Risk Factors Comparison 2025-02-27 to 2024-03-14 Form: 10-K

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Risks Related to the Development of Our Product Candidates Our preclinical studies and clinical trials may fail to demonstrate adequately the safety and efficacy of any of our product candidates, which would prevent or delay development, regulatory approval, and commercialization. Before obtaining regulatory approvals for the commercial sale of our current and future product candidates, we must demonstrate the safety and efficacy of our investigational product candidates for use in each target indication through lengthy, complex, and expensive preclinical studies and clinical trials. If the results of our ongoing or future preclinical studies and clinical trials are inconclusive with respect to the safety and efficacy of our product candidates, if we do not meet the clinical endpoints with statistical and clinically meaningful significance, or if there are safety concerns associated with our product candidates, we may be prevented or delayed in obtaining marketing approval for such product candidates. In some instances, there can be significant variability in safety or efficacy results between different preclinical studies and clinical trials of the same product candidate due to numerous factors, including changes in and adherence to clinical trial procedures set forth in protocols, differences in the size and type of the patient populations, and the rate of dropout among clinical trial participants **. Additionally, we and third parties may have limited preclinical and clinical data, and a more limited understanding generally, with respect to certain indications for which our product candidates are being developed, including autoimmune diseases, and we cannot predict the extent to which the safety and efficacy of a product candidate may vary across indications. We may encounter significant challenges creating appropriate models and assays for evaluating the safety and efficacy of our product candidates and may not be able to provide sufficient data or other evidence, to the satisfaction of regulatory authorities, that certain unexpected results observed in preclinical and clinical testing of our product candidates are not indicative of the potential safety issues of such product candidates. We may develop program plans and timelines for certain product candidates based on our experience with such product candidates in different indications or with other product candidates that incorporate or were developed with the same technologies based on our expectation that such product candidates will perform and act similarly. However, our product candidates may reveal unexpected, important differences, including with respect to safety or efficacy, when developed in different indications or as compared to such other product candidates, including differences that may require changes to the manufacturing process or clinical development plan that require additional time and resources beyond what we initially anticipated. Any such occurrence could require us to adjust or alter our development plans, which could delay, harm, or prevent our ability to develop and commercialize or receive regulatory approval for such product candidates** . In addition to our ongoing clinical trials of zipalertinib, patients have been, and will likely continue to be, treated with zipalertinib under an expanded access or " compassionate use " program. To the extent the experiences of patients being treated in this program are inconsistent with or less favorable than the results of our ongoing or planned company-sponsored clinical trials with zipalertinib, it may negatively affect perceptions of zipalertinib, our other product candidates, or our business. In addition, the United States (" U. S.") Food and Drug Administration (the " FDA"), or foreign regulatory authorities may require us to obtain and submit additional clinical data due to these inconsistent or unfavorable results, which could delay clinical development or marketing approval of zipalertinib or potentially our other product candidates . Our approach to the identification,..... is unsuccessful, our business will suffer . Preclinical and clinical development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future preclinical studies or clinical trial results. If our preclinical studies and clinical trials are not sufficient to support regulatory approval of any of our product candidates, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development of such product candidate. Our preclinical studies and future clinical trials may not be successful. It is impossible to predict when or if any of our product candidates will prove effective and safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical studies and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical development testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials even after achieving promising results in earlier stage clinical trials. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates. Additionally, some of the clinical trials we conduct are and in the future may be open- label in trial design and may be conducted at a limited number of clinical sites on a limited number of patients. An " open- label " clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open- label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open- label clinical trials are subject to various limitations that may exaggerate any therapeutic effect, as patients in open- label clinical trials are aware when they are receiving treatment. Open- label clinical trials may be subject to a " patient bias " where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. Moreover, patients selected for early clinical studies often include the most severe sufferers and their symptoms may have been bound to improve notwithstanding the new treatment. In addition, open- label clinical trials may be subject to an " investigator bias "

where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. Because some of our clinical trials are open- label in clinical trial design, the results from these clinical trials may not be predictive of future clinical trial results with this or other product candidates for which we conduct an open- label clinical trial when studied in a controlled environment with a placebo or active control. Moreover, principal investigators for our current and future clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates. If a sufficient number of our product candidates generally prove to be ineffective, unsafe or commercially unviable, our entire pipeline may have little, if any, value, which would have a material and adverse effect on our business, financial condition, results of operations and prospects. We may encounter substantial delays in preclinical and clinical trials or may not be able to conduct or complete preclinical or clinical trials on the expected timelines, if at all. We may experience delays in initiating or completing preclinical studies or clinical trials, including as a result of delays in obtaining, or failure to obtain, the FDA' s clearance to initiate clinical trials under future investigational new drug applications (" INDs"). Additionally, we cannot be certain that preclinical studies or clinical trials for our product candidates will not require **a** redesign, enroll an adequate number of subjects on time, or be completed on schedule, if at all. We may experience numerous adverse or unforeseen events during, or as a result of, preclinical studies and clinical trials that could delay or terminate our clinical trials, or delay or prevent our ability to receive marketing approval or commercialize our product candidates, including: • we may receive feedback from regulatory authorities that requires us to modify the design or implementation of our preclinical studies or clinical trials, including our ability to commence a clinical trial; • we may fail or be delayed in reaching agreement on acceptable terms with prospective contract research organizations (" CROs"), and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites; • we may be unable to add or be delayed in adding a sufficient number of clinical trial sites and obtaining institutional review board (" IRB"), or **research ethics committee (" REC ")** approval at each clinical trial site; • preclinical studies or clinical trials of our product candidates may fail to show safety or efficacy or otherwise produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or abandon our research efforts for our other product candidates; • preclinical studies or clinical trials of our product candidates may not produce differentiated or clinically significant results across **indications or** tumor types ~~or indications~~ ; • the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of our clinical trials or fail to return for post- treatment follow- up at a higher rate than we anticipate; • our third- party contractors may fail to comply with regulatory requirements, fail to maintain adequate quality controls or be unable to provide us with sufficient product supply to conduct and complete preclinical studies or clinical trials of our product candidates in a timely manner, or at all; • we or our investigators might have to suspend or terminate clinical trials of our product candidates for various reasons, including non- compliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics or a finding that the participants are being exposed to unacceptable health risks; • the cost of clinical trials of our product candidates may be greater than we anticipate, for example, if we experience delays or challenges in identifying patients with the mutations required for our clinical trials, we may have to reimburse sites for genetic sequencing costs in order to encourage sequencing of additional patients; • clinical trial sites may deviate from the clinical trial protocol or drop out of a clinical trial; • we may be unable to obtain or be delayed in obtaining sufficient product supply of a product candidate for use in preclinical studies or clinical trials from third- party suppliers; • the quality of our product candidates or other materials necessary to conduct preclinical studies or clinical trials of our product candidates may be insufficient or inadequate, and any transfer of manufacturing activities may require unforeseen manufacturing or formulation changes; • reports from clinical testing of other therapies may raise safety or efficacy concerns about our product candidates; • regulators may revise the requirements for ~~approving~~ **development, approval and marketing** our product candidates, or such requirements may not be as we anticipate; and • collaborators may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us. If we are required to conduct additional preclinical studies or clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these studies, trials or tests are not positive or are only moderately positive or if there are safety concerns, our business and results of operations may be adversely affected and we may incur significant additional costs. We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs, or RECs of the institutions in which such clinical trials are being conducted, by the data safety monitoring board, if any, for such clinical trial or by the FDA or other **comparable** regulatory authorities. Such authorities may suspend, place on clinical hold, or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical trial protocols, inspection of the clinical trial operations or trial site by the FDA or other **comparable** regulatory authorities, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from the product candidates, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. We are early in our development efforts and are substantially dependent on our lead product candidates. If we are unable to advance these or any of our other current and future product candidates through clinical development, or to obtain regulatory approval

and ultimately commercialize any such product candidates, either by ourselves or with or by third parties or if we experience significant delays in doing so, our business may be materially harmed. We are early in our development efforts. **We are developing** ~~Our lead unpartnered product candidate,~~ CLN- ~~619~~ **978** , ~~is in a~~ **our lead product candidate, for autoimmune diseases through an ongoing** Phase 1 clinical trial **in SLE in the U. S., Europe, and Australia and plan to initiate a company- sponsored Phase 1 clinical trial in RA in Europe. Our lead unpartnered oncology product candidate, CLN-619, is in a Phase 1 clinical trial** . In collaboration with our partners at Taiho **Pharmaceutical Co., Ltd (“ Taiho ”)** , we are evaluating zipalertinib in a pivotal Phase 2b clinical trial in patients with EGFRex20 non- small ~~-~~cell lung cancer **(" NSCLC")** who progressed after prior systemic therapy, and in a global Phase 3 clinical trial in combination with chemotherapy as a potential first- line treatment for EGFRex20 NSCLC adult patients. Additionally, our **other** product candidates ~~CLN- 978~~ , CLN- 049 ~~, CLN- 418,~~ and CLN- 617, are each in Phase 1 clinical trials. Our ability to generate product revenues, which we do not expect will occur for ~~many~~ years, if ever, will depend heavily on the successful clinical development and eventual commercialization of our current and future product candidates, if approved. The success of our current and future product candidates will depend on several factors, including the following: • sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials; • successful completion of preclinical studies; • regulator acceptance of and maintenance of INDs, clinical trial authorizations (“ CTAs ”), or comparable foreign applications that allow commencement and continuation of our planned clinical trials or future clinical trials; • successful initiation of clinical trials; • successful patient enrollment in and completion of clinical trials; • positive results from our preclinical data and clinical trials that support a demonstration of safety and effectiveness and an acceptable risk- benefit profile for our product candidates that are satisfactory to the FDA or any foreign regulatory authority for marketing approval in the intended population; • receipt of marketing approvals for our product candidates and any companion diagnostics from applicable regulatory authorities; • the extent of any required post- marketing approval commitments to applicable regulatory authorities; • obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates; • making arrangements with third- party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of our product candidates, if any product candidates are approved; • establishing sales, marketing, and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others; • acceptance of our products, if and when approved, by patients, the medical community and third- party payors; • effectively competing with other **autoimmune and** cancer therapies; • obtaining and maintaining third- party coverage and adequate pricing and reimbursement decisions; and • maintaining a continued acceptable safety, tolerability, and efficacy profile of our products following approval. If we do not succeed in one or more of these factors in a timely manner or at all, we could experience significant delays in our ability to successfully commercialize our current and future product candidates or be unable to commercialize product candidates at all. If we are unable to advance our preclinical- stage product candidates to clinical development, successfully complete clinical trials for our current and future product candidates, obtain regulatory approval, and ultimately commercialize our current and future product candidates, our business may be materially harmed. There is no guarantee that the results obtained in ~~current~~ preclinical studies or our ~~ongoing~~ clinical trials of our current and future product candidates will be sufficient to obtain regulatory approval or marketing authorization for such product candidates. **Additionally** ~~For example~~ , **even if regulatory authorities agree with** the **design and implementation of the** ~~FDA may require us to complete~~ clinical trials **set forth** in ~~addition to~~ **an IND** ~~our~~ **or** ~~ongoing pivotal Phase 2b~~ **other applicable regulatory submission, such regulatory authorities may change their requirements or recommendations in the future. The FDA, European Medicines Agency (“ EMA ”) or comparable foreign regulatory authorities may require the analysis of data from** clinical ~~trial~~ **trials** ~~and global Phase 3~~ **assessing different doses of a product candidate alone or in combination with other therapies to justify the selected dose prior to the initiation of larger** clinical ~~trial~~ **trials in a specific indication. Any delays** ~~for~~ **or** ~~zipalertinib in collaboration with~~ **failure to obtain regulatory approvals** ~~our~~ **or** ~~partners~~ **clearances to initiate our clinical trials may prevent us from completing our clinical trials or commercializing our current and future product candidates on a timely basis, if** at **all** ~~Taiho prior to granting regulatory approval~~ . Although we believe our product candidates and programs are uncorrelated, negative results in the development process of one product candidate could impact other product candidates or programs. **In autoimmune diseases, our product candidates may demonstrate different safety and or efficacy in each of the different diseases we plan on evaluating in our clinical trials.** For each of our **oncology** product candidates, antitumor activity may be different in each of the different tumor types we plan on evaluating in our clinical trials. Even as we build clinical experience with our product candidates, we may need to further discuss or meet with the FDA **and other comparable foreign regulatory authorities** to agree on the optimal patient population, clinical trial design, and size for each clinical trial in order to obtain regulatory approval, any of which may require significant additional resources and delay the timing of our clinical trials and ultimately the approval, if any, of any of our product candidates. **.Our approach to the identification,discovery,and development of targeted oncology product candidates may never lead to marketable products** .The scientific evidence to support the feasibility of developing product candidates based on our discoveries to date is both preliminary and limited.The patient populations for certain of our product candidates are limited to those with specific target mutations,and we will need to screen and identify these patients with the targeted mutations.Successful identification of patients is dependent on several factors,including achieving certainty as to how specific genetic alterations and larger classes of mutations,such as epidermal growth factor receptor **(" EGFR")** exon 20 insertion mutations,respond to our product candidates,and developing companion diagnostics to identify such genetic alterations.Furthermore,even if we are successful in identifying patients,we cannot be certain that the resulting patient populations for each mutation or class of mutations will be large enough to allow us to successfully obtain indications for each mutation type and to commercialize our ~~product~~ **products** ~~candidates~~ and achieve profitability.The FDA and other ~~comparable~~ regulatory authorities may not agree with our approach to seek labeling for groups of related mutations,rather than individual mutations,and may require us to conduct additional clinical trials and obtain separate approvals

for each individual mutation,which may further affect our ability to successfully commercialize our ~~product~~ **products** ~~candidates~~ ,if approved.In addition ~~,in autoimmune diseases,we may be unable to identify clinical features or biomarkers predictive of response,presenting potential challenges to broad development of our product candidates in one or more potential indications.Similarly~~ ,even if our approach is successful in showing clinical benefit for tumors harboring certain targeted mutations,we may never successfully identify additional oncogenic mutations.Therefore,we do not know if our approach **of treating patients with targeted oncology therapies** will be successful,and if our approach is **unsuccessful,our business will suffer** Difficulty in enrolling patients could delay or prevent clinical trials of our product candidates ~~,~~ and ultimately delay or prevent regulatory approval. Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of completion of our clinical trials depends in part on the speed at which we can recruit patients to participate in testing our product candidates, and we may experience delays in our clinical trials if we encounter difficulties in enrollment. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll enough eligible patients to participate in these clinical trials as required by the FDA or similar regulatory authorities outside the U. S., or as needed to provide appropriate statistical power for a given clinical trial. For example **, in early phase autoimmune disease development, identification of patients with appropriate disease severity and / or willingness to accept the potential risks associated with a novel approach to treating their disease could impair enrollment. Similarly** , because we are focused on patients with specific genetic mutations for the development of zipalertinib, our ability to enroll eligible patients may be limited or enrollment may be slower than we anticipate due to the small eligible patient population. In addition to the potentially small populations, the eligibility criteria of our planned clinical trials **for some of our product candidates** will further limit the pool of available clinical trial participants as we require that patients have specific characteristics, such as a certain severity or stage of disease progression, to include them in a clinical trial. Additionally, the process of finding eligible patients may prove costly. We also may not be able to identify, recruit, and enroll a sufficient number of patients to complete our clinical studies because of the perceived risks and benefits of the product candidate under clinical trial, the availability and efficacy of competing therapies and clinical trials, the proximity and availability of clinical trial sites for prospective patients **, the availability of patients with appropriate disease severity and extent of prior therapy in autoimmune disease indications** , the availability of genetic sequencing information for patient tumors so that we can identify patients with the targeted genetic mutations **for our oncology studies** , and the patient referral practices of physicians. If patients are unwilling to participate in our studies for any reason, the timeline for recruiting patients, conducting studies, and obtaining regulatory approval of potential products may be delayed. The enrollment of patients further depends on many factors, including: • the proximity of patients to clinical trial sites; • the design of the clinical trial; • our ability to recruit clinical trial investigators with the appropriate competencies and experience; • our ability to obtain and maintain patient consents; • our ability to enroll a diverse patient base in our clinical trials to meet FDA recommended guidance; • reporting of the preliminary results of any of our clinical trials; • the risk that patients enrolled in clinical trials will drop out of the clinical trials before clinical trial completion; and • factors we may not be able to control, such as **future** ~~current or potential~~ pandemics that may limit patients, principal investigators or staff or clinical site availability ~~(e. g., the COVID- 19 pandemic)~~ . In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us because some patients who might have opted to enroll in our clinical trials may instead opt to enroll in a clinical trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites. Moreover, because certain of our product candidates represent a departure from more commonly used methods for **autoimmune diseases or** cancer treatment and because certain of our product candidates have not been tested in humans before, potential patients and their doctors may be inclined to use conventional therapies, such as **conventional immune suppressing medications in autoimmune diseases or** chemotherapy **in oncology** , rather than enroll patients in any future clinical trial of our product candidates. If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenue from any of these product candidates could be delayed or prevented. Interim, " topline ", and preliminary data from our clinical trials that we announce or publish may change as more patient data become available and are subject to confirmation, audit, and verification procedures that could result in material changes in the final data. From time to time, we may publicly disclose preliminary or topline data from our preclinical studies and clinical trials, which ~~is~~ **are** based on a preliminary analysis of then- available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations, and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated **. For example, in April 2024, we announced the expansion of the development of CLN- 978 in autoimmune diseases based the treatment of three patients in a Phase 1 dose escalation trial of CLN- 978 in patients with relapsed / refractory B cell non- Hodgkin lymphoma (" B- NHL "). Results from our Phase 1b trials of CLN- 978 in systemic lupus erythematosus or other future trials may differ from the results of our prior Phase 1 trial in CLN- 978 in relapsed / refractory B- NHL** . Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. From time to time, we may also disclose interim data from our clinical trials. Interim data from clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment and treatment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data and final data could

