our suppliers ceases its operations for any reason or is unable or unwilling to supply API or drug product in sufficient quantities or on the timelines necessary to meet our needs it could significantly and adversely affect our business, the supply of our current or future drug candidates or any future approved drugs and our financial condition. For bezuclastinib and any other product candidates, we intend to identify and qualify additional manufacturers to provide such API and drug product prior to submission of a New Drug Application (" NDA ") to the FDA and / or a Marketing Authorization Application (" MAA ") to the EMA. We are not certain, however, that our single- source suppliers will be able to meet our demand for their products, either because of the nature of our agreements with those suppliers, our limited experience with those suppliers or our relative importance as a customer to those suppliers. It may be difficult for us to assess their ability to timely meet our demand in the future based on past performance and they may subordinate our needs in the future to their other customers. While we seek to maintain adequate inventory of the API and drug product used in our current or future drug candidates and any future approved drugs, any interruption or delay in the supply of components or materials, or our inability to obtain such API and drug product from alternate sources at acceptable prices in a timely manner could impede, delay, limit or prevent our development efforts, which could harm our business, results of operations, financial condition and prospects. Risks Related to Regulatory Approval of Our Drug Candidates and Other Legal Compliance Matters The FDA regulatory approval process is lengthy and time- consuming, and we may experience significant delays in the clinical development and regulatory approval of our product candidates. We currently have one drug candidate in clinical development for three indications and its risk of failure is high. We are unable to predict when or if any of our drug candidates will prove effective or safe in humans or will obtain marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of any drug candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. While bezuclastinib is a highly potent and selective KIT D816V inhibitor that is being developed to treat SM and GIST patients, we may find that patients treated with bezuclastinib have or develop mutations that confer resistance to treatment. If patients have or develop resistance to treatment with our drug candidates, we may be unable to successfully complete our clinical trials, and may not be able to obtain regulatory approval of, and commercialize, our drug candidates. Our product development costs will increase if we experience delays in preclinical studies or clinical trials or in obtaining marketing approvals. We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to obtain marketing approval or commercialize our drug candidates. We may utilize companion diagnostics in our planned clinical trials in the future in order to identify appropriate patient populations for our drug candidates. 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. Regulatory authorities, including the FDA, may disagree with our regulatory plan and we may fail to obtain regulatory approval of our product candidates. We are conducting clinical trials with our lead product candidate, bezuclastinib, in patients with GIST, AdvSM and Non- AdvSM. The FDA may not agree with some or all of our regulatory plans for initial registration of bezuclastinib in some or all of these indications and may require additional clinical trials to be conducted prior to approval. Our clinical trial results may also not support approval. In addition, our product candidates could fail to receive regulatory approval for many reasons, including if we are unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that our product candidates are safe and effective for any of their proposed indications, or that our product candidates' clinical and other benefits outweigh their safety risks. Moreover, our clinical trial results may also not support approval. 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, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. We may also submit marketing applications in other countries. Obtaining foreign regulatory approvals and compliance with foreign 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 fail to comply with the regulatory requirements in international markets and / or 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. The impact of healthcare legislation and other changes in the healthcare industry and in healthcare spending on us is currently unknown, and may adversely affect our business model. Our revenue prospects could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition. ~~There~~ **Many federal and state legislatures have considered, and adopted, healthcare policies intended to curb rising healthcare costs, such** ~~has~~ - **as** ~~been increasing legislative and enforcement interest in~~ **the Inflation Reduction Act of 2022. These cost- containment**

measures may include, among ~~the~~ **other** ~~United States~~ **measures: requirements for pharmaceutical companies to negotiate prescription drug prices** with ~~respect~~ **government healthcare programs; controls on government- funded reimbursement for drugs; new or increased requirements** to ~~specialty~~ **pay prescription drug rebates to government healthcare programs, including if drug prices increase at a higher rate than inflation; controls on healthcare providers; challenges to or limits on the pricing of drugs, including pricing controls or limits or prohibitions on reimbursement for specific products through other means; requirements to try less expensive products or generics before a more expensive branded product; and public funding for cost effectiveness research, which may be used by government and private third- party payors to make coverage and payment decisions. Political, economic and regulatory developments may further complicate developments in healthcare systems and pharmaceutical** drug pricing ~~practices~~. ~~In fact~~ **These developments could** , ~~both~~ **for example, impact our potential licensing agreements as commercial and collaborative partners may also consider the impact of** ~~the~~ **these pressures on** ~~federal and state governments in the~~ **their licensing strategies. Any** ~~United States and foreign governments continue to propose and pass~~ new ~~legislation,~~ **laws or** regulations **that have** ~~, and policies affecting coverage and reimbursement rates, which are designed to contain or reduce~~ the **effect of imposing additional** ~~cost~~ **costs or regulatory burden on pharmaceutical manufacturers** ~~of health care. Further federal and state proposals and healthcare reforms are likely~~ , ~~which~~ **or otherwise negatively affect the industry,** could **adversely affect our ability to successfully commercialize our** ~~limit the prices that can be charged for the~~ product candidates ~~that we develop and may further limit our commercial opportunity~~ . ~~There~~ -- **The implementation** ~~may be future changes that result in reductions in potential coverage and reimbursement levels for our product candidates, if approved and commercialized, and we cannot predict the scope~~ of any ~~future changes or the impact that those changes would have on our operations. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and / or impose~~ price controls ~~may~~ **, caps on prescription drugs or price transparency requirements could** adversely affect ~~us~~ **our business, operating results and financial condition** . Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements. We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under the regulations of the FDA and other similar foreign regulatory bodies will increase significantly, and our costs associated with compliance with such laws and regulations are also likely to increase. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and 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. We face potential liability related to the privacy of health information we obtain from clinical trials sponsored by us. Most healthcare providers, including research institutions from which we obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA, as amended by the HITECH. We are not currently classified as a covered entity or business associate under HIPAA and thus are not directly subject to its requirements or penalties. However, any person may be prosecuted under HIPAA' s criminal provisions either directly or under aiding- and- abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA- covered healthcare provider or research institution that has not satisfied HIPAA' s requirements for disclosure of individually identifiable health information. In addition, we may maintain sensitive personally identifiable information, including health information, that we receive throughout the clinical trial process, in the course of our research collaborations, and directly from individuals (or their healthcare providers) who enroll in our patient assistance programs. As such, we may be subject to state laws requiring notification of affected individuals and state regulators in the event of a breach of personal information, which is a broader class of information than the health information protected by HIPAA. Furthermore, certain health privacy laws, data breach notification laws, consumer protection laws and genetic testing laws may apply directly to our operations and / or those of our collaborators and may impose restrictions on our collection, use and dissemination of individuals' health information. Patients about whom we or our collaborators obtain health information, as well as the providers who share this information with us, may have statutory or contractual rights that limit our ability to use and disclose the information. We may be required to expend significant capital and other resources to ensure ongoing compliance with applicable privacy and data security laws. Claims that we have violated individuals' privacy rights or breached our contractual obligations, even if we are not found liable, could be expensive and time- consuming to defend and could result in adverse publicity that could harm our business. Additionally, we are subject to state and foreign equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope and may apply regardless of the payor. If we are unable to successfully develop companion diagnostic tests for our drug candidates that require such tests, or experience significant delays in doing so, we may not realize the full commercial potential of these drug candidates. We may develop, either by ourselves or with collaborators, in vitro companion diagnostic tests for our drug candidates for certain indications. To be successful, we or our collaborators will need to address a number of scientific, technical, regulatory, and logistical challenges. The FDA regulates in vitro companion diagnostics as medical devices that will likely be subject to clinical trials in conjunction with the clinical trials for our drug candidates, and which will require regulatory clearance or approval prior to commercialization. We may rely on third parties for the design, development, and manufacture of companion diagnostic tests for our therapeutic drug candidates that require such tests. If these parties are unable to successfully develop companion diagnostics for these therapeutic drug candidates, or experience delays in doing so, the development of these therapeutic drug candidates may be adversely affected or may not obtain marketing approval, and we may not realize the full commercial

potential of any of these therapeutics that obtain marketing approval. **Pharmaceutical and biological product marketing is subject to substantial regulation in the U. S. and any failure by us or our commercial and collaborative partners to comply with applicable statutes or regulations can adversely affect our business. Any marketing activities associated with our product candidates, if approved for commercialization, will be subject to numerous federal and state laws governing the marketing and promotion of pharmaceutical and biological products. The FDA regulates post- approval promotional labeling and advertising to ensure that they conform to statutory and regulatory requirements. In addition to FDA restrictions, the marketing of prescription drugs is subject to laws and regulations prohibiting fraud and abuse under government healthcare programs. Similarly, many states have similar statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, and, in some states, such statutes or regulations apply regardless of the payor. In addition, government authorities may also seek to hold us responsible for any failure of our commercialization or collaborative partners to comply with applicable statutes or regulations. If we, or our commercial or collaborative partners, fail to comply with applicable FDA regulations or other laws or regulations relating to the marketing of our product candidates, if approved for commercialization, we could be subject to criminal prosecution, civil penalties, seizure of products, injunctions and exclusion of our product candidates from reimbursement under government programs, as well as other regulatory or investigatory actions against our future product candidates, our commercial or collaborative partners or us.