significantly harm our business prospects and our ability to obtain approval for, and commercialize, our product candidates may be harmed. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock. We may not be able to file INDs ~~or ,~~ IND amendments **or other similar regulatory submissions outside of the U. S.** to commence additional clinical trials on the timelines we expect, and even if we are able to, the FDA or foreign regulatory authorities may not permit us to proceed. Each of our product candidates have INDs which are currently in effect. However, we may not be able to file future INDs for our other product candidates on the timelines we expect. Additionally, we may experience manufacturing delays or other delays with IND- enabling studies, or the FDA or other **comparable** regulatory authorities may require additional preclinical studies that we did not anticipate. Moreover, we cannot be sure that submission of an IND **or similar regulatory submissions** will result in the FDA **or other comparable regulatory authority** allowing clinical trials to begin, or that, once begun, issues will not arise that result in a decision by us, by IRBs or independent ethics committees, or by the FDA or other **comparable** regulatory authorities to suspend or terminate clinical trials, including as a result of a clinical hold. Additionally, even if the FDA or other **comparable** regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND **or other similar regulatory submission** , we cannot guarantee that they will not change their requirements or expectations in the future. These considerations also apply to new clinical trials we may submit as amendments to existing INDs or to a new IND. Any failure to file INDs **or similar regulatory submissions** on the timelines we expect or to obtain regulatory approvals for our clinical trials may prevent us from completing our clinical trials or commercializing our products on a timely basis, if at all **.** Our product candidates may cause undesirable side effects or have other properties that delay or prevent their regulatory approval,limit their commercial potential,or result in significant negative consequences following any potential marketing approval.Our product candidates may cause undesirable side effects.Additionally,the administration process or related procedures also can cause adverse side effects.Adverse events that occur in our clinical trials may cause us,or cause the FDA ~~,the EMA~~ or other **comparable** regulatory authorities,or IRBs,RECs,or equivalent organizations to order us to halt,delay or amend preclinical development or clinical development of our product candidates and could result in more restrictive ~~labelling~~ **labeling** or the denial of regulatory approval of our product candidates for any or all targeted indications.Even if serious adverse events are unrelated to study treatment,such occurrences could affect patient enrollment or the ability of enrolled patients to complete the clinical trial.In addition,if any of our product candidates are tested or used in combination with other drugs,such as our plans to potentially use CLN- 619 in combination with other agents,these combinations may have additional side effects,which could be more severe than those caused by either therapy alone.Furthermore,clinical trials by their nature utilize a sample of the potential patient population.With a limited number of patients and limited duration of exposure,rare and severe side effects of our product candidates or those of our competitors may only be uncovered when a significantly larger number of patients have been exposed to the ~~drug~~ **product candidate** .For example,while we believe that **CLN- 978,** zipalertinib and CLN- 619 have demonstrated manageable tolerability profiles thus far,there can be no assurance that they or any of our other product candidates will not cause more severe side effects in a greater proportion of patients.Moreover,if we elect,or are required,to delay,suspend or terminate any clinical trial of any of our product candidates,the commercial prospects of such product candidates or our other product candidates may be harmed,and our ability to generate product revenues from any of these product candidates may be delayed or eliminated.Any of these occurrences may harm our ability to develop other product candidates and may harm our business,financial condition,results of operations,and prospects significantly.If our product candidates receive marketing approval and we or others identify undesirable side effects caused by such product candidates (or any other similar drugs or biologics) after such approval,a number of potentially significant negative consequences could result,including:• regulatory authorities may withdraw or limit their approval of such product candidates;• regulatory authorities may require the addition of labeling statements,such as a " boxed " warning or a contraindication;• we may be required to change the way such product candidates are distributed or administered,conduct additional clinical trials or change the labeling of the product candidates **with the potential restriction of their clinical use** ;• regulatory authorities may require a Risk Evaluation and Mitigation Strategy (" REMS") plan to mitigate risks,which could include medication guides,physician communication plans,or elements to assure safe use,such as restricted distribution methods,patient registries,and other risk minimization tools;• we may be subject to regulatory investigations and government enforcement actions;• we may decide to remove such product candidates from the marketplace;• **personal** ~~we could be sued and held liable for~~ injury ~~caused to individuals~~ **claims,actions,lawsuits and proceedings that may arise from** ~~exposed~~ - **exposure** to or taking our product candidates;and • our reputation may suffer.We believe that any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidates and could substantially increase the costs of commercializing our product candidates,if approved,and significantly impact our ability to successfully commercialize our product candidates and generate revenues.Since the number of patients that have been and will be dosed in our ongoing clinical trials is small,the results from such clinical trials,once completed,may be less reliable than results achieved in larger clinical trials,which may hinder our efforts to obtain regulatory approval for our product candidates.The preliminary results of clinical trials with smaller sample sizes can be disproportionately influenced by various biases associated with the conduct of small clinical trials,such as the potential failure of the smaller sample size to accurately depict the characteristics of the broader patient population,which limits the ability to generalize the results across a broader community,thus making the clinical trial results less reliable than clinical trials 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.Further,the FDA or other **comparable** regulatory authorities may require us to conduct additional and larger clinical trials than we may plan to support applications for marketing authorization.If we conduct any future clinical trials of our current and future product candidates,we may not achieve a positive or statistically significant result or the same level of statistical significance,if any,that we might have anticipated based on prior results.We are currently conducting and may in the future conduct clinical trials for product candidates outside the U.S.,and the FDA and comparable foreign regulatory authorities may not accept data from such trials.We are ~~evaluating our current product~~

~~candidates in clinical trials that include centers located inside and outside of the U.S.We may also in the future choose to conduct~~ **conducting** ~~one~~ **clinical trials** ~~or~~ **for our product candidates** ~~more additional clinical trials~~ outside the U.S.,including in Europe and Australia.The acceptance of study data from clinical trials conducted outside the U.S.or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all.If data from foreign clinical trials are intended to serve as the basis for marketing approval in the U.S.,the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S.population and U.S.medical practice,and (ii) the clinical trials were performed by clinical investigators of recognized competence and pursuant to good clinical practice (" GCP") regulations.Additionally,the FDA' s clinical trial requirements,including sufficient size of patient populations and statistical powering,must be met.Many foreign regulatory authorities have similar approval requirements.In addition,foreign clinical trials are subject to the applicable local laws of the foreign jurisdictions where the clinical trials are conducted.We would need to conduct additional trials if the FDA or any comparable foreign regulatory authority does not accept data from clinical trials conducted outside of the U.S.or the applicable foreign jurisdiction,which could be costly and time- consuming,and which may result in product candidates that we may develop not **receiving approval for commercialization in the U.S.or any such foreign jurisdiction** . We intend to develop CLN- 619 and potentially other product candidates in combination with other therapies, which exposes us to additional risks. We intend to develop CLN- 619 and potentially other product candidates in combination with one or more approved or unapproved therapies to treat cancer or other diseases. Even if any product candidate we develop were to receive marketing approval for use in combination with other approved therapies, the FDA, the EMA, or comparable foreign regulatory authorities outside of the U. S. could still revoke approval of the therapy used in combination with our product. If the therapies used in combination with our product candidates are replaced as the standard of care for the indications we choose for any of our product candidates, the FDA, EMA or comparable foreign regulatory authorities may require us to conduct additional clinical trials. The occurrence of any of these risks could result in our own products, if approved, being removed from the market or being less successful commercially. Further, we will not be able to market and sell any product candidate we develop in combination with an unapproved ~~cancer~~ therapy for a combination indication if that unapproved therapy does not ultimately obtain marketing approval either alone or in combination with our product. In addition, unapproved ~~cancer~~ therapies face the same risks described with respect to our product candidates currently in development and clinical trials, including the potential for serious adverse effects, delay in their clinical trials and lack of FDA approval. If the FDA, EMA or comparable foreign regulatory authorities do not approve these other products or revoke their approval of, or if safety, efficacy, quality, manufacturing or supply issues arise with the products we choose to evaluate in combination with our product candidate, we may be unable to obtain approval of or market such combination therapy. If we are unable to successfully validate, develop, and obtain regulatory approval for any required companion diagnostic tests for our product candidates or experience significant delays in doing so, we may fail to obtain approval or may not realize the full commercial potential of these product candidates. In connection with the clinical development of our product candidates for certain indications, we need to develop or obtain access to in vitro companion diagnostic tests to identify patient subsets within a disease category who may derive benefit from our product candidates, as we are targeting certain genetically defined populations for our treatments. Such companion diagnostics may be used during our clinical trials and may be required in connection with the FDA approval of our product candidates. To be successful, we or our collaborators will need to address a number of scientific, technical, regulatory, and logistical challenges. Companion diagnostics are subject to regulation by the FDA, the EMA, and other **comparable** regulatory authorities as medical devices and require separate regulatory approval prior to commercialization. Given our limited experience in developing and commercializing diagnostics, we may rely on third parties for the design, development, and manufacture of companion diagnostic tests for our product candidates that may require such tests. If we enter into such collaborative agreements, we will be dependent on the sustained cooperation and effort of our future collaborators in developing and obtaining approval for these companion diagnostics. We and our future collaborators may encounter difficulties in developing and obtaining approval for the companion diagnostics, including issues relating to selectivity / specificity, analytical validation, reproducibility, or clinical validation of companion diagnostics. We and our future collaborators also may encounter difficulties in developing, obtaining regulatory approval for, manufacturing, and commercializing companion diagnostics similar to those we face with respect to our product candidates themselves, including issues with achieving regulatory clearance or approval, production of sufficient quantities at commercial scale and with appropriate quality standards, and in gaining market acceptance. If we are unable to successfully develop companion diagnostics for these product candidates, or experience delays in doing so, the development of these ~~therapeutic~~ product candidates may be adversely affected or these product candidates may not obtain marketing approval or such approval may be delayed, and we may not realize the full commercial potential of any of these product candidates that obtain marketing approval. As a result, our business, results of operations, and financial condition could be materially harmed. In addition, a diagnostic company with whom we contract may decide to discontinue developing, selling or manufacturing the companion diagnostic test that we anticipate using in connection with development and commercialization of our product candidates or our relationship with such diagnostic company may otherwise terminate. We may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our product candidates or do so on commercially reasonable terms, which could adversely affect and / or delay the development or commercialization of our product candidates. Our product candidates may cause undesirable side..... or any such foreign jurisdiction. Risks Related to Our Financial Condition and Capital Requirements Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability. We began substantive operations in 2017. Our operations to date have **involved** ~~been limited to~~ organizing and staffing our company, business planning, raising capital, identifying, acquiring, and investing in potential product candidates, undertaking clinical trials, building our intellectual property portfolio, and establishing arrangements and collaborating with third

parties for identification, discovery and research activities, preclinical studies, clinical trials, and the manufacture of initial quantities of our product candidates and component materials. We have not yet demonstrated our ability to successfully conduct late- stage ~~clinical trials, complete any~~ clinical trials, obtain marketing approvals, manufacture a commercial- scale product or arrange for a third party to do so on our behalf, or conduct sales, marketing, and distribution activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history. We have incurred significant losses since inception, and we expect to incur losses over the next several years and may not be able to achieve or sustain revenues or profitability in the future. Investment in biopharmaceutical product development is a highly speculative undertaking and entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval, and become commercially viable. We are still in the early stages of development of our product candidates. 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. We have financed our operations primarily through the sale of equity securities. We have ~~incurred~~ **a history of** significant net losses ~~in each period~~ since we began substantive operations ~~, with the exception of 2022~~. For **2024 and** 2023 ~~and 2022~~, we reported a net loss of $ **167. 6 million and $** 155. 1 million ~~and net income of $ 109. 2 million~~, respectively. As of December 31, ~~2023~~ **2024**, we had an accumulated deficit of $ ~~200~~ **368**. ~~9~~ **2** million. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase substantially if and as we: • continue our research and development efforts and submit INDs for our current and future product candidates; • conduct preclinical studies and clinical trials for our current and future product candidates; • experience any delays or encounter any issues with any of the above, including but not limited to failed studies, complex results, safety issues, or other regulatory challenges; • develop the necessary processes, controls, and manufacturing capabilities to obtain marketing approval for our product candidates and to support manufacturing on a commercial scale; • seek regulatory approvals for any product candidates that successfully complete clinical trials, if any; • hire and retain additional personnel, such as non- clinical, clinical, pharmacovigilance, quality assurance, regulatory affairs, manufacturing, distribution, legal, compliance, medical affairs, finance, general and administrative, commercial, and scientific personnel; • establish a sales, marketing, and distribution infrastructure and scale- up manufacturing capabilities, whether alone or with third parties, to commercialize any current and future product candidates for which we may obtain regulatory approval; and • develop, maintain, expand, and protect our intellectual property portfolio. Because of the numerous risks and uncertainties associated with developing pharmaceutical product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all. 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 seek regulatory approval for additional product candidates or additional indications. We may encounter unforeseen expenses, difficulties, complications, delays, and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. We have not generated any revenue from the sale of our product candidates and may never be profitable. Our ability to become profitable depends upon our ability to generate revenue. Other than a previous licensing agreement, we have not generated any other license or collaboration revenue or any sales revenue from any of our product candidates. We do not expect to generate significant sales revenue or commercial revenue from the sale or license of one or more of our preclinical programs or product candidates unless or until we successfully complete clinical development and obtain regulatory approval of, and then successfully commercialize, at least one of our product candidates or, alternatively, enter into agreements with third parties for the purchase, collaboration, or license of one of our product candidates. We are currently advancing CLN- ~~619~~ **978**, CLN- ~~978~~ **619**, zipalertinib (pursuant to the co-development agreement with **an affiliate of** Taiho), CLN- 049 ~~, CLN- 418~~, and CLN- 617 in clinical development, in addition to our other programs that are in the preclinical stages of development and will require additional preclinical studies. All of our product candidates will require additional clinical development, regulatory review and approval, substantial investment, access to sufficient commercial manufacturing capacity, and significant marketing efforts before we can generate any revenue from product sales. Our ability to generate revenue depends on a number of factors, including, but not limited to: • timely completion of our preclinical studies and clinical trials, which may be significantly slower or cost more than we currently anticipate and will depend substantially upon the performance of third- party contractors; • our ability to complete IND- enabling studies and successfully submit INDs or comparable applications for our product candidates; • whether we are required by the FDA or similar foreign regulatory authorities to conduct additional clinical trials or other studies beyond those planned to support the approval and commercialization of our current and future product candidates; • our ability to timely seek and obtain regulatory and marketing approvals for any of our current and future product candidates; • the prevalence, duration, and severity of potential side effects or other safety issues experienced by patients receiving our current and future product candidates; • the willingness of physicians, operators of clinics, and patients to utilize or adopt any of our current and future product candidates over alternative or more conventional therapies, such as chemotherapy; • the actual and perceived availability, cost, risk profile, and efficacy of our current and future product candidates, if approved, relative to existing and future alternative ~~cancer~~ therapies and competitive product candidates and technologies; • the equal cost- sharing structure for clinical development and commercialization costs of zipalertinib in the U. S. and the equal profit- sharing structure from potential future U. S. sales of zipalertinib, each pursuant to the co- development agreement with **an affiliate of** Taiho; • our ability and the ability of third parties with whom we contract to manufacture adequate clinical and commercial supplies of our current and future product candidates, remain in good standing with regulatory authorities and develop, validate, and maintain commercially viable manufacturing processes that are compliant with current good manufacturing practices (" cGMP"); • our ability to successfully develop a commercial strategy and thereafter commercialize our current and future product candidates in the U. S. and

internationally, if approved for marketing, reimbursement, sale, and distribution in such countries and territories, whether alone or in collaboration with others; • patient demand for our current and future product candidates, if approved; and • our ability to establish and enforce intellectual property rights in and for our current and future product candidates. Many of the factors listed above are beyond our control and could cause us to experience significant delays or prevent us from obtaining regulatory approvals or commercializing our current and future product candidates. Even if we are able to commercialize our current and future product candidates, we may not achieve profitability soon after generating product sales, if ever. If we are unable to generate sufficient revenue through the commercial sale of our current and future product candidates, or from agreements with third parties for the purchase, collaboration, or license of one or more of our product candidates, we may be unable to continue operations without continued funding. We will require substantial additional funding to develop and commercialize our current and future product candidates. If we are unable to raise capital when needed, we would be compelled to delay, reduce, or eliminate our product development programs or other operations. The development of pharmaceutical products is capital intensive. We are currently advancing CLN- ~~619~~ **978**, CLN- ~~978~~ **619**, zipalertinib (pursuant to the co- development agreement with **an affiliate of** Taiho), CLN- 049 ~~, CLN- 418~~, and CLN- 617 in clinical development and making further investments in our preclinical programs. We expect our expenses to increase in parallel with our ongoing activities, as described above under the risk factor entitled " We have incurred significant losses since inception, and we expect to incur losses over the next several years and may not be able to achieve or sustain revenues or profitability in the future. " We have estimated our current additional funding needs based on assumptions that may prove to be wrong. Changing circumstances may cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We cannot be certain that additional funding will be available on acceptable terms, or at all. Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through a combination of public or private equity offerings, debt financings, governmental funding, collaborations, strategic partnerships, and alliances, or marketing, distribution, or licensing arrangements with third parties. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce, or eliminate our identification, discovery, and preclinical or clinical development programs, or any future commercialization efforts. ~~We~~ **As of December 31, 2024, we** had cash ~~and~~ **,** cash equivalents, **and** short- term investments **of $ 399. 0 million**, **and long- term investments** and interest receivable of $ ~~468~~ **207**. ~~3~~ **9** million ~~as of December 31, 2023~~. We believe that, based upon our current operating plan, our existing capital resources will be sufficient to fund our anticipated operations into ~~the second half of 2026~~ **2028**. Our future capital requirements will depend on many factors, including: • the scope, progress, results, and costs of drug discovery, laboratory testing, manufacturing and preclinical and clinical development for our current and future product candidates; • the extent to which we enter into additional collaboration arrangements with regard to product discovery or acquire or in- license products or technologies; • our ability to establish additional discovery collaborations on favorable terms, if at all; • the costs, timing, and outcome of regulatory review of our product candidates; • the costs of future commercialization activities, including product sales, marketing, manufacturing, and distribution, for any of our product candidates for which we receive marketing approval; • revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval, or from licensing or collaboration agreements pursuant to which we may receive milestone, royalty, or other revenue from third parties developing or commercializing our product candidates; and • the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property- related claims. If we engage in acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks. **We have** ~~In June 2022, we sold our equity interest in Cullinan Pearl, formerly a development subsidiary of the Company, to Taiho and we entered into~~ a co- development agreement with an affiliate of Taiho to co- develop and, at our option, co- commercialize zipalertinib in the U. S. Pursuant to the terms of the co- development agreement with **an affiliate of** Taiho, development costs for zipalertinib ~~incurred after the sale of our equity interest in Cullinan Pearl~~ are shared equally between us and Taiho, with each party receiving 50 % of any future pre- tax profits from potential U. S. sales of zipalertinib. We intend to engage in various acquisitions and strategic partnerships in the future, including licensing or acquiring products, intellectual property rights, technologies, or businesses. Any acquisition or strategic partnership, including the co- development agreement with **an affiliate of** Taiho, may entail numerous risks to us, including: • increased operating expenses and cash requirements; • the assumption of indebtedness or contingent liabilities; • the issuance of equity securities which would result in dilution; • assimilation of operations, intellectual property, products, and product candidates of an acquired company, including difficulties associated with integrating new personnel; • the diversion of financial and managerial resources from our existing product programs and initiatives in pursuing such an acquisition or strategic partnership; • retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships; • risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; • our inability to generate revenue from acquired intellectual property, technology, and / or products sufficient to meet our objectives or even to offset the associated transaction and maintenance costs; • risk of conducting research and development activities in new therapeutic areas or treatment modalities in which we have little to no experience; • successfully negotiating a proposed acquisition, in- license or investment in a timely manner and at a price or on terms and conditions favorable to us; • successfully combining and integrating a potential acquisition into our existing business to fully realize the benefits of such acquisition; • the impact of regulatory reviews on a proposed acquisition, in- license or investment; and • the outcome of any legal proceedings that may be instituted with respect to the proposed acquisition, in- license or investment. If we fail to properly evaluate potential acquisitions, in- licenses, investments or other transactions associated with the creation of new research and development programs or the maintenance of existing ones, we might not achieve the anticipated benefits of any such transaction, we might incur costs in excess of what we anticipate, and management resources and attention might be diverted from other necessary or

valuable activities. 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 on unfavorable terms to us. To the extent that we raise additional capital through the sale of equity or convertible debt securities, existing ownership interests will be diluted, and the terms may include liquidation or other preferences that adversely affect the rights of our stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take certain actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through strategic partnerships with third parties, we may have to relinquish valuable rights to our technologies or product candidates, future revenue streams, research programs or product candidates or grant licenses on terms that are not favorable to us. If we are unable to raise additional capital when needed, we would be required to delay, limit, reduce or terminate our product development or commercialization efforts for our current and future product candidates. Our stockholders will experience substantial additional dilution if outstanding stock options are exercised for common stock. As of ~~March 1~~ **February 19** , ~~2024~~ **2025** , the number of shares of our common stock outstanding excludes approximately ~~12~~ **13** . ~~1~~ **7** million shares of common stock issuable upon the exercise of stock options, having a weighted- average exercise price of $ 15. ~~84~~ **31** per share. The exercise of outstanding stock options for common stock would be substantially dilutive to existing stockholders. As of ~~March 1~~ **February 19** , ~~2024~~ **2025** , the number of shares of our common stock outstanding also excludes approximately ~~1~~ **0** . ~~6~~ **3 million shares of common stock issuable upon the exercise of pre- funded warrants having an exercise price of $ 0. 001 per share, approximately 2. 3** million shares of common stock issuable upon vesting of restricted stock units (assuming the Company achieves its corporate stock price metrics at the target achievement level), approximately ~~2~~ **1** . ~~2~~ **8** million shares of common stock reserved for future issuance under our 2021 Stock Option and Incentive Plan and ~~1~~ **2** . ~~7~~ **2** million shares of common stock reserved for future issuance under our 2021 Employee Stock Purchase Plan, as amended. Any dilution or potential dilution may cause our stockholders to sell their shares, which may contribute to a downward movement in the stock price of our common stock. Our operations and financial condition have been and could continue to be adversely affected by global and regional economic conditions in ways we may not be able to predict or control. Our operations and financial condition have been and could continue to be adversely affected by global or regional economic conditions if markets decline in the future, whether related to a public health crisis similar to the COVID- 19 pandemic, the Russian invasion of Ukraine, the Israel- Hamas war, U. S **.** - China relations, U. S.- Iran relations, higher inflation or interest rates, recession, natural disasters, impacts of and issues related to climate change, business disruptions, our ability to adequately staff operations or otherwise. Additionally, escalation in interest rates, in conjunction with banking failures, may lead to financial institutions being more prudent with capital deployment and tightening lending, especially in relation to construction and real estate development. Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses. Our operations, and those of our CROs, **contract manufacturing organizations (“** CMOs **”)** and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man- made disasters or business interruptions. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third- party manufacturers to produce our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man- made or natural disaster or other business interruption. Risks Related to Our Corporate Structure We may not be successful in our efforts to build a pipeline of product candidates with commercial value. ~~A key~~ We may not be successful in our efforts in building a pipeline of product candidates for the treatment of various ~~autoimmune diseases and~~ cancers through acquisitions,licensing or through internal development or in progressing these product candidates through clinical development.Although we analyze whether we can replicate scientific results observed prior to our acquisition or investment in a product candidate,we may not be successful in doing so after our investment.For example, ~~pharmacodynamic activity of B cell depleting agents such as CLN- 978 has not always been associated with sufficient anti- disease activity to support broad development in indications of sufficient commercial opportunity.Similarly,~~ we may not be successful in identifying additional genetic mutations which are oncogenic and which can be “ basketed ” into a group that is large enough to present **a sufficient commercial opportunity or that is druggable with one chemical compound.Additionally,we are pursuing additional in- licenses or acquisitions of development- stage assets or programs,which entails additional risk to us.** element of our strategy is to form or seek strategic alliances, create joint ventures or collaborations, or enter into licensing arrangements with third parties for programs, product candidates, technologies or intellectual property that we believe are novel, employ differentiated mechanisms of action, are more advanced in development than competitors, or have a combination of these attributes. We face significant competition in seeking appropriate strategic partners and licensing and acquisition opportunities, and the negotiation process is time- consuming and complex. We may not be successful in our..... which entails additional risk to us. Identifying, selecting, and acquiring promising product candidates requires substantial technical, financial and human resources expertise. Efforts to do so may not result in the actual acquisition or license of a successful product candidate, potentially resulting in a diversion of our management’ s time and the expenditure of our resources with no resulting benefit. For example, if we are unable to identify programs that ultimately result in approved products, we may spend material amounts of our capital and other resources evaluating, acquiring, and developing products that ultimately do not provide a return on our investment. We have terminated programs and expect to terminate programs in the future if they do not meet our criteria for advancement **. For example, following a review of the data from our Phase 1 clinical trial in CLN- 418, we decided to discontinue development of CLN- 418 and terminated the license agreement with Harbour BioMed US Inc** . We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success. Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other

product candidates or for other indications that later prove to have greater commercial potential. If we do so, we may never realize the anticipated benefits of these decisions and, as a result, we may be required to forego or delay other opportunities. In addition, our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Certain agreements provide our licensors, collaborators, or other shareholders in our development subsidiaries with rights that could delay or impact the potential sale of our development subsidiaries or could impact our ability to sell assets, or enter into strategic alliances, collaborations, or licensing arrangements with other third parties. We license intellectual property from third parties for several of our product candidates and have raised capital from third- party investors for CLN- 619, CLN- 049 and CLN- 617. These third parties have certain rights that could delay collaboration, licensing or other arrangement with another third party, and the existence of these rights may adversely impact the ability to attract an acquirer or partner. These rights include rights of negotiation and fees payable upon a sale of assets or change of control of a subsidiary that are contained in license agreements, as well as rights such as drag- along rights in agreements with shareholders of the subsidiary. In addition, we will also owe the licensors of CLN- 049 and CLN- 617 a success fee in the event of a sale or other disposition of the majority of the assets of the development subsidiaries holding these product candidates. These fees will reduce the net proceeds we receive from any such sale or disposition of assets. We have also entered into investor rights and voting agreements with third- party investors, which may delay or impact our ability to sell our equity interests in or the assets of our development subsidiaries. For example, we would need to comply with certain notice and other provisions, such as a drag- along provision in the event of sale of the subsidiary, which may delay or prevent a specific transaction or make transacting with our subsidiaries and us less attractive to third parties. We may enter into similar agreements with future partners or investors that in each case may contain similar provisions or other terms that are not favorable to us. Our reliance on a ~~central team consisting of a~~ limited number of employees presents operational challenges that may adversely affect our business. As of December 31, ~~2023~~ **2024** , we had ~~85~~ **111** full- time employees upon which we rely for various research and development, administrative and other support services. **The** ~~While we believe this structure enables us to reduce certain infrastructure costs, the~~ small size of our ~~centralized~~ team may limit our ability to devote adequate personnel, time, and resources to our research and development activities, and the management of financial, accounting, and reporting matters. If our ~~centralized~~ team fails to provide adequate research and development, administrative, or other services ~~across our entire organization~~ , our business, financial condition, and results of operations could be harmed **. We will no longer qualify as an " emerging growth company " nor a " smaller reporting company " after December 31, 2024, and, as a result, we will have to comply with increased disclosure and compliance requirements. Prior to December 31, 2024, we were an " emerging growth company " (" EGC ") as defined in the Jumpstart Our Business Startups Act and a " smaller reporting company " (" SRC ") under the Securities and Exchange Commission (" SEC ") rules. However, because (i) the market value of our common stock held by non- affiliates exceeded $ 700 million as of June 30, 2024, (ii) we have been a public company for more than one year, and (iii) we have filed at least one annual report, we no longer qualified as an EGC or a SRC as of December 31, 2024 and became a large accelerated filer beginning January 1, 2025. As a large accelerated filer, we are subject to certain disclosure and compliance requirements that apply to other public companies but that did not previously apply to us due to our status as an EGC and a SRC. These requirements include, but are not limited to: • the requirement that our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting under Section 404 (b) of the Sarbanes- Oxley Act of 2002; • compliance with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor' s report providing additional information about the audit and the financial statements; • the requirement that we provide more detailed disclosures regarding executive compensation; and • the requirement that we hold a non- binding advisory vote on executive compensation and obtain stockholder approval of any golden parachute payments not previously approved. We expect that the loss of EGC and SRC status and compliance with the additional requirements of being a large accelerated filer will increase our legal, accounting and financial compliance costs, and cause management and other personnel to divert attention from operational and other business matters to devote substantial time to public company reporting requirements. In addition, if we are not able to comply with changing requirements in a timely manner, the market price of our stock could decline and we could be subject to sanctions or investigations by the stock exchange on which our common stock is listed, the SEC or other regulatory authorities, which would require additional financial and management resources** . Risks Related to Potential Commercialization Even if we obtain regulatory approval of our product candidates, the products may not gain market acceptance among physicians, patients, hospitals, ~~cancer~~ treatment centers, and others in the medical community. The use of ~~targeted~~ **T cell engagers in immunology and** oncology ~~medicines as a potential cancer treatment~~ is a recent development and may not become broadly accepted by physicians, patients, hospitals, ~~cancer~~ treatment centers, and others in the medical community. Various factors will influence whether our product candidates are accepted in the market, including: • the clinical indications for which our product candidates are licensed; • physicians, hospitals, ~~cancer~~ treatment centers, and patients considering our product candidates as a safe and effective treatment; • the potential and perceived advantages of our product candidates over alternative treatments; • the prevalence and severity of any side effects caused by our product candidates; • the prevalence and severity of any side effects for other precision medicines and public perception of other precision medicines; • product labeling or product insert requirements of the FDA or other **comparable** regulatory authorities; • limitations or warnings contained in the labeling approved by the FDA; • the timing of market introduction of our product candidates as well