** Risks Related to Our Intellectual Property If our efforts to protect the proprietary nature of the intellectual property related to our technologies are not adequate, we may not be able to compete effectively in our market. We rely upon a combination of patents, confidentiality agreements, trade secret protection and license agreements to protect the intellectual property related to our technologies. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market **. While we undertake efforts to protect our trade secrets and other confidential information from disclosure, others may independently discover trade secrets and proprietary information, and in such cases, we may not be able to assert any trade secret rights against such party. Enforcing a claim that a party illegally obtained and is using our trade secrets is challenging and the outcome is unpredictable. In addition, courts outside of the U. S. may be less willing to protect trade secrets. Costly and time- consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position** . Currently, we have patents issued from our in- licensed portfolio under our license agreement with Plexxikon. in multiple territories, including but not limited to, Australia, Brazil, Canada, China, Colombia, Europe (validated in Germany, Spain, France, Great Britain, Italy, the Netherlands, as well as various other EU countries), Hong Kong, India, Indonesia, Israel, Japan, Mexico, New Zealand, Peru, the Philippines, Republic of Korea, Russia, Singapore, South Africa, Taiwan, and the United States. We also have **in- licensed** patent applications pending in Australia, Brazil, Canada, China, Egypt, Europe, India, Indonesia, Israel, Japan, Korea, Mexico, Philippines, Singapore, South Africa, and the United States **. In addition, we have our own US and international patent applications** . We anticipate additional patent applications will be filed both in the United States and in other countries, as appropriate. There is no guarantee that patent applications will provide meaningful protection or result in patents being issued and granted. **In addition, patent grant standards by the U. S. Patent and Trademark Office (the " USPTO ") and its foreign counterparts are not always uniform or predictable, and subject to change. For example, the America Invents Act enacted a number of changes to U. S. patent laws, which may prevent us from adequately protecting our or our licensors' inventions and discoveries, including our ability to seek injunctive relief, pursue infringement claims, and obtain substantial damage awards. An example of a major provision of the America Invents Act is the change in the U. S. patent policy from a first- to- invent to a first- to- file practice. Additionally, the USPTO and patent offices in other jurisdictions have often required that patent applications directed to pharmaceutical and / or biotechnology- related inventions be limited or narrowed substantially to cover only the specific innovations exemplified in the patent application, thereby limiting the scope of protection against competitive challenges. Accordingly, even if we or our licensors are able to obtain patents, the patents might be substantially narrower than anticipated. Thus, there is no assurance as to the degree and range of protections any of our or our licensors' patents, if issued, may afford us or whether patents will be issues. Foreign counterparts to this law are also not uniform, and there is no worldwide policy governing the subject matter and scope of claims granted in a pharmaceutical or biotechnology patent. Uncertainty arising from changing laws can impact our ability to protect our or our licensors' patents and other proprietary rights.** Third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our **or our licensors'** patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. If the breadth or strength of protection provided by the patent applications we hold with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced. We depend on intellectual property licensed from third parties and termination of any of these licenses could result in the loss of significant rights, which would harm our business. We are dependent on patents, know- how and proprietary technology, both our own and licensed from others. In particular, bezuclastinib and other molecules are subject to a license from Plexxikon. We expect in the future to be party to additional material license or collaboration agreements. Any termination of our current or future licenses could result in the loss of significant rights and could harm our ability to commercialize our product candidates. These licenses do and future licenses may include provisions that impose obligations and restrictions on us. This could delay or otherwise negatively impact a transaction that we may wish to enter into. Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement. 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 be unable to successfully develop and commercialize the affected product candidates. We are generally also subject to all of the same risks with respect to protection of intellectual property that we license, as we are for intellectual property that we own, which are described below. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize products could suffer. We may not be successful in obtaining or maintaining necessary rights to product components and processes for our development pipeline through acquisitions and in- licenses. Presently we have rights to certain intellectual property, through licenses from third parties and under patent applications that we own or will own, related to bezuclastinib, and certain other product candidates. Because additional product candidates may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in- license or use these proprietary rights. Our product candidates may also require specific formulations to work effectively and efficiently and these rights may be held by others. Similarly, efficient production or delivery of our product candidates may also require specific compositions or methods, and the rights to these may be owned by third parties. We may be unable to acquire or in- license any compositions, methods of use, processes or other third- party intellectual property rights from third parties that we identify. 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. Third- party claims of intellectual property infringement may prevent or delay our product discovery and development efforts. Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Third parties may assert that we are employing their proprietary technology without authorization. While we do not believe that any claims that could materially adversely affect commercialization of our product candidates, if approved, are valid and enforceable, we may be incorrect in this belief, or we may not be able to prove it in litigation. There may be third- party patents of which we are currently unaware with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We may fail to identify relevant patents or incorrectly conclude that a patent is invalid, not enforceable, exhausted, or not infringed by our activities. If any third- party patents were held by a court of competent jurisdiction to cover the manufacturing process of our product candidates, molecules used in or formed during the manufacturing process, or any final product itself, the holders of any such patents may be able to block our ability to commercialize the product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third- party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy or patient selection methods, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, if we are unable to obtain a necessary license to a third- party patent on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business. Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Defense of these claims, regardless of their merit, could involve substantial litigation expense and would be a substantial diversion of employee resources from our business. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need or may choose to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our product candidates, which could harm our business significantly. 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. Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time- consuming. An adverse result in any litigation or defense proceedings could put one or more of our **or our licensors'** patents at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our **or our licensors'** patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. An unfavorable outcome of any post-grant proceedings, including interference proceedings, provoked by third parties or brought by the USPTO could result in a loss of our current patent rights and 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. Litigation or post- grant proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States. Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or the USPTO. If we or one of our licensing partners initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate, as applicable, is invalid and / or unenforceable. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such proceedings could result in

revocation or amendment to our **or our licensors'** patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. 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 our product candidates. Such a loss of patent protection could have a material adverse impact on our business **. Patent terms may be inadequate to protect our competitive position on our product candidates and any future products 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. The patent term of a U. S. patent may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in granting a patent, or may be shortened if a patent is terminally disclaimed over another patent having an earlier expiration date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a Patent Term Extension, or PTE, of up to five years beyond the normal expiration of the patent to compensate patent owners for loss of enforceable patent term due to the lengthy regulatory approval process. A PTE grant cannot extend the remaining term of a patent beyond a total of 14 years from the date of the product approval. Further, PTE may only be applied once per product, and only with respect to an approved indication — in other words, only one patent (for example, covering the product itself, an approved use of said product, or a method of manufacturing said product) can be extended by PTE. Moreover, the scope of protection during the period of the PTE does not extend to the full scope of the claim, but instead only to the scope of the product as approved. We anticipate applying for PTE in the United States. Similar extensions may be available in other countries where we are prosecuting patents and we likewise anticipate applying for such extensions. The granting of such patent term extensions is not guaranteed and is subject to numerous requirements. We might not be granted an extension because of, for example, failure to apply within applicable periods, failure to apply prior to the expiration of relevant patents, failure to exercise due diligence during the testing phase or regulatory review process or any other failure to satisfy any of the numerous applicable requirements. In addition, to the extent we wish to pursue patent term extension based on a patent that we in- license from a third party, we would need the cooperation of that third party. Moreover, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our or our licensors' patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to obtain approval of competing products following our or our licensors' patent expiration by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. If this were to occur, it could have a material adverse effect on our ability to generate revenue. Changes to patent law in the United States and in foreign jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our product candidates and future products. As is the case with other biotechnology and biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology and biopharmaceutical industry involves both technological and legal complexity, and is therefore costly, time- consuming and inherently uncertain. Moreover, recent U. S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our or our licensors' 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 federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our or our licensors' ability to obtain new patents or to enforce our or our licensors' existing patents and patents that we or our licensors might obtain in the future. We cannot predict how future decisions by the courts, Congress or the USPTO may impact the value of our or our licensors' patents. Similarly, any adverse changes in the patent laws of other jurisdictions could have a material adverse effect on our business and financial condition. Changes in the laws and regulations governing patents in other jurisdictions could similarly have an adverse effect on our ability to obtain and effectively enforce our patent rights. Further, a new court system recently became operational in the European Union. The Unified Patent Court, or UPC, began accepting patent cases on June 1, 2023. The UPC is a common patent court with jurisdiction over patent infringement and revocation proceedings effective for multiple member states of the European Union. The broad geographic reach of the UPC could enable third parties to seek revocation of any of our European patents in a single proceeding at the UPC rather than through multiple proceedings in each of the individual European Union member states in which the European patent is validated. Under the UPC, a successful revocation proceeding for a European Patent under the UPC would result in loss of patent protection in those European Union countries. Accordingly, a single proceeding under the UPC could result in the partial or complete loss of patent protection in numerous European Union countries. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize our technology and product candidates. Moreover, the controlling laws and regulations of the UPC will develop over time and we cannot predict what the outcomes of cases tried before the UPC will be. The case law of the UPC may adversely affect our ability to enforce or defend the validity of our or our licensors' European patents. Patent owners have the option to opt- out their European Patents from the jurisdiction of the UPC, defaulting to pre- UPC enforcement mechanisms. We may not be able to seek or obtain patent protection throughout the world or enforce such patent protection once obtained. We may not be able to pursue patent coverage of our product candidates in certain countries outside of the United States. Filing, prosecuting and defending patents on product**

candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States may be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. The breadth and strength of our or our licensors' patents issued in foreign jurisdictions or regions may not be the same as the corresponding patents issued in the United States. Consequently, we may not be able to prevent third parties from practicing our or our licensors' inventions in all countries outside the United States, or from selling or importing products made using our or our licensors' 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 certain territories where we 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' 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 foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protections, particularly those relating to biotechnology and biopharmaceutical products. This difficulty with enforcing patents could make it difficult for us to stop the infringement of our or our licensors' patents or marketing of competing products otherwise generally in violation of our proprietary rights. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our or our licensors' patents at risk of being invalidated or interpreted narrowly, put our or our licensors' patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our 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. If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our trademarks of interest and our business may be adversely affected. Our current or future trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. As a means to enforce our trademark rights and prevent infringement, we may be required to file trademark claims against third parties or initiate trademark opposition proceedings. This can be expensive and time- consuming, particularly for a company of our size. We may not be able to protect our rights to our trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. During trademark registration proceedings, we may receive rejections. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Moreover, any name we propose to use for our products in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. Similar requirements exist in Europe. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed product names, we may be required to expend significant additional resources in an effort to identify a usable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected . Risks Related to Employee Matters and Managing Growth We are highly dependent on our key personnel, and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy. Our inability or failure to successfully attract and retain qualified personnel, particularly at the management level, could adversely affect our ability to execute our business plan and harm our operating results. We are highly dependent on our management, scientific and medical personnel, including our Chief Executive Officer and President, our Chief Financial Officer, our Chief Technology Officer, our Chief Scientific Officer, our Chief Medical **Officer, our Chief Commercial** Officer and our Chief Legal Officer. The loss of the services of any of our executive officers, other key employees and other scientific and medical advisors, and an inability to find suitable replacements could result in delays in product development and harm our business. Competition for skilled personnel in our market is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid- level and senior managers as well as junior, mid- level and senior scientific and medical personnel. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. The employment agreements with our key employees provide for at- will employment, which means that any of our employees could leave our employment at any

time, with or without notice. We have ~~undergone~~ **experienced** significant growth ~~over~~ **and expect to continue to expand our company to support research, development and future commercial capabilities and may face challenges in managing our growth. During** the past two years ~~and we may face challenges in managing our growth. During the past two years,~~ we increased our headcount from ~~77~~ **138** to ~~164~~ **205** full time employees through the expansion of our research, development, manufacturing and G & A infrastructure ~~, and we moved into new offices and labs in Massachusetts and Colorado, respectively~~ . We need to continue to recruit, train and retain qualified personnel to support our growth and we may be unable to do so effectively. ~~As of December 31, 2023, we are no longer an emerging growth company (" EGC "), as defined in the JOBS Act and, as the market value of our common stock that was held by non- affiliates exceeded $ 700 million as of June 30, 2023, we are now a large accelerated filer and we are now subject to certain disclosure requirements that were not applicable to use as an EGC or as a smaller reporting company. Additionally, our independent registered public accounting firm is required to attest to the effectiveness of our internal control over financial reporting.