as competitive products; • the cost of treatment in relation to alternative treatments; • the availability of adequate coverage, reimbursement and pricing by third- party payors and government authorities; • the willingness of patients to pay out- of- pocket in the absence of coverage by third- party payors and government authorities; • relative convenience and ease of administration, including as compared to alternative treatments and competitive therapies; and • the effectiveness of our sales and marketing efforts. If our product candidates are licensed but fail to achieve market acceptance among physicians, patients, hospitals, ~~cancer~~ treatment centers or others in the medical community, we will not be able to generate significant revenue. Even if our product candidates achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our products, are more cost effective or render our products obsolete. We face substantial competition, which may result in others discovering, developing, or commercializing products before or more successfully than we do. The biotechnology and pharmaceutical industries are characterized by the rapid evolution of technologies and understanding of disease etiology, intense competition, and a strong emphasis on intellectual property. We face, and will continue to face, competition from companies focused on more traditional therapeutic modalities, such as small- molecule inhibitors. We believe that our differentiated business model, approach, scientific capabilities, know- how, and experience provide us with competitive advantages. However, we expect substantial competition from multiple sources, including major pharmaceutical, specialty pharmaceutical, and existing or emerging biotechnology companies, academic research institutions, governmental agencies, and public and private research institutions worldwide. Many of our competitors, either alone or through collaborations, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Smaller or early- stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and recruiting patients in clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result, our competitors may discover, develop, license or commercialize products before or more successfully than we do. Product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition, and the availability of reimbursement from government and other third- party payors. Our competitors may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidates. The availability of reimbursement from government and other third- party payors will also significantly affect the pricing and competitiveness of our products. Our competitors may also obtain FDA or other **comparable** regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. If our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient to administer, are less expensive or with a more favorable label than our product candidates, we could see a reduction or elimination in our commercial opportunity. For additional information regarding our competition, see the section of this Annual Report on Form 10- K titled " Business — Competition. " The insurance coverage and reimbursement status of newly- approved products is uncertain. Our product candidates may become subject to unfavorable pricing regulations, third- party coverage and reimbursement practices, or healthcare reform initiatives, which would harm our business. Failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue. The regulations that govern marketing approvals, pricing, coverage, and reimbursement for new drugs vary widely from country to country. Some countries require approval of the sale price of a drug before the product can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval. In the U. S. and markets in other countries, patients generally rely on third- party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental authorities or healthcare programs, such as Medicare and Medicaid, and private payors, such as health plans, is critical to new product acceptance. Our ability to successfully commercialize our product candidates will depend in part on the extent to which adequate coverage and reimbursement for these products and related treatments will be available from government authorities and programs as well as private health insurers and other organizations. Government authorities and other third- party payors decide which products will be covered and establish reimbursement levels for the products (or the services provided using the products). If coverage and adequate reimbursement is not available, or is available but limited, we may not be able to successfully commercialize our product candidates. Under such circumstances, we may not be able to establish or maintain pricing sufficient to realize a sufficient return on our investment. Within the U. S., no uniform policy of coverage and reimbursement for drug products exists among third- party payors. Coverage and reimbursement for new drug products is uncertain and, if applicable, can differ significantly from payor to payor. New products face particular coverage and reimbursement challenges. To obtain or maintain coverage and reimbursement for any approved drug product, we may need to conduct expensive pharmacoeconomic studies or otherwise provide evidence to demonstrate the medical necessity and cost- effectiveness of our product. These studies will be in addition to the studies required to obtain or maintain regulatory approvals. If third- party payors do not consider a product to be cost- effective compared to other available therapies, they may not cover the product or, if they do, the level of payment may not be sufficient to allow sale of a product at a profit. Even if third- party

payors provide some coverage, the third- party payors may impose limits on the coverage or controls to manage utilization of products. Third- party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication and can exclude drugs from their formularies in favor of competitor drugs or alternative treatments. Payors may also impose step edits that require patients to try alternative, including generic, treatments before authorizing payment for our products, limit the types of diagnoses for which coverage will be provided, require pre-approval (known as " prior authorization ") for coverage of a prescription for each patient (to allow the payor to assess medical necessity) or impose a moratorium on coverage for products while the payor makes a coverage decision. Moreover, a third-party payor' s decision to provide coverage for a product does not mean that an adequate reimbursement rate will be approved. We may be required to provide mandatory discounts or rebates to certain purchasers to obtain coverage under federal healthcare programs, or to sell products to government purchasers. We also may have to offer discounts or rebates to private third- party payors to obtain favorable coverage. **There has been significant consolidation in the health insurance industry, increasing the leverage of large insurers and pharmacy benefit managers in pricing and other negotiations and potentially impacting potential drug product sales, business and results of operations.** Reimbursement rates may vary according to the use of the drug and the clinical setting in which the drug is used; they may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Adequate third- party reimbursement may not be available to enable us to maintain net price levels sufficient to realize an appropriate return on our investment in product development **. The containment of healthcare costs has become a priority of federal and state governments, and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption or enhancement of price controls and cost- containment measures could further limit a company' s revenue generated from the sale of any approved products. Coverage policies and third- party payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future** . Our inability to promptly obtain coverage and profitable payment rates from both government- funded and private payors for any approved products we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize product candidates, and our overall financial condition. Outside the U. S., governmental authorities and other third- party payors have also attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the U. S. Other countries allow companies to fix their own prices for medicines, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the U. S., the reimbursement for products may be reduced compared with the U. S. and may be insufficient to generate commercially reasonable revenues and profits. Additionally, we may develop companion diagnostic tests for use with our product candidates. We, or our collaborators, may be required to obtain coverage and reimbursement for these tests separate and apart from the coverage and reimbursement we seek for our product candidates, once approved. Even if we obtain regulatory approval or clearance for such companion diagnostics, there is significant uncertainty regarding our ability to obtain coverage and adequate reimbursement for the same reasons applicable to our product candidates. Our inability to promptly obtain coverage and adequate reimbursement from both third- party payors for the companion diagnostic tests that we develop and for which we obtain regulatory approval could have a material and adverse effect on our business, financial condition, results of operations and prospects. We expect ongoing initiatives from government and private payors to control utilization and costs of healthcare generally and drug products specifically, which initiatives could reduce demand for any product candidates for which we obtain marketing approval or limit the prices that we may charge for such products. Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations. The U. S. and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our product candidates or any future product candidates, restrict or regulate post- approval activities and affect our ability to profitably sell a product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record- keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. In the U. S. and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory reforms affecting the delivery of, and payment for, healthcare services, including cost-containment measures that may limit coverage and reimbursement for newly approved drugs and affect our ability to profitably sell any product candidates for which we obtain marketing approval. In particular, there have been and continue to be a number of initiatives at the U. S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For additional information regarding healthcare reform, see the section of this Annual Report on Form 10- K titled " Business — Governmental Regulation — Healthcare Reform. " Within the U. S., for example, the ACA was enacted in 2010 and has substantially changed the way healthcare is financed by both governmental and private insurers and significantly affected the pharmaceutical industry. Since its enactment, there have been judicial, congressional, and executive branch challenges to the ACA. For example, tax reform legislation was enacted that eliminated the tax penalty established by ACA for individuals who do not maintain mandated health insurance coverage beginning in 2019 and, in 2021, the U. S. Supreme Court dismissed the latest judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Beyond the ACA, there have been ongoing healthcare reform efforts ~~, including under the Biden administration~~ . Significantly,

the **Inflation Reduction Act (the"** IRA **") of 2022** includes a number of healthcare reform provisions. The IRA, which has varying implementation dates, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces; eliminates the " donut hole " under the Medicare Part D program by lowering the beneficiary maximum out- of- pocket cost and establishing a new manufacturer discount program; imposes new Medicare Part B and Part D drug price inflation rebates, and implements a drug price negotiation program for certain high spend Medicare Part B and D drugs. **The IRA is anticipated to have a significant impact on the pharmaceutical industry.** Such healthcare reform efforts have been and likely will continue to be subject to legal challenge. Further, there has been heightened governmental scrutiny in the U. S. of pharmaceutical pricing practices in light of the rising cost of prescription drugs. Such scrutiny has resulted in several congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing; review the relationship between pricing and manufacturer patient programs **; assess the role of pharmacy benefit managers in prescription drug pricing** ; and reform government program reimbursement methodologies for products. For example, in addition to the IRA drug pricing reforms, federal legislation ~~enacted in 2021~~ eliminated the statutory cap on Medicaid drug rebate program rebates (currently set at 100 % of a drug' s " average manufacturer price ") effective January 1, 2024. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third- party payors or other restrictions could harm our business, financial condition, results of operations and prospects. In addition, hospitals and health systems are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare services. This could reduce the ultimate demand for our product candidates, if approved, or put pressure on our product pricing, which could negatively affect our business, financial condition, results of operations and prospects. **Drug pricing and payment reform was a focus of the prior Trump administration and that focus is likely to continue under the new Trump administration. Other potential healthcare reform efforts under the Trump administration may affect access to healthcare coverage or the funding of health care benefits. There is significant uncertainty regarding the nature or impact of any such reform implemented by the Trump administration through executive action or by Congress.** The continuing efforts of the government as well as third- party payors to **limit access to healthcare, reduce the scope of coverage of healthcare,** contain or reduce costs of healthcare and / or impose price controls may adversely affect: • the demand for our product candidates, if we obtain regulatory approval; • our ability to set a price that we believe is fair for our products; • our ability to obtain coverage and reimbursement approval for a product; • our ability to generate revenue and achieve or maintain profitability; • the level of taxes that we are required to pay; and • the availability of capital. General legislative cost control measures may also affect reimbursement for our product candidates. The Budget Control Act, as amended, resulted in the imposition of reductions in Medicare (but not Medicaid) payments to providers in 2013 and will remain in effect through 2032 ~~(except May 1, 2020 to March 31, 2022)~~ unless additional ~~Congressional~~ **congressional** action is taken. Any significant spending reductions affecting Medicare, Medicaid or other publicly funded or subsidized health programs that may be implemented and / or any significant taxes or fees that may be imposed on us could have an adverse impact on our results of operations. We expect that current and any future healthcare **reform** or budget ~~reform~~ measures in the U. S. or abroad may result in more rigorous coverage criteria, new payment methodologies and additional downward pressure on the payment that we receive or price that we may charge for any approved product. The implementation of such reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates, if approved. 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 litigation as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, product liability claims may result in: • decreased demand for our product candidates or products that we may develop; • injury to our reputation; • withdrawal of clinical trial participants; • initiation of investigations by regulators; • costs to defend the related litigation; • a diversion of management' s time and our resources; • substantial monetary awards to clinical trial participants or patients; • product recalls, withdrawals or labeling, marketing or promotional restrictions; • loss of revenue; • exhaustion of any available insurance and our capital resources; • the inability to commercialize any product candidate; and • a decline in our share price. Failure to obtain or retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of product candidates we develop, alone or with corporate collaborators. Although we have clinical trial insurance, our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise. If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business. We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures

and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the **handling, use, storage, treatment and** disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. Although we maintain workers' compensation insurance to cover us for costs and expenses, we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials. The market opportunities for our product candidates **and forecasts of market growth** may **not** be ~~relatively~~ **accurate, and the actual market for our products may be** ~~small~~ **smaller** ~~since~~ **than we estimate, and even if** the ~~patients who~~ **markets in which we compete achieve the forecasted growth, our business** may ~~potentially be treated~~ **not grow at similar rates, or at all. The precise incidence and prevalence for all the conditions we aim to address** with our product candidates are **unknown. Our** ~~those who are ineligible for or have failed prior treatments, and our~~ estimates ~~of the prevalence of our target patient populations may be inaccurate. Cancer therapies are sometimes characterized by line of therapy (first line, second line, third line, fourth line, etc.), and the FDA often approves new therapies initially only for a particular line or lines of use. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first line therapy, usually chemotherapy, antibody drugs, tumor- targeted small molecules, hormone therapy, radiation therapy, surgery, or a combination of these, proves unsuccessful, second line therapy may be administered. Second line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor- targeted small molecules, or a combination of these. Third line therapies can include chemotherapy, antibody drugs and small- molecule tumor- targeted therapies, more invasive forms of surgery, and new technologies. There is no guarantee that our product candidates, even if approved as a second or third or subsequent line of therapy, would be approved for an earlier line of therapy, and, prior to any such approvals, we may have to conduct additional clinical trials. Our projections~~ of both the number of people who have ~~the~~ **these diseases** ~~cancers we are targeting, who may have their tumors genetically sequenced~~ , as well as the subset of people with these **diseases** ~~cancers in a position to receive a particular line of therapy and~~ who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including **sales of our competitors,** scientific literature, surveys of clinics, patient foundations or market research, and may prove to be incorrect **in general, or as to their applicability to our company** . Further, new ~~therapies~~ **trials** may change the estimated incidence or prevalence of ~~the~~ **these diseases** ~~cancers that we are targeting~~ . ~~Consequently, even~~ **Even** if **the markets in which we compete meet our size estimates and growth forecasts, our business may not grow at similar rates, or at all. The total addressable market across all of** our product candidates ~~are~~ **will ultimately depend upon, among other things, the diagnosis criteria included in the final label for each of our product candidates** approved for **sale** ~~a second or~~ **for** ~~third line of therapy, the~~ **these indications, the ability of our product candidates to improve on the safety, convenience, cost and efficacy of competing therapies or therapies in development, acceptance by the medical community and patients, drug pricing and reimbursement. The** number of patients ~~that may be eligible for treatment with our product candidates~~ **in the U. S., other major markets and elsewhere** may turn out to be ~~much~~ lower than expected ~~. In addition~~ , ~~we have~~ **patients may** not ~~yet conducted~~ **be otherwise amenable to treatment with our product candidates or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our business, financial condition, results of operations and prospects. Further, even if we obtain significant** market **share** ~~research to determine how treating physicians would expect to prescribe a product that is approved~~ for ~~multiple tumor types if there~~ **our product candidates, because some of our potential target populations** are ~~different lines of approved therapies for each~~ **very small, we may never achieve profitability despite obtaining** such ~~tumor type~~ **significant market share** . We currently have no marketing and sales organization and have no experience in marketing products. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if approved, we may not be able to generate product revenue. We currently have no sales, marketing or distribution capabilities and have no experience in marketing products. If we commercialize ourselves any of our product candidates that may be approved, we will need to develop an in-house marketing organization and sales force, which will require significant capital expenditures, management resources and time. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel. If we are unable or decide not to establish internal sales, marketing and distribution capabilities, we will pursue arrangements with third- party sales, marketing, and distribution collaborators regarding the sales and marketing of our products, if approved. However, there can be no assurance that we will be able to establish or maintain such arrangements on favorable terms or at all, or if we are able to do so, that these third- party arrangements will provide effective sales forces or marketing and distribution capabilities. Any revenue we receive will depend upon the efforts of such third parties, which may not be successful. We may have little or no control over the marketing and sales efforts of such third parties and our revenue from product sales may be lower than if we had commercialized our product candidates ourselves. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates. There can be no assurance that we will be able to develop in- house sales and distribution capabilities or establish or maintain relationships with third-party collaborators to commercialize any product in the U. S. or overseas. Risks Related to Government Regulation If we are not able to obtain, or are delayed in obtaining, required regulatory approvals for our product candidates, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired. Our product candidates and the activities associated with their development and commercialization,

including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import, and export are subject to comprehensive regulation by the FDA and other **comparable** regulatory agencies in the U. S. and by comparable authorities in other countries. Before we can commercialize any of our product candidates, we must obtain marketing approval. Whether the results from our current ongoing clinical trials and other trials will suffice to obtain approval will be a review issue and the FDA may not grant approval and may require that we conduct one or more controlled clinical trials to obtain approval. Additionally, even if the FDA grants approval for one or more of our product candidates, it may be for a narrower indication than we seek. Regulatory authorities, including the FDA, also may impose significant limitations in the form of narrow indications, warnings, or a REMS. These regulatory authorities may require labeling that includes precautions or contra- indications with respect to conditions of use, or they may grant approval subject to the performance of costly post- marketing clinical trials. In addition, regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of any product candidates we may develop. To date, we have had interactions with **various** regulatory authorities **globally** ~~in Australia, mainland China, Hong Kong, Italy, Netherlands, Poland, Singapore, South Korea, Spain, Taiwan, and the U. S. for our current product candidates. There is limited experience of regulatory authorities outside of the U. S. with the approval of tumor- agnostic precision cancer medicines~~ . Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Further, our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. The process of obtaining regulatory approvals, both in the U. S. and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity, and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted IND, CTA, Biologics License Application (" BLA"), New Drug Application (" NDA"), marketing authorization application, or equivalent application type, may cause delays in the approval or rejection of an application. The FDA and other competent authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. Our product candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following: • the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials; • the FDA or comparable foreign regulatory authorities may disagree with our ~~tumor- agnostic~~ development strategy; • we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication or a related companion diagnostic is suitable to identify appropriate patient populations; • the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval; • we may be unable to demonstrate that a product candidate' s clinical and other benefits outweigh its safety risks; • the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials; • the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a BLA, NDA or other submission or to obtain regulatory approval in the U. S. or elsewhere; • the FDA or comparable foreign regulatory authorities may determine that the manufacturing processes or controls or the facilities of third- party manufacturers with which we contract for clinical and commercial supplies are inadequate; and • the ~~approval~~ policies or regulations of the FDA or comparable foreign regulatory authorities **regarding development, approval, and marketing of biological products** may significantly change ~~in~~ **, including, but not limited to, as** a ~~manner rendering~~ **result of the 2024 U. S. presidential election, and** our clinical data **may be rendered** insufficient for approval **or we may not be able to market our product candidates in the manner in which we anticipate** . Of the large number of product candidates in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations, and prospects **. The U. S. Supreme Court' s June 2024 decision in Loper Bright Enterprises v. Raimondo overturned the longstanding Chevron doctrine, under which courts were required to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The Loper decision could result in additional legal challenges to regulations and guidance issued by federal agencies, including the FDA, on which we rely. Any such legal challenges, if successful, could have a material impact on our business. Additionally, the Loper decision may result in increased regulatory uncertainty, inconsistent judicial interpretations, and other impacts to the agency rulemaking process, any of which could adversely impact our business and operations. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action or as a result of legal challenges, either in the U. S or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, our business could be materially harmed** . We may in the future seek orphan drug status for some of our current and future product candidates, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug status, including market exclusivity, which may cause our revenue, if any, to be reduced. Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200, 000 in the U. S., or a patient population greater than 200, 000 in the U. S. when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the U. S. will be recovered from sales in the U. S. for that drug or biologic. Orphan drug designation must be requested before submitting a BLA or NDA. In the U. S., orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user- fee waivers.

After the FDA grants orphan drug designation, the generic identity of the drug or biologic and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. If a product that has orphan drug designation subsequently receives the first FDA approval for a particular drug for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a BLA or NDA, to market the same drug for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. As a result, even if one of our product candidates receives orphan exclusivity, that exclusivity may not effectively protect the product candidate from competition because different product candidates can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve a later product candidate that is the same drug as the drug with orphan exclusivity for the same condition if the FDA concludes that the later product candidate is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care compared with the product that has orphan exclusivity. Orphan drug exclusivity may also be lost if the FDA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition. The FDA has historically taken the position that the scope of orphan exclusivity aligns with the approved indication or use of a product, rather than the disease or condition for which the product received orphan designation. However, on September 30, 2021, the U. S. Court of Appeals for the Eleventh Circuit issued a decision in Catalyst Pharms., Inc. v. Becerra holding that the scope of orphan drug exclusivity must align with the disease or condition for which the product received orphan designation, even if the product' s approval was for a narrower use or indication. We may seek orphan drug designation for some ~~or all~~ of our current and future product candidates in additional orphan indications in which there is a medically plausible basis for the use of these products. Even when we obtain orphan drug designation, exclusive marketing rights in the U. S. may be limited if we seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. In addition, although we intend to seek orphan drug designation for other product candidates, we may never receive such designations. For example, the FDA has expressed concerns regarding the regulatory considerations for orphan drug designation as applied to tumor- agnostic therapies, and the FDA may interpret the federal Food, Drug and Cosmetic Act, as amended (the" FDCA"), and regulations promulgated thereunder in a way that limits or blocks our ability to obtain orphan drug designation or orphan drug exclusivity, if our product candidates are approved, for our targeted indications. On August 18, 2017, the FDA Reauthorization Act of 2017 (" FDARA") was enacted. FDARA, among other things, codified the FDA' s pre- existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The legislation was made in response to a court ruling holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period of a company obtains approval of a drug designated as an orphan drug, regardless of a showing of clinical superiority. Moreover, in the Consolidated Appropriations Act, 2021, Congress did not further change this interpretation when it clarified that the interpretation codified in FDARA would apply in cases where the FDA issued an orphan designation before the enactment of FDARA but where product approval came after the enactment of FDARA. Additionally, the Catalyst decision regarding interpretation of the Orphan Drug Act' s exclusivity provisions as applied to drugs and biologics approved for orphan indications being narrower than the product' s orphan designation has the potential to significantly broaden the scope of orphan exclusivity for such products. The FDA announced on January 24, 2023 that despite the Catalyst decision, it will continue to apply its longstanding regulations, which tie the scope of orphan exclusivity to the uses or indications for which the drug is approved, rather than to the designation. The FDA' s application of its orphan drug regulations post- Catalyst could be the subject of future legislation or to further challenges in court, which could impact our ability to obtain or seek to work around orphan exclusivity and might affect our ability to retain orphan exclusivity that the FDA previously has recognized for our product candidates. The FDA and legislators may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted. A Fast Track designation by the FDA, even if granted for any of our current or future product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval. If a drug or biologic is intended for the treatment of a serious or life- threatening condition and the product demonstrates the potential to address unmet medical needs for this condition, the product sponsor may apply for FDA Fast Track designation for a particular indication. We may seek Fast Track designation for certain current or future product candidates, but there is no assurance that the FDA will grant this status to any of our proposed product candidates. Marketing applications filed by sponsors of products in Fast Track development may qualify for priority review under the policies and procedures offered by the FDA, but the Fast Track designation does not assure any such qualification or ultimate marketing approval by the FDA. The FDA has broad discretion whether or not to grant Fast Track designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive Fast Track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a Fast Track designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. In addition, the FDA may withdraw any Fast Track designation at any time. The Breakthrough Therapy designation by the FDA, even if granted for any of our

current or future product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that any of our product candidates will receive marketing approval. In January 2022, the FDA granted Breakthrough Therapy designation for zipalertinib for the treatment of patients with locally advanced or metastatic NSCLC harboring epidermal growth factor exon 20 insertion mutations who have previously received platinum- based systemic chemotherapy. We may also seek Breakthrough Therapy designation for certain current or future product candidates. A Breakthrough Therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life- threatening disease or condition and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. Sponsors of product candidates that have been designated as Breakthrough Therapies are eligible to receive more intensive FDA guidance on developing an efficient drug development program, an organizational commitment involving senior managers, and eligibility for rolling review and priority review. Drugs and biologics designated as Breakthrough Therapies by the FDA may also be eligible for other expedited approval programs, including accelerated approval. Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy designation for zipalertinib or any other product candidate may not result in a faster development process, review or approval compared to candidate products developed and considered for approval that have not received Breakthrough Therapy designation and does not assure ultimate approval by the FDA. Even though we may seek Breakthrough Therapy designation for some or all of our current or future product candidates for the treatment of various **autoimmune diseases or** cancers, there can be no assurance that we will receive Breakthrough Therapy designation for such product candidates. Accelerated approval by the FDA, even if granted for zipalertinib or any other current or future product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive marketing approval. We may seek approval of zipalertinib, and certain of our other current and future product candidates using the FDA' s accelerated approval pathway. A product may be eligible for accelerated approval if it treats a serious or life- threatening condition, generally provides a meaningful advantage over available therapies, and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. As a condition of approval, the FDA requires that a sponsor of a product receiving accelerated approval perform a post- marketing confirmatory clinical trial or trials. These confirmatory trials must be completed with due diligence. In addition, the FDA currently requires as a condition for accelerated approval pre- approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. The Food and Drug Omnibus Reform Act of 2022 (" FDORA "), enacted on December 29, 2022 as part of the Consolidated Appropriations Act, 2023, includes numerous reforms to the accelerated approval process for drugs and biologics and enables the FDA to require, as appropriate, that a post- approval study be underway prior to granting accelerated approval. FDORA also expands the expedited withdrawal procedures already available to the FDA to allow the agency to use expedited procedures if a sponsor fails to conduct any required post- approval study of the product with due diligence. FDORA also adds the failure of a sponsor of a product approved under accelerated approval to conduct with due diligence any required post- approval study with respect to such product or to submit timely reports with respect to such product to the list of prohibited acts in the FDCA. Even if we do receive accelerated approval, we may not experience a faster development or regulatory review or approval process, and receiving accelerated approval does not provide assurance of ultimate full FDA approval. In connection with the receipt of accelerated approval, we may be required to complete additional confirmatory clinical trials. Conducting such additional confirmatory clinical trials could delay or prevent our ability to receive full approval of our product. Accelerated approval may also be withdrawn if, among other things, a confirmatory trial required to verify the predicted clinical benefit of the product fails to verify such benefit or if such trial is not conducted with due diligence. If approved, our investigational products regulated as biologics may face competition from biosimilars approved through an abbreviated regulatory pathway. Most of our current product candidates, with the exception of zipalertinib, will be regulated by the FDA as biologics, which must be licensed by the FDA prior to marketing under a BLA. The ACA includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 (the" BPCIA"), which created an abbreviated approval pathway for biologic products that are biosimilar to or interchangeable with an FDA- licensed reference biologic product. Under the BPCIA, a reference biological product is granted 12 years of data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12- year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a BLA for the competing product containing the sponsor' s own preclinical data and data from adequate and well- controlled clinical trials to demonstrate the safety, purity, and potency of the other company' s product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. **In December 2022, Congress clarified through FDORA, that the FDA may approve multiple first interchangeable biosimilar biological products so long as the products are all approved on the same first day on which such a product is approved as interchangeable with the reference product and the exclusivity period may be shared amongst multiple first interchangeable products. More recently, in October 2023, the FDA issued its first interchangeable exclusivity determination under the BPCIA.** We believe that any of our product candidates approved as a biologic product under a BLA should qualify for the 12- year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our investigational medicines to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar, once licensed, will be substituted for any one of our reference products

in a way that is similar to traditional generic substitution for non- biologic products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. If competitors are able to obtain marketing approval for biosimilars referencing our products, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences. **Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor' s own preclinical data and data from adequate and well- controlled clinical trials to demonstrate the safety, purity and potency of the product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. There have been recent government proposals to reduce the 12- year reference product exclusivity period, but none has been enacted to date. Since passage of the BPCIA, many states have passed laws or amendments to laws, which address pharmacy practices involving biosimilar products. The Consolidated Appropriations Act, which was enacted on December 27, 2020 required that the " patent dance " lists be made public in the FDA' s Database of Licensed Biological Products (the " Purple Book "). In particular, within 30 days of exchanging a patent list (patents with expiry dates) with a biosimilar applicant, reference product BLA holders must submit that patent list, as well as any supplemental lists, to the FDA. This information was previously maintained as confidential as between the BLA holder and biosimilar applicant. A BLA holder may still assert other patents against future filers, and publication of these lists does not exclude enforcement of newly granted patents. Additionally, under the Consolidated Appropriations Act, 2021, the FDA must now update the Purple Book every 30 days and publish in the Purple Book the following information about patented biological products: • a list of each biological product, by nonproprietary name, for which a biologics license is in effect; • the date of licensure and the application number; • the licensure status and, as available, the marketing status; and • exclusivity periods.** If the FDA or comparable foreign regulatory authorities approve generic versions of any of our small- molecule investigational products that receive marketing approval, or such authorities do not grant our products appropriate periods of exclusivity before approving generic versions of those products, the sales of our products, if approved, could be adversely affected. Once an NDA is approved, the product covered thereby becomes a " reference listed drug " in the FDA' s publication, " Approved Drug Products with Therapeutic Equivalence Evaluations, " commonly known as the Orange Book. Manufacturers may seek approval of generic versions of reference listed drugs through submission of abbreviated new drug applications (" ANDAs"), in the U. S. In support of an ANDA, a generic manufacturer need not conduct clinical trials to assess safety and efficacy. Rather, the applicant generally must show that its product has the same active ingredient (s), dosage form, strength, route of administration and conditions of use or ~~labelling~~ **labeling** as the reference listed drug and that the generic version is bioequivalent to the reference listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference listed drug is typically lost to the generic product. The FDA may not approve an ANDA for a generic product until any applicable period of non- patent exclusivity for the reference listed drug has expired. The FDCA provides a period of five years of non- patent exclusivity for a new drug containing a new chemical entity. Specifically, in cases where such exclusivity has been granted, an ANDA may not be submitted to the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference listed drug. Generic drug manufacturers may seek to launch generic products following the expiration of any applicable exclusivity period we obtain if our products are approved, even if we still have patent protection for such products. Competition that our products could face from generic versions of our products could materially and adversely affect our future revenue, profitability, and cash flows and substantially limit our ability to obtain a return on the investments we have made in those product candidates. 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. For example, even if the FDA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing, and promotion of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the U. S., including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the U. S., a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval. We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the U. S. have requirements for approval of product candidates with which we must comply prior to marketing in those jurisdictions. 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. Even if we receive regulatory approval of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates. Any product candidate for which we obtain marketing approval will be subject to extensive and ongoing regulatory requirements governing, among other things, the

research, development, testing, manufacturing, labeling, packaging, distribution, storage, advertising, promotion, import, export, recordkeeping, monitoring, and reporting of our products. These requirements include submissions of safety and other post-marketing information and reports, facility registration and drug listing requirements, as well as continued compliance with cGMPs, good laboratory practices, regulations, and GCPs, for any clinical trials that we conduct post- approval. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post- marketing testing and surveillance to monitor the safety or efficacy of the product. The FDA may require a REMS ~~,~~ in order to approve our product candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third- party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things: • restrictions on the marketing or manufacturing of our product candidates, withdrawal of the product from the market or voluntary or mandatory product recalls; • manufacturing delays and supply disruptions where regulatory inspections identify observations of noncompliance requiring remediation; • revisions to the labeling, including limitation on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings; • imposition of a REMS, which may include distribution or use restrictions; • requirements to conduct additional post- market clinical trials to assess the safety of the product; • fines, warning letters or holds on clinical trials; • refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals; • product seizure or detention, or refusal to permit the import or export of our product candidates; and • injunctions or the imposition of civil or criminal penalties. The FDA' s and other **comparable** regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U. S. or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability. The FDA and other **comparable** regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off- label uses. The FDA and other regulatory agencies closely regulate the post- approval marketing and promotion of products to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other **comparable** regulatory agencies impose stringent restrictions on manufacturers' communications regarding off- label use. If any of our product candidates are approved and we are found to have promoted such off- label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off- label use and has enjoined several companies from engaging in off- label promotion. Violation of the FDCA, and other statutes, including the False Claims Act (the" FCA") and equivalent legislation in other countries relating to the promotion and advertising of prescription products may also lead to investigations or allegations of violations of federal and state and other countries' health care fraud and abuse laws and state consumer protection laws. Even if it is later determined we were not in violation of these laws, we may be faced with negative publicity, incur significant expenses defending our actions and have to divert significant management resources from other matters. Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business. The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U. S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns or other disruptions could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations. Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements which could have a significant adverse impact on our business. We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and / or negligent conduct that fails to: comply with the regulations of the FDA and other similar foreign regulatory authorities, provide true, complete and accurate information to the FDA and other similar foreign regulatory authorities, comply with manufacturing standards we have established, comply with healthcare fraud and abuse laws in the U. S. and similar foreign fraudulent misconduct laws or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the U. S., our potential exposure under such laws and regulations will increase significantly, and our costs associated with compliance with such laws and regulations are also likely to increase. These laws may impact, among other things, our current activities involving principal investigators and research patients, as well as proposed and future sales, marketing and education programs. We adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this

activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions. We are or may become subject to additional healthcare regulation and enforcement by various government entities, and our failure to strictly adhere to these regulatory regimes could have a significant adverse impact on our business. Pharmaceutical manufacturers and their products are subject to extensive federal and state regulation, including laws intended to prevent fraud and abuse in the healthcare industry. These laws may constrain the business or financial arrangements and relationships through which we conduct business, including how we conduct research regarding, market, sell, and distribute our products. In the U. S., these laws include, but are not limited to the following, some of which are likely to apply only if or when we obtain marketing approval for a product candidate: • federal false claims, false statements, and civil monetary penalties laws prohibiting, among other things, any person from knowingly presenting, or causing to be presented, a false claim for payment of government funds or knowingly making, or causing to be made, a false statement to get a false claim paid; • the federal anti- kickback law, which prohibits, among other things, persons from offering, soliciting, receiving, or providing remuneration, directly or indirectly, to induce either the referral of an individual for, or the purchasing or ordering of, a good or service for which payment may be made under federal healthcare programs such as Medicare and Medicaid; • the federal Health Insurance Portability and Accountability Act of 1996 (" HIPAA "), which, in addition to privacy protections applicable to healthcare providers and other entities, prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters; • the FDCA, which among other things, strictly regulates drug marketing, prohibits manufacturers from marketing products prior to approval or for off- label use and regulates the distribution of samples; • federal laws that require pharmaceutical manufacturers to **calculate,** report **and certify** certain ~~calculated~~ **complex** product prices **and other data** to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs **, which data may be used in the calculation of reimbursement and / or discounts on approved products** ; • the federal Open Payments (or federal " sunshine " law), which requires pharmaceutical and medical device companies to monitor and report certain financial interactions with certain healthcare providers to the Center for Medicare & Medicaid Services within the U. S. Department of Health and Human Services for re- disclosure to the public, as well as ownership and investment interests held by physicians and their immediate family members; • federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; • analogous state laws and regulations, including state anti- kickback and false claims laws, consumer protection and unfair competition laws and laws governing privacy, security and breaches of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and • state laws that require pharmaceutical companies to comply with specific compliance standards, restrict financial interactions between pharmaceutical companies and healthcare providers, report drug product pricing information, financial interactions with health care providers, or marketing expenditures and / or require the registration of pharmaceutical sales representatives **. The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record- keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products** . Ensuring compliance is time- consuming and costly. Given the breadth of the laws and regulations, limited guidance for certain laws and regulations and evolving government interpretations of the laws and regulations, governmental authorities may possibly conclude that our business practices are non- compliant. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management' s attention from the operation of our business. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations, and prospects. Outside the U. S., our activities may also be subject to extensive regulation, including anti- kickback and false claims laws. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to induce or reward improper performance generally is usually governed by the national anti- bribery laws of EU member states, and the Bribery Act 2010 in the UK. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001 / 83 / EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the UK despite its departure from the EU. Payments made to physicians in certain EU member states must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician' s employer, his or her competent professional organization and / or the regulatory authorities of the individual EU member states. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU member states. Failure to comply with these requirements could result in administrative, civil and criminal penalties, damages, fines, disgorgement, the exclusion from participation in federal and state healthcare programs, individual imprisonment, reputational harm, and the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non- compliance with these laws. Data collection is governed by restrictive regulations governing the use, processing and cross- border transfer of personal information. We may be subject to additional data privacy

restrictions as we continue to enroll subjects in our ongoing or future clinical trials. The collection, use, storage, disclosure, transfer, or other processing of personal data regarding individuals in the EEA, including personal health data, is subject to the EU General Data Protection Regulation (the" GDPR") which became effective on May 25, 2018. The GDPR is wide- ranging in scope and imposes numerous requirements on companies that are established in the EEA or which are not established in the EEA but collect and use personal data in relation to (i) offering goods or services to, or (ii) monitoring the behavior of, individuals located in the EEA. The GDPR imposes stringent operational requirements for controllers and processors of personal data, including, for example, requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing and maintaining a process to address data subject rights, implementing safeguards to protect the security and confidentiality of personal data, providing notification to data subjects and government authorities of data breaches, and taking certain measures when engaging third- party processors. The GDPR also imposes strict rules on the transfer of personal data to most countries outside the EEA, including the U. S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to € 20 million or 4 % of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. The GDPR increased our responsibility and potential liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries within the EEA. Compliance with the GDPR will continue to be a rigorous and time- intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European data processing activities. Following the UK' s exit from the EU, our processing of personal data of persons located in the United Kingdom subjects us to the UK Data Protection Act 2018 and the " UK GDPR " as defined by the Data Protection Act 2018, as amended by the Data Protection, Privacy and Electronic Communications (Amendments etc.) (EU Exit) Regulations 2019 (SI 2019 / 419) (" UK GDPR "). The UK GDPR imposes similar obligations on data controllers and processors to those found in the GDPR and carries with it fines similar to those of the GDPR. **The UK' s data protection authority, the Information Commissioner' s Office, had indicated that it will continue to enforce the UK GDPR in line with the enforcement of GDPR in the EU, and currently the UK GDPR and EU GDPR are broadly aligned. However, the UK government on October 23, 2024 introduced a draft Data (Use and Access) Bill which is currently making its way through the House of Lords, and proposes certain amendments to the data protection regime in the UK, and once passed, will create slight divergences between the EU and UK data protection regimes.** Recent legal developments in the EU and UK have also created complexity and uncertainty regarding transfers of personal data from the EEA and the UK to the U. S. and other countries. On ~~December 13~~ **July 10** , ~~2022~~ **2023** , the European Commission **issued an** ~~published a draft~~ EU- U. S. data adequacy decision ~~which sets out a~~ **on the basis of the** new framework for transatlantic data flows, ~~but there is~~ **the** ~~remains uncertainty as to when the proposed~~ **EU- U. S. Data Privacy** ~~framework~~ **Framework (" DPF "). Companies must self- certify to the U. S. Department of Commerce that they comply with the principles of the DPF in order to benefit from the new mechanism to transfer personal data from the EU (and the UK and Switzerland under the respective extensions to the DPF) and the U. S. Companies who have not certified to the DPF** will ~~become~~ **continue to be subject to the current rules on** ~~operational~~ **international** ~~. It is also likely~~ **transfers under the GDPR and UK GDPR, including, for example, ensuring** that the ~~proposed framework will be~~ **Standard Contractual Clauses, published by the European Commission in 2021, are in place where required. The DPF has already been** ~~subject~~ **subjected** to legal challenge **, and it is likely to be subjected to further challenges in the future** . The impact of these developments on the ability to lawfully transfer personal information from the EEA and UK to the U. S. and other countries has led to increased scrutiny on data transfers out of the EEA and UK and may increase our costs of compliance with data privacy legislation. In addition, several U. S. states have recently enacted or are considering enacting comprehensive privacy legislation. Most notably, California recently enacted the California Consumer Privacy Act (the" CCPA"), which creates new GDPR- like individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on covered businesses handling personal data of California consumers or households. The CCPA requires covered businesses to provide new disclosures to consumers about such businesses' data collection, use and sharing practices, provide such consumers new ways to opt- out of certain sales or sharing of personal information, and provide consumers with additional causes of action in the event of a data security breach. The CCPA went into effect on January 1, 2020, and the California Attorney General commenced enforcement actions for violations on July 1, 2020. Further, the California Privacy Rights Act (the" CPRA"), was passed by California voters on November 3, 2020. The CPRA, which amends the CCPA, creates additional obligations with respect to processing and storing personal information that took effect on January 1, 2023 (with certain provisions having retroactive effect to January 1, 2022). While there are currently exceptions in the CCPA for protected health information that is subject to HIPAA and information collected in research studies, including clinical trials, that are conducted in accordance with certain regulations, we continue to monitor the impact the CCPA may have on our business activities. New data privacy laws have been proposed in more than half of the states in the U. S. and in the U. S. Congress, reflecting a trend toward more stringent privacy legislation in the U. S., which trend may accelerate under the current U. S. presidential administration. The effects of this legislation are potentially far - reaching and may require us to modify our data processing practices and policies and to incur substantial costs and expenses in an effort to comply. Compliance with U. S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with U. S. and international data protection laws and regulations could result in government enforcement actions (which could include civil or criminal penalties), class action litigation and / or adverse publicity and could

negatively affect our operating results and business. Moreover, clinical trial subjects about whom we or our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, 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. Risks Related to Our Intellectual Property If we are unable to obtain and maintain patent and other intellectual property protection for our current and future product candidates and technology, or if the scope of intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to commercialize any of our current or future product candidates or technology may be adversely affected. Our success depends in large part on our ability to obtain and maintain patent and other intellectual property protection in the U. S. and other countries with respect to our product candidates, their respective components, formulations, combination therapies, methods used to manufacture them and methods of treatment and development that are important to our business, as well as successfully defending these patents against third- party challenges. If we do not adequately protect our intellectual property rights, competitors may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. We intend to rely upon a combination of patent applications, confidentiality agreements, trade secret protection and license agreements to protect the intellectual property related to our product candidates and 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. We, or any future partners, collaborators, or licensees, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to establish our patent position. To protect our proprietary position, we have filed or in- licensed, and plan to file or in- license, patents and patent applications in the U. S. and abroad relating to our product candidates that are important to our business. Our ability to stop unauthorized third parties from making, using, selling, offering to sell, or importing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. If we are unable to secure or maintain patent protection with respect to any of our current or future product candidates, or any other proprietary products and technology we develop, our business, financial condition, results of operations, and prospects would be materially harmed. The degree of patent protection we require to successfully compete in the marketplace may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any patents we may own, have licensed, or in- license in the future will have, or that any of our patent applications that mature into issued patents will include, claims with a scope sufficient to protect our current and future product candidates or otherwise provide any competitive advantage. In addition, to the extent that we currently or in the future in- license intellectual property, we cannot assure you that those licenses will remain in force. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the U. S. Furthermore, patents have a limited lifespan, and the term of any patents we may own or in- license may be inadequate to protect our competitive position of our product candidates or technology for an adequate amount of time. In the U. S., the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however, 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 new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Even if they are unchallenged, our patent applications, if issued, and any patents we may own or in- license, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent any patents we may own or in- license by developing similar or alternative technologies or therapeutics in a non- infringing manner. For example, a third party may develop a competitive therapy that provides benefits similar to one or more of our product candidates but that uses a formulation and / or a device that falls outside the scope of any patent protection we may have in the future. If the patent protection provided by our patent applications or any patents, we may pursue with respect to our product candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our product candidates could be negatively affected, which would harm our business. Patent positions of life sciences companies can be uncertain and involve complex factual and legal questions. Changes in either the patent laws or their interpretation in any jurisdiction that we seek patent protection may diminish our ability to protect our inventions, maintain and enforce our intellectual property rights; and, more generally, may affect the value of our intellectual property, including the narrowing of the scope of our patent applications or any patents we may own or in- license. The patent prosecution process is complex, expensive, time- consuming, and inconsistent across jurisdictions. Patent license negotiations also can be complex and protracted, with uncertain results. We may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent rights at a commercially reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. It is possible that we will fail to identify important patentable aspects of our research and development efforts in time to obtain appropriate or any patent protection. While we enter into non- disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development efforts, including for example, our employees, corporate collaborators, external academic scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose results before a patent application is filed, thereby endangering our ability to seek patent protection. In addition, publications of discoveries in the scientific and scholarly literature often lag behind the actual discoveries, and patent applications in the U. S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Consequently, we cannot be certain that we were the first to file for patent protection on the inventions claimed in our patent applications. It is possible that defects of form in the preparation or filing of our patent applications, or any patents we may own or in- license, may exist or may arise in the future, for example with respect to proper

priority claims, inventorship, claim scope, or requests for patent term adjustments. If we or our partners, collaborators, licensees, or licensors fail to establish, maintain, or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our partners, collaborators, licensees, or licensors are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our patent applications or patents we may own or in- license, such patents may be invalid and / or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business. Additionally, we cannot be certain that the claims in our patent applications covering composition of matter of our product candidates or technology will be considered patentable by the U. S. Patent and Trademark Office (the" USPTO") or by patent offices in foreign countries, or that the claims in any issued patents we may own or in- license will be considered patentable by courts in the U. S. or foreign countries. Method of use patents protect the use of a product for the specified method. These types of patents do not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products " off- label. " Although off- label prescriptions may induce or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute. The patent position of pharmaceutical and biotechnology companies generally is highly uncertain and involves complex legal and factual questions for which many legal principles remain unresolved. In recent years, patent rights have been the subject of significant litigation. As a result, the issuance, scope, validity, enforceability, and commercial value of any rights we may have from our patent applications are highly uncertain. Our patent applications may not result in patents being issued in the U. S. or in other jurisdictions which protect our technology or products, or which effectively prevent others from commercializing competitive technologies and products. Moreover, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art, including our own previously filed patent applications and scientific publications, allow our inventions to be patentable over the prior art. Even if our patent applications issue as patents, third parties could challenge the validity of such patents based on such scientific publications and we could potentially lose valuable patent rights. Further, the scope of the invention claimed in a patent application can be significantly reduced before the patent is issued, and this scope can be reinterpreted after issuance. Even where our patent applications, whether owned or in- licensed, issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with a competitive advantage. Any patents that eventually issue may be challenged, narrowed, or invalidated by third parties. Consequently, we do not know whether any of our product candidates will be protectable or remain protected by valid and enforceable patent rights. Our competitors or other third parties may be able to evade any rights we may have by developing new compounds or alternative technologies or products in a non- infringing manner. The issuance or grant of a patent is not irrefutable as to its inventorship, scope, validity, or enforceability, and any of our current or future patents, whether owned or in-licensed may be challenged in the courts or patent offices in the U. S. and abroad. Such challenges may result in the patent claims of any such patents being narrowed, invalidated, or held unenforceable, which could limit our ability to stop or prevent us from stopping others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. We may in the future, become subject to a third- party pre- issuance submission of prior art or opposition, derivation, revocation, re- examination, post- grant and inter partes review, or interference proceeding and other similar proceedings challenging any rights we may have from our patent applications or the patent rights of others in the USPTO or other foreign patent office, or in declaratory judgment actions or counterclaims. An unfavorable determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, any rights we may have from our patents or patent applications, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or extinguish our ability to manufacture or commercialize products without infringing third- party patent rights. Moreover, some of our intellectual property ~~,~~ may be co- owned with third parties. If we are unable to obtain an exclusive license to any such third-party co- owners' interest in such intellectual property, including patents or patent applications, such co- owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we or our licensors may need the cooperation of any such co- owners of our owned and in- licensed intellectual property, including patents and patent applications, in order to enforce such intellectual property against third parties, and such cooperation may not be provided to us or our licensors. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects. If we fail to comply with our obligations in any agreements under which we may license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business. We are currently, and may in the future be, party to license or collaboration agreements with third parties to advance our research or allow commercialization of our product candidates. Our current agreements impose, and we expect that future agreements may impose numerous obligations, such as development, diligence, payment, commercialization, funding, milestone, royalty, sublicensing, insurance, patent prosecution, enforcement and other obligations on us and may require us to meet development timelines, or to exercise commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the licenses. If our licensors conclude that we have materially breached our license agreements they may seek to terminate the license agreements, thereby removing or limiting our ability to develop and commercialize products and technologies covered by these license agreements. Any termination of these licenses, or if the underlying patents fail to provide the intended

exclusivity, could result in the loss of significant rights and could harm our ability to commercialize our product candidates, and competitors or other third parties would have the freedom to seek regulatory approval of, and to market, products identical to ours and we may be required to cease our development and commercialization of certain of our product candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects. Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including: • the scope of rights granted under the license agreement and other interpretation- related issues; • whether and the extent to which our technology and processes infringe, misappropriate or otherwise violate intellectual property rights of the licensor that is not subject to the licensing agreement; • our right to sublicense patent and other rights to third parties under collaborative development relationships; • our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations; • the priority of invention of any patented technology; and • the ownership of inventions and know- how resulting from the joint creation or use of intellectual property by our licensors and us and our partners. In addition, licensing agreements are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. For example, we will owe the licensors of CLN- 049 and CLN- 617 a success fee in the event of a sale or other disposition of the majority of the assets of the development subsidiaries holding these product candidates. These fees will reduce the net proceeds we receive from any such sale or disposition of assets. Moreover, if disputes over intellectual property prevent or impair our ability to maintain licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations and prospects. If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. In addition to the protection afforded by our owned and in- licensed patents, we seek to rely on trade secret protection, confidentiality agreements, and license agreements to protect proprietary know- how that is not patentable, processes for which patents are difficult to enforce and any other elements of our product identification, discovery, and development processes, including our differentiated hub- and- spoke business model that involve proprietary know- how, information, or technology that is not covered by patents. Although we require all of our employees, consultants, advisors and any third parties who have access to our proprietary know- how, information, or technology to enter into confidentiality agreements, trade secrets can be difficult to protect, and we have limited control over the protection of trade secrets used by our collaborators and suppliers. We cannot be certain that we have or will obtain these agreements in all circumstances, and we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary information. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time- consuming, and the outcome is unpredictable. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. Further, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our business and competitive position could be harmed. Third- party claims of intellectual property infringement, misappropriation or other violations may be costly and time consuming and may prevent or delay our product identification, discovery and development efforts. The intellectual property landscape around precision medicine is crowded, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating, or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. Our commercial success depends upon our ability, or the ability of our third parties, to develop, manufacture, market and sell our current and future product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including derivation, interference, reexamination, inter partes review, and post grant review proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We or any of our licensors or strategic partners may be party to, exposed to, or threatened with, future adversarial proceedings or litigation by third parties having patent or other intellectual property rights alleging that our current or future product candidates and / or proprietary technologies infringe, misappropriate or otherwise violate their intellectual property rights. We cannot assure you that our product candidates and other technologies that we have developed, are developing or may develop in the future do not or will not infringe, misappropriate or otherwise violate existing or future patents or other intellectual property rights owned by third parties. Numerous U. S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. 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. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product candidates, technologies, or methods. If a third party claims that we infringe, misappropriate or otherwise violate its intellectual property rights, we may face a number of issues, including, but not limited to: • infringement, misappropriation and