~~ We continue to enhance our operational, financial and management controls and systems, reporting systems and infrastructure, and policies and procedures to support the establishment and maintenance of effective disclosure and financial controls and corporate governance. Our management and other personnel devote a ~~s~~ substantial amount of time to these compliance initiatives, and these increase our legal and financial costs and make some activities more time- consuming and costly. We may not be able to implement enhancements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our development timelines may be delayed, our ability to generate revenue could be reduced, and we may not be able to implement our business strategy. Our business and operations could suffer in the event of system failures or unauthorized or inappropriate use of or access to our systems. We are increasingly dependent on our information technology systems and infrastructure for our business. We collect, store, use and transmit personal information and sensitive information including intellectual property, proprietary business information, and health- related information, in connection with business operations. The secure maintenance of this information is critical to our operations and business strategy. Due to the size and complexity and the increasing amounts of confidential information that are maintained, our internal information technology systems and those of our third- party CROs, vendors and other contractors and consultants are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security incidents or breaches from inadvertent or intentional actions by our employees and / or third parties with whom we do business, or from cyber- attacks by malicious third parties (including the deployment of harmful malware, ransomware, digital extortion, denial- of- service attacks, supply chain attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information), which may compromise our system infrastructure or those of our partners or lead to data leakage. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. 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 data. Likewise, similar events relating to the information technology systems of our third- party collaborators who we rely on for the manufacture of our product candidates and to conduct clinical trials could also have a material adverse effect on our business. In addition, changes in how our employees work and access our systems, when part of our workforce is working remotely, could also lead to opportunities for bad actors to launch cyber-attacks or for employees to cause inadvertent security risks or incidents. The prevalent use of mobile devices also increases the risk of data security incidents. To the extent that any disruption, security breach or unauthorized or inappropriate use or access to our systems were to result in a loss of or damage to our data, or inappropriate disclosure of confidential or proprietary information, including but not limited to patient, employee or vendor information, we could, under certain circumstances, be subject to notification obligations to affected individuals and / or government agencies, liability, including potential lawsuits from patients, collaborators, employees, stockholders or other third parties and liability under foreign, federal and state laws that protect the privacy and security of personal information which could take the form of, amongst other things, administrative fines, and the development and potential commercialization of our product candidates could be delayed. While we maintain cyber insurance at levels that we believe are appropriate for our business, we cannot assure our investors that it will be sufficient in type or amount to cover us against all claims related to security compromises or breaches, cyberattacks and other related breaches. Risks Related to Our Financial Position and Need for Additional Capital We will require substantial additional funding. If we fail to obtain additional financing when needed, or on attractive terms, we may be unable to complete the development and commercialization of our product candidates. Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts to continue the clinical and preclinical development of our current and future product candidates, including our clinical trials for bezuclastinib. If approved, we will require significant additional amounts in order to launch and commercialize our product candidates. We cannot be certain that additional funding will be available on acceptable terms, or at all. Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates or other research and development initiatives. Our license agreements may also be terminated if we are unable to meet the payment and other obligations under the agreements. We could be required to seek collaborators for our product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to our product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves. Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline. We have incurred net losses in every year since our inception and anticipate that we will continue to

incur net losses in the future. We are a clinical- stage biopharmaceutical company with a limited operating history. Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval and become commercially viable. We have no products approved for commercial sale and have not generated any revenue from product sales to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we are not profitable and have incurred losses in each period since our inception in March 2014. For further information, see " Management' s Discussion and Analysis of Financial Condition and Results of Operations. " There can be no assurance that the product candidates under development by us will be approved for sale in the United States or elsewhere. Furthermore, there can be no assurance that if such products are approved, they will be successfully commercialized, which would have an adverse effect on our business prospects, financial condition and results of operation. **The commercial success of our products, if approved, will depend on many factors, including, but not limited to: • the availability of coverage and adequate and timely reimbursement from managed care plans, private insurers, government payors (such as Medicare and Medicaid and similar foreign authorities) and other third- party payors for our products; • patients' ability and willingness to pay out- of- pocket for our products in the absence of coverage and / or adequate reimbursement from third- party payors; • patient demand for our products; • our ability to establish and enforce intellectual property rights in and to our products; and • our ability to avoid third- party patent interference, intellectual property challenges or intellectual property infringement claims.** Even if we succeed in commercializing one or more of our product candidates, we will continue to incur substantial research and development and other expenditures to develop and market additional product candidates. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. Our ability to use net operating losses and tax credit carryforwards to offset future taxable income may be subject to certain limitations. In general, under Sections 382 and 383 of the Code, a corporation that undergoes an " ownership change " is subject to limitations on its ability to utilize its pre- change net operating losses or tax credits, or NOLs or credits, to offset future taxable income or taxes. As a result of the shares issued in July 2020 related to the acquisition of Kiq and the sale of Series A convertible preferred stock, the Company has experienced a change in ownership, as defined by Section 382. As a result of the ownership change, utilization of the federal and state net operating loss carryforwards and research and development tax credit carryforwards is subject to annual limitation under Section 382. Under Section 382, the annual limitation is determined by first multiplying the value of the Company' s stock at the time of the ownership change by the applicable long- term tax- exempt rate, and then could be subject to additional adjustments, as required. As of December 31, ~~2023~~ **2024** , approximately $ ~~69~~ **73** . ~~7~~ **0** million and $ ~~4~~ **1** . ~~0~~ **5** million of federal and state net operating losses, respectively ~~, as well as $ 3. 5 million of future amortization for federal purposes~~ , were subject to the July 2020 limitation of $ 0. 3 million per year. A second ownership change occurred in December 2020 as a result of the underwritten public offering of common stock which resulted in a limitation of tax attributes generated from July 2020 to December 2020. The December 1, 2020 ownership change is not expected to have a material impact to the Company' s net operating loss carryforwards or research and development tax credit carryforwards as these net operating losses and tax credit carryforwards may be utilized, subject to annual limitation, assuming sufficient taxable income is generated before expiration. The Company has not performed a Section 382 analysis since December 2020 **. We may be subject to adverse legislative or regulatory tax changes that could negatively impact our financial condition. The rules dealing with U. S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U. S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect our stockholders or us. We assess the impact of various tax reform proposals and modifications to existing tax treaties in all jurisdictions where we have operations to determine the potential effect on our business and any assumptions we have made about our future taxable income. We cannot predict whether any specific proposals will be enacted, the terms of any such proposals or what effect, if any, such proposals would have on our business if they were to be enacted. For example, the United States enacted the Inflation Reduction Act of 2022, which implements, among other changes, a 1 % excise tax on certain stock buybacks. In addition, beginning in 2022, the Tax Cuts and Jobs Act eliminated the previously available option to deduct research and development expenditures and requires taxpayers to amortize them generally over five years for research activities conducted in the United States and over 15 years for research activities conducted outside the United States. Such changes, among others, may adversely affect our effective tax rate, results of operation and general business condition** . 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 continue to be highly volatile. Market prices for our common stock could be subject to wide fluctuations in response to various factors. In addition, the stock market in general, and The Nasdaq Global Select Market and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. If the market price of our common stock does not exceed your purchase price, you may not realize any return on your investment in us and may lose some or all of your investment. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company' s securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management' s attention and resources, which would harm our business, operating results, or financial condition. Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant influence over matters subject to stockholder approval. Our executive officers, directors, and ≥ 5 % stockholders beneficially owned approximately ~~65~~ **55** . ~~1~~ **9** % of our outstanding common stock as of December 31, ~~2023~~ **2024** . These stockholders will have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of our directors, amendments

to 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 may be in the best interests of our stockholders. An active trading market for our common stock may not be sustained. Given the low trading volumes of our common stock, there is a risk that an active trading market for our shares may not be sustained, which could put downward pressure on the market price of our common stock and thereby affect the ability of our stockholders to sell some or all of their shares at attractive prices, at the times and in the volumes that they would like to sell them, or at all. Future sales and issuances of our common stock or rights to purchase common stock could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall. We expect that significant additional capital may be needed in the future to continue our planned operations, including conducting clinical trials, commercialization efforts, research and development activities, and incurring costs associated with operating as a public company. To raise capital, we may sell common stock, convertible securities, or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities, or other equity securities, investors may be materially diluted by such sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences, and privileges senior to the holders of our common stock. Anti- takeover provisions under our charter documents and Delaware law could delay or prevent a change of control, which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management. Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15 % or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then- current board of directors and could also delay or impede a merger, tender offer, or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline. Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees. Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, any action to interpret, apply, enforce, or determine the validity of our certificate of incorporation or bylaws or any action asserting a claim against us that is governed by the internal affairs doctrine. The choice of 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 such lawsuits against us and our directors, officers, and other employees. Alternatively, if a court were to find the choice of forum provision contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.