other intellectual property claims which, regardless of merit, may be expensive and time- consuming to litigate and may divert our management' s attention from our core business and may impact our reputation; • substantial damages for infringement, misappropriation or other violations, which we may have to pay if a court decides that the product candidate or technology at issue infringes, misappropriates or violates the third party' s rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner' s attorneys' fees; • a court prohibiting us from developing, manufacturing, marketing or selling our current and future product candidates, or from using our proprietary technologies, unless the third party licenses its product rights to us, which it is not required to do, on commercially reasonable terms or at all; • if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and / or grant cross- licenses to intellectual property rights for our products, or the license to us may be non- exclusive, which would permit third parties to use the same intellectual property to compete with us; • redesigning our product candidates or processes so they do not infringe, misappropriate or violate third- party intellectual property rights, which may not be possible or may require substantial monetary expenditures and time; and • there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition, results of operations or prospects. We may choose to challenge the patentability of claims in a third party' s U. S. patent by requesting that the USPTO review the patent claims in an ex- parte re-exam, inter partes review or post- grant review proceedings. These proceedings are expensive and may consume our time or other resources. We may choose to challenge a third party' s patent in patent opposition proceedings in the European Patent Office (the" EPO") or other foreign patent office. The costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent office then we may be exposed to litigation by a third party alleging that the patent may be infringed by our product candidates or proprietary technologies. Third parties may assert that we are employing their proprietary technology without authorization. Patents issued in the U. S. by law enjoy a presumption of validity that can be rebutted only with evidence that is " clear and convincing, " a heightened standard of proof. There may be issued third- party patents of which we are currently unaware with claims to compositions, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Patent applications can take many years to issue. In addition, because some patent applications in the U. S. may be maintained in secrecy until the patents are issued, patent applications in the U. S. and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications covering our product candidates or technology. If any such patent applications issue as patents, and if such patents have priority over our patent applications or patents we may own or in- license, we may be required to obtain rights to such patents owned by third parties which may not be available on commercially reasonable terms or at all, or may only be available on a non- exclusive basis. There may be currently pending patent applications which may later result in issued patents that may be asserted in infringement claims against our current and future product candidates. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our current and future product candidates or other technologies, could be found by a court of competent jurisdiction to be infringed by our product candidates or other technologies. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Moreover, 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, such a license may not be available on commercially reasonable terms or at all. 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. In the event of a successful claim of infringement, misappropriation or other violation 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 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 not be successful in obtaining or maintaining

necessary rights to product components and processes for our development pipeline through acquisitions and in- licenses. We own **five patent families related to CLN- 978. We own** four patent families related to CLN- 619. We ~~own six patent families related to CLN- 978. We~~ have in- licensed ~~six~~ **seven** patent families related to zipalertinib as part of our co- development agreement with **an affiliate of** Taiho. We have in- licensed one ~~and own another~~ patent family related to CLN- 049 ~~. We have in- licensed six U. S. patent applications related to CLN- 418~~ . We have in- licensed one patent family and own two patent families related to CLN- 617. 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 as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third- party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be nonexclusive, thereby giving our competitors access to the same technologies licensed to us. In such circumstances, we may be required to expend significant time and resources to develop or license replacement technology. Moreover, the molecules that will be used with our product candidates may be covered by the intellectual property rights of others. Additionally, we sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions provide us with an option to negotiate a license to any of the institution' s rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program and allowing third parties to compete with us. If we are unable to successfully obtain rights to required third- party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer. The licensing and acquisition of third- party intellectual property rights is a competitive area, and companies, which may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third- party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to in- license or acquire third- party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire. If we are unable to successfully obtain rights to required third- party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business, results of operations, financial condition and prospects could suffer. We may be involved in lawsuits to protect or enforce our owned or in- licensed intellectual property rights, which could be expensive, time- consuming and unsuccessful. Competitors may infringe any patents we may own or in- license. In addition, any patents we may own, or in- license may become involved in inventorship, priority, validity or unenforceability disputes. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time- consuming. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. In addition, in an infringement proceeding, a court may decide that one or more of any patents we may own or in- license is not valid or is unenforceable or that the other party' s use of our technology that may be patented falls under the safe harbor to patent infringement under 35 U. S. C. § 271 (e) (1). There is also the risk that, even if the validity of these patents is upheld, the court may refuse to stop the other party from using the technology at issue on the grounds that any of our owned or in- licensed patents do not cover the technology in question or that such third party' s activities do not infringe our patents. An adverse result in any litigation or defense proceedings could put one or more of our owned or in- licensed patents at risk of being invalidated, held unenforceable, or interpreted narrowly, or could put our 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. 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. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Post- grant proceedings provoked by third parties or brought by the USPTO may be necessary to determine the validity or priority of inventions with respect to our owned or in- licensed patents or patent applications. These proceedings are expensive and an unfavorable outcome 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 a party prevailing against us does not offer us a license on commercially

reasonable terms. In addition to potential USPTO review proceedings, we may become a party to patent opposition proceedings in the EPO or similar proceedings in other foreign patent offices, where our foreign patents are challenged. The costs of these opposition or similar proceedings could be substantial, and may result in a loss of scope of some claims or a loss of the entire patent. An unfavorable result at the USPTO, EPO or other patent office may result in the loss of our right to exclude others from practicing one or more of our inventions in the relevant country or jurisdiction, which could have a material adverse effect on our business. 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, misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the U. S. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. We may not be able to detect infringement against any of our owned or in- licensed patents. Even if we detect infringement by a third party, we may choose not to pursue litigation against or settlement with the third party. If we later sue such third party for patent infringement, the third party may have certain legal defenses available to it, which otherwise would not be available except for the delay between when the infringement was first detected and when the suit was brought. Such legal defenses may make it impossible for us to enforce any patents we may own or in- license against such third party. Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and patent protection could be reduced or eliminated for non- compliance with these requirements. Periodic maintenance fees, renewal fees, annuity fees and various other government fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and following the issuance of a patent. While an inadvertent lapse can in some cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent include, but are not limited to, failure to respond to official actions within prescribed time limits, non- payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market with similar or identical products or platforms, which could have a material adverse effect on our business prospects and financial condition. Changes to patent law in the U. S. and in foreign jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products. As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity, and are therefore costly, time- consuming and inherently uncertain. 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 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 ability to obtain new patents or to enforce patents that we might obtain in the future. For example, in the case Assoc. for Molecular Pathology v. Myriad Genetics, Inc., the U. S. Supreme Court held that certain claims to DNA molecules are not patentable. 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 any rights we may have in our patent applications or any patents we may own or in- license. Recent or future patent reform legislation could also increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any patents we may own or in- license. The U. S. has enacted and implemented wide- ranging patent reform legislation. On September 16, 2011, the Leahy- Smith America Invents Act, was signed into law, which includes a number of significant changes to U. S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art, may affect patent litigation, establish a new post- grant review system and switch the U. S. patent system from a " first- to- invent " system to a " first- to- file " system. Under a " first- to- file " system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. We have limited foreign intellectual property rights and may not be able to protect our intellectual property rights throughout the world. We may not be able to pursue generic coverage of our product candidates outside of the U. S. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and intellectual property rights in some countries outside the U. S. can be less extensive than those in the U. S. 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 U. S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U. S., or from selling or importing products made using our inventions in and into the U. S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but where enforcement is not as strong as that in the U. S. These products may compete with our product candidates and in jurisdictions where we do not have any issued patents or patent applications or other intellectual property rights, we may not have effective or sufficient protection to prevent them from competing. Our patent portfolio is at the very early stages of prosecution. We will need to decide whether and in which

jurisdictions to pursue protection for the various inventions in our portfolio prior to applicable deadlines. 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 protection, particularly those relating to biopharmaceutical products, which could make it difficult for us to stop the infringement of any patents we may own or in- license or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce any rights we may have in our patents and patent applications in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put any of our owned or in- licensed patents at risk of being invalidated or interpreted narrowly and our 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. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patents. If we are forced to grant a license to third parties with respect to any of our owned or in- licensed patents that are relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected. We may be subject to claims challenging the inventorship or ownership of any intellectual property, including any patents we may own or in- license. We may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in- licensed patents, trade secrets, or other intellectual property as an inventor or co- inventor. For example, we may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates or other technologies. We generally enter into confidentiality and intellectual property assignment agreements with our employees, consultants, and contractors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, those agreements may not be honored and may ineffectively assign intellectual property rights to us. Moreover, there may be some circumstances where we are unable to negotiate for such ownership rights. Disputes regarding ownership or inventorship of intellectual property can also arise in other contexts, such as collaborations and sponsored research. If we are subject to a dispute challenging our rights in or to patents or other intellectual property, such a dispute could be expensive and time consuming. Litigation may be necessary to defend against these and other claims challenging inventorship of any of our owned or in- licensed patents, trade secrets or other intellectual property. If we were unsuccessful, in addition to paying monetary damages, we could lose valuable rights in intellectual property that we regard as our own, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates and other technologies. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects. We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information or alleged trade secrets of third parties or competitors or are in breach of non- competition or non- solicitation agreements with our competitors. We have received confidential and proprietary information from third parties. In addition, as is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors, in some cases until recently. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information or trade secrets of these third parties or our employees' former employers or our consultants' or contractors' current or former clients or customers. In addition, we may become subject to claims that we caused an employee to breach the terms of his or her non- competition or non- solicitation agreement. Litigation or arbitration may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims and possible aftermath could result in substantial cost and be a distraction to our management and employees. Any litigation or the threat thereof may adversely affect our ability to hire employees. A loss of key personnel or their work product could hamper or prevent our ability to commercialize product candidates, which could have an adverse effect on our business, results of operations and financial condition. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace. If we do not obtain patent term extension and data exclusivity for any of our current or future product candidates we may develop, our business may be materially harmed. Depending upon the timing, duration and specifics of any FDA marketing approval of any of our current or future product candidates we may develop, one or more U. S. patents we may own or in- license may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 (the" Hatch- Waxman Amendments"). The Hatch- Waxman Amendments permit a patent term extension of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering

the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is shorter than what we request, our competitors may obtain approval of competing products following expiration of any patents that issue from our patent applications, and our business, financial condition, results of operations, and prospects could be materially harmed. If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our marks of interest and our business may be adversely affected. Our trademarks or trade names may be challenged, infringed, diluted, circumvented, or declared generic or determined to be infringing on other marks. We intend to rely on both registration and common law protection for our trademarks. We may not be able to protect our rights to these 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. During the trademark registration process, we may receive Office Actions from the USPTO objecting to the registration of our trademark. Although we would be given an opportunity to respond to those objections, 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 / or to seek the cancellation of registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we are unable to obtain a registered trademark or 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 Our Reliance on Third Parties We currently rely and expect to continue to rely on the outsourcing of the majority of our development functions to third parties to conduct our preclinical studies and clinical trials. 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. We utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs, CMOs, and strategic partners to conduct and support our preclinical studies and clinical trials under agreements with us and expect to rely on such parties in the future. We negotiate budgets and contracts with CROs, clinical trial sites and CMOs and we may not be able to do so on favorable terms, which may result in delays to our development timelines and increased costs. We rely heavily on these third parties over the course of our preclinical studies and 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 our preclinical studies and clinical trials and the management of data developed through preclinical studies and clinical trials than would be the case if we relied entirely upon our own staff. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with good manufacturing, clinical, laboratory practices (" GxPs"), which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GxPs through periodic inspections of clinical trial sponsors, principal investigators and clinical trial sites. If we or any of these third parties fail to comply with applicable GxP 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. We cannot assure you that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GxP regulations. In addition, our clinical trials must be conducted with pharmaceutical product produced under GxP regulations and will require a large number of test patients. Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of patients may delay ongoing or planned clinical trials or require us to repeat clinical trials, which would delay the regulatory approval process. Failure by us or by third parties we engage to comply with regulatory requirements can also result in fines, adverse publicity, and civil and criminal sanctions. 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. Any third parties conducting our clinical trials are not and will not be our employees and, except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our current and future preclinical studies and clinical trials. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed. Switching or adding third parties to conduct our preclinical studies and clinical trials involves substantial cost and requires extensive time and focus of our management. In addition, there is a natural transition period when a new third party commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Additionally, we do not directly control the manufacturing facilities where our product candidates are made, and we must depend on CMOs to make our product candidates according to standards for quality and reliability. We do not own any manufacturing facilities or equipment. We cannot provide assurance that we will be able to obtain qualified contract manufacturing services on reasonable terms. If any CMO with whom we contract fails to perform its obligations or has challenges sourcing raw materials, we may be forced to enter into an agreement with a different CMO, which we may not be able to do on reasonable terms, if at all. In such a

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. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We may need to verify, such as through a manufacturing comparability or bridging study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another **comparable** regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to advance clinical trials or otherwise develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a CMO may possess technology related to the manufacture of our product candidate that such CMO owns independently, which may 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 us to conduct further additional clinical trials. In addition to our existing collaborations, we may form or seek additional collaborations or strategic alliances or enter into additional licensing arrangements in the future, and we may not realize the benefits of such collaborations, alliances or licensing arrangements. As noted above, ~~in June 2022,~~ we **may receive up** ~~completed the sale of our equity interest in Cullinan Pearl, formerly a development subsidiary of the Company,~~ to ~~Taiho for an upfront payment of~~ $ ~~275~~ **130** . 0 million **from Taiho** ~~. We may receive up to an additional $ 130. 0 million~~ upon the achievement of certain **U. S.** regulatory milestones related to zipalertinib. There is no guarantee that these milestones will be achieved or that we will receive any of the ~~additional~~ $ 130. 0 million. **We have** ~~In connection with the sale of our equity interest in Cullinan Pearl, we entered into~~ a co- development agreement with an affiliate of Taiho to co- develop and, at our option, co- commercialize zipalertinib in the U. S. Pursuant to the terms of the co-development agreement, we ~~will~~ each equally contribute to the ~~future~~ clinical development costs of zipalertinib in the U. S., and will each receive 50 % of any future pre- tax profits from potential U. S. sales of zipalertinib. There is no guarantee that the co-development and co- commercialization will be successful or that we will receive any net profits and we could lose money. We may form or seek additional 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. 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. Further, collaborations involving our product candidates are subject to numerous risks, which may include the following: • collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration; • collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization of our product candidates based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities; • collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing; • collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates; • a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to their marketing and distribution; • collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability; • disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our product candidates, or that result in costly litigation or arbitration that diverts management attention and resources; • collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates; and • collaborators may own or co- own intellectual property covering our product candidates that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property. As a result, if we enter into additional collaboration agreements and strategic partnerships or license our product candidates, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture, which could delay our timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction. Any delays in entering into new collaborations or strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates in certain geographies for certain indications, which would harm our business prospects, financial condition and results of operations. We currently rely and expect to rely in the future on the use of manufacturing suites in third- party facilities or third parties to manufacture our product candidates. Our business could be harmed if we are unable to use third-party manufacturing suites or if the third- party manufacturers fail to provide us with sufficient quantities of our product candidates or fail to do so at acceptable quality levels or prices. We do not currently own any facility that may be used as our clinical- scale manufacturing and processing facility and must currently rely on outside vendors to manufacture our product candidates. We will need to negotiate and maintain contractual arrangements with these outside vendors for the supply of our product candidates and we may not be able to do so on favorable terms. We have not yet caused our product candidates to be manufactured on a commercial scale and may not be able to do so for any of our product candidates. Our anticipated reliance on

a limited number of third- party manufacturers exposes us to a number of risks, including the following: • we may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA must inspect any manufacturers for cGMP compliance as part of our marketing application; • a new manufacturer would have to be educated in, or develop substantially equivalent processes for, the production of our current and future product candidates; • our third- party manufacturers might be unable to timely manufacture our current and future product candidates or produce the quantity and quality required to meet our clinical and commercial needs, if any; • contract manufacturers may not be able to execute our manufacturing procedures and other logistical support requirements appropriately; • our future contract manufacturers may not perform as agreed, may not devote sufficient resources to our current and future product candidates or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store, and distribute our products, if any; • manufacturers are subject to ongoing periodic unannounced inspection by the FDA and corresponding state agencies, as well as foreign regulatory authorities, to ensure strict compliance with cGMP and other government regulations and corresponding foreign standards and we have no control over third- party manufacturers' compliance with these regulations and standards; • we may not own, or may have to share, the intellectual property rights to any improvements made by our third- party manufacturers in the manufacturing process for our current and future product candidates; • our third- party manufacturers could breach or terminate their agreements with us; • raw materials and components used in the manufacturing process, particularly those for which we have no other source or supplier, may not be available or may not be suitable or acceptable for use due to material or component defects; and • our contract manufacturers and critical reagent suppliers may be subject to inclement weather, as well as natural or man- made disasters. Each of these risks could delay or prevent the completion of our clinical trials or the approval of any of our current and future product candidates by the FDA, result in higher costs or adversely impact commercialization of our current and future product candidates. In addition, we will rely on third parties to perform certain specification tests on our product candidates prior to delivery to patients. If these tests are not appropriately done and test data are not reliable, patients could be put at risk of serious harm and the FDA could place significant restrictions on our company until deficiencies are remedied. Significant non- compliance could also result in the imposition of sanctions, including warning or untitled letters, fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage our reputation and our business. Additionally, for some of our product candidates, we rely on third parties located in China to manufacture and supply certain raw materials, drug substances, and / or drug products ~~used in our product candidates~~, and we expect to continue to use such third- party manufacturers **as needed** ~~for such purposes~~. A natural disaster, epidemic or pandemic disease outbreak, trade war, political unrest or other event (s) in China or in adjacent geopolitical territories could disrupt the business or operations of our CMOs with whom we conduct business now or in the future. Any disruption in China or in adjacent geopolitical territories that significantly impacts such third parties, including their ability to produce and deliver materials according to our contracts in adequate quantities to meet our needs could impede, delay, limit, or prevent the research and development of our current and future product candidates. In addition, for any activities conducted in China, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the policies of the U. S. or Chinese governments, political unrest or unstable economic conditions in China. For example, ~~in February 2024,~~ **recently proposed legislation (BIOSECURE Act) by** certain U. S. lawmakers called for possible ~~sanctions~~ **restrictions** against ~~the~~ **certain named** Chinese CMOs, **such as** WuXi AppTec and WuXi Biologics ~~(collectively, " WuXi "), over alleged ties to China' s Communist Party and its military~~. Any unfavorable government policies on international trade, such as export controls, capital controls or tariffs, new legislation or regulations, renegotiation of existing trade agreements, or any retaliatory trade actions due to recent trade tension, may impede, delay, limit, or increase the cost of manufacturing our product candidates including pursuant to any of our manufacturing service arrangements with WuXi **AppTec or WuXi Biologics**. Such events could have an adverse effect on our business, financial condition and results of operations. The manufacture of drug products, and particularly biologics, is complex and our third- party manufacturers may encounter difficulties in production. If any of our third- party manufacturers encounter such difficulties, our ability to provide supply of our current and future product candidates, if approved, could be delayed or prevented. Manufacturing drugs, particularly biologics, especially in large quantities, is often complex and may require the use of innovative technologies to handle living cells. Each lot of an approved biologic must undergo thorough testing for identity, strength, quality, purity, **and** potency ~~and stability~~. Manufacturing biologics requires facilities specifically designed for and validated for this purpose, and sophisticated quality assurance and quality control procedures are necessary. Slight deviations anywhere in the manufacturing process, including filling, labeling, packaging, storage and shipping **,** and quality control ~~and~~ testing, may result in lot failures, product recalls or spoilage. When changes are made to the manufacturing process, we may be required to provide preclinical and clinical data showing the comparable identity, strength, quality, purity or potency of the products before and after such changes. If microbial, viral or other contaminations are discovered at the facilities of our manufacturers, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely harm our business. In addition, there are risks associated with large scale manufacturing for clinical trials or commercial scale including, among others, cost overruns, potential problems with process scale- up, process reproducibility, stability issues, compliance with good manufacturing practices, lot consistency and timely availability of raw materials. Even if we obtain marketing approval for any of our current and future product candidates, there is no assurance that our manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other comparable foreign regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential commercial launch of the product or to meet potential future demand. If our manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects. If

our third- party manufacturers use hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages. Our research and development activities involve the controlled use of potentially hazardous substances, including chemical and biological materials, by our third- party manufacturers. Our manufacturers are subject to federal, state and local laws and regulations in the U. S. governing the use, manufacture, storage, handling and disposal of medical and hazardous materials. Although we believe that our manufacturers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury resulting from medical or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. We do not have any insurance for liabilities arising from medical or hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations. Risks Related to Managing Growth and Employee Matters We are highly dependent on our key personnel. If we are not successful in retaining highly qualified personnel, we may not be able to successfully implement our business strategy. Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our senior management, including scientific and medical personnel, and other key employees. While we expect to engage in an orderly transition process as we integrate newly appointed officers and managers, we face a variety of risks and uncertainties relating to management transition, including diversion of management attention from business concerns, failure to retain other key personnel or loss of institutional knowledge. In addition, 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. In particular, due to our small number of employees, the loss of one employee may have a larger impact on our business than compared to a loss at one of our peers. We conduct our operations at our facilities in Cambridge, Massachusetts. The Massachusetts region is headquarters to many other biopharmaceutical companies and many academic and research institutions. 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. Changes to U. S. immigration and work authorization laws and regulations, including those that restrain the flow of scientific and professional talent, can be significantly affected by political forces and levels of economic activity. Our business may be materially adversely affected if legislative or administrative changes to immigration or visa laws and regulations impair our hiring processes and goals or projects involving personnel who are not U. S. citizens. To encourage valuable employees to remain at our company, in addition to salary and cash incentives, we have provided equity that vests over time. The value to employees of stock options that vest over time may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific, and development teams may terminate their employment with us on short notice. Although we have employment agreements with our key employees, these employment agreements provide for at- will employment, which means that any of our employees could leave our employment at any time, with or without notice. 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. We will need to grow the size of our organization, and we may experience difficulties in managing this growth. As of December 31, ~~2023~~ **2024**, we had ~~85~~ **111** full- time employees. As our development and commercialization plans and strategies develop, we expect to need additional managerial, operational, sales, marketing, financial and other personnel. Future growth would impose significant added responsibilities on members of management, including: • identifying, recruiting, integrating, maintaining and motivating additional employees; • managing our internal development efforts effectively, including the clinical and FDA review process for our product candidates, while complying with our contractual obligations to contractors and other third parties; and • improving our operational, financial and management controls, reporting systems and procedures. Our future financial performance and our ability to commercialize our current and future product candidates that are approved for marketing will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day- to- day activities in order to devote a substantial amount of time to managing these growth activities. If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and potentially commercialize our current and future product candidates and, accordingly, may not achieve our research, development and commercialization goals. Our internal computer systems, or those used by our third- party CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption to the development programs of our current and future product candidates. Despite the implementation of security measures, our internal computer systems and those of our current and future CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, and telecommunication and electrical failures. While we have not experienced any such material system failure or security breach to date, 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 data from completed or future preclinical studies and clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed. We

may be unable to adequately protect our information systems from cyberattacks, which could result in the disclosure of confidential or proprietary information, including personal data, damage our reputation, and subject us to significant financial and legal exposure. We rely on information technology systems that we or our third- party providers operate to process, transmit and store electronic information in our day- to- day operations. In connection with our product discovery efforts, we may collect and use a variety of personal data, such as name, mailing address, email addresses, phone number and clinical trial information. A successful cyberattack could result in the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. We also continue to provide for remote work for our employees, which may increase our vulnerability to cyber and other information technology risks. Cyberattacks could include wrongful conduct by hostile foreign governments, industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, denial- of- service **, ransomware, business email compromise, phishing attacks** , social engineering fraud or other means to threaten data security, confidentiality, integrity and availability. A successful cyberattack could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. Although we devote resources to protect our information systems, we realize that cyberattacks are a threat, and there can be no assurance that our efforts will prevent information security breaches that would result in business, legal, financial or reputational harm to us, or would have a material adverse effect on our results of operations and financial condition. Any failure to prevent or mitigate security breaches or improper access to, use of, or disclosure of our clinical data or patients' personal data could result in significant liability under state (e. g., state breach notification laws), federal (e. g., HIPAA, as amended by HITECH), and international law (e. g., the GDPR) and may cause a material adverse impact to our reputation, affect our ability to conduct new studies and potentially disrupt our business. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In some cases, data cannot be reproduced. To the extent that any disruption or security breach was to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur material legal claims and liability, damage to our reputation, and the further development of our devices and drugs or any future product candidate could be delayed. If a security breach results in the exposure or unauthorized disclosure of personal information, we could incur additional costs associated with data breach notification and remediation expenses, investigation costs, regulatory penalties and fines, and legal proceedings. Our insurance coverage may not be adequate to cover all the costs related to such breaches or attacks. **Furthermore, we cannot be sure that insurance will continue to be available to us on commercially reasonable terms, if at all, or that any insurer will not deny coverage as to any future claim.** In addition, the computer systems of various third parties on which we rely, including our CROs and other contractors, consultants and law and accounting firms, may sustain damage from computer viruses, unauthorized access, data breaches, phishing attacks, cybercriminals, natural disasters (including hurricanes and earthquakes), terrorism, war and telecommunication and electrical failures. We rely on our third- party providers to implement effective security measures and identify and correct for any such failures, deficiencies or breaches. If we or our third- party providers fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to our information technology systems, we or our third- party providers could have difficulty preventing, detecting and controlling such cyber- attacks and any such attacks could result in losses described above as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating expenses, expenses or lost revenues or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows. Any failure by such third parties to prevent or mitigate security breaches or improper access to or disclosure of such information could have similarly adverse consequences for us. If we are unable to prevent or mitigate the impact of such security or data privacy breaches, we could be exposed to litigation and governmental investigations, which could lead to a potential disruption to **our business. As cybersecurity threats continue to evolve, we may be required to expend significant additional resources to continue to modify or enhance our protective measures or to investigate and remediate any information security vulnerabilities. The inability to implement, maintain and upgrade adequate safeguards could have a material adverse effect on** our business. Risks Related to Ownership of Our Common Stock The price of our stock may be volatile, and you could lose all or part of your investment. The trading price of our common stock is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this " Risk Factors " section and elsewhere in this Annual Report on Form 10- K, these factors include: • the results of our ongoing, planned or any future preclinical studies, clinical trials or clinical development programs; • the commencement, enrollment, or results of clinical trials of our current and future product candidates, or changes in the development status of our product candidates; • adverse results or delays in preclinical studies and clinical trials, including as a result of clinical holds; • our decision to initiate a clinical trial, not to initiate a clinical trial, or to terminate an existing clinical trial; • any delay in our regulatory filings or any adverse regulatory decisions, including failure to receive regulatory approval of our current and future product candidates; • changes in laws or regulations applicable to our products, including but not limited to clinical trial requirements for approvals; • adverse developments concerning our manufacturers or our manufacturing plans; • our inability to obtain adequate product supply for any licensed product or inability to do so at acceptable prices; • our inability to establish collaborations if needed; • our failure to commercialize our current and future product candidates; • additions or departures of key scientific or management personnel; • unanticipated serious safety concerns related to the use of our current and future product candidates; • introduction of new products or services offered by us or our competitors; • announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors; • our ability to effectively

manage our growth; • the size and growth of our initial ~~cancer~~ target markets; • our ability to successfully treat additional types of **autoimmune diseases or** cancers or at different stages; • actual or anticipated variations in quarterly operating results; • our cash position; • our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public; • publication of research reports about us or our industry, or immunotherapy in particular, or positive or negative recommendations or withdrawal of research coverage by securities analysts; • changes in the market valuations of similar companies; • overall performance of the equity markets; • sales of our common stock by us or our stockholders in the future; • trading volume of our common stock; • changes in accounting practices; • ineffectiveness of our internal controls; • disputes or other developments relating to intellectual property or proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies; • significant lawsuits, including intellectual property or stockholder litigation; • general political and economic conditions; and • other events or factors, many of which are beyond our control. In addition, the stock market in general, and The Nasdaq Global Select Market and market for 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. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. 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, financial condition, results of operation and future prospects. We expect our financial condition and results of operations to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance. We do not intend to pay dividends on our common stock, so any returns will be limited to the value of our stock. We currently anticipate that we will retain future earnings for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, we may enter into agreements that prohibit us from paying cash dividends without prior written consent from our contracting parties, or which other terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited to the appreciation of their stock, which may never occur. Our principal stockholders and management own a significant percentage of our stock and ~~will~~ **could** be able to exert significant influence over matters subject to stockholder approval. Our executive officers, directors, and 5 % stockholders beneficially owned approximately ~~53~~ **41** . 8 % of our voting stock, based on ~~44~~ **58** , ~~108~~ **618** , ~~892~~ **729** shares of our common stock deemed to be outstanding as of December 31, ~~2023~~ **2024** , which assumes conversion of ~~1~~ **108** , **119** ~~208, 809~~ shares of outstanding ~~Series A~~ convertible preferred stock into shares of common stock. These stockholders **could** have the ability to influence us through their ownership position ~~. Accordingly, and significantly affect these -- the outcome of stockholders may be able to determine~~ all matters requiring stockholder approval. For example, these stockholders may be able to ~~control~~ **significantly affect the outcome of** elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders ~~. We are an emerging growth company and a smaller reporting company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies will make our common stock less attractive to investors. We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act (the" JOBS Act"), enacted in April 2012. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes- Oxley Act of 2002 (as amended, the" Sarbanes- Oxley Act"), reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the closing of our initial public offering, (b) in which we have total annual gross revenue of at least $ 1. 235 billion or (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common stock that is held by non- affiliates to exceed $ 700 million as of the last business day of the most recently completed second fiscal quarter, and (2) the date on which we have issued more than $ 1 billion in non- convertible debt during the prior three- year period. Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to not " opt out " of this exemption from complying with new or revised accounting standards and, therefore, we will adopt new or revised accounting standards at the time private companies adopt the new or revised accounting standard and will do so until such time that we either (i) irrevocably elect to " opt out " of such extended transition period or (ii) no longer qualify as an emerging growth company. Even after we no longer qualify as an emerging growth company, we may still qualify as a " smaller reporting company, " which would allow us to continue to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes- Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We may take advantage of scaled disclosures available to smaller reporting companies until the fiscal year following the determination that either (i) the market value of our voting and non- voting common stock held by non- affiliates is greater than $ 700 million, as measured on the last business day of the most recently completed second fiscal quarter, or (ii) the market value of our voting and non- voting common stock held by non- affiliates, as measured on the last business day of our most recently completed second fiscal quarter, is less than $ 700 million but greater than $ 250 million and our annual revenues during our most recently completed fiscal year are greater than $ 100 million. We cannot predict if investors will find our common stock less attractive~~

~~because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile~~ . Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an " ownership change " (generally defined as a greater than 50 % change (by value) in its equity ownership by 5 % stockholders over a three- year period), the corporation' s ability to use its pre- change net operating loss (" NOL") carryforwards and other pre- change tax attributes to offset its post- change taxable income may be limited. As a result of our most recent private placements and other transactions that have occurred over the past three years, we may have experienced, and may experience, an " ownership change. " We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As of December 31, ~~2023~~ **2024** , we had U. S. federal and state NOL carryforwards of $ ~~54~~ **125** . 3 million and $ ~~56~~ **128** . ~~8~~ **2** million, respectively, which could be limited if we experience an " ownership change. " As of December 31, ~~2023~~ **2024** , $ ~~52~~ **123** . 9 million our federal NOLs can be carried forward indefinitely and $ 1. 4 million, which were generated prior to 2018, expire in 2037. As of December 31, ~~2023~~ **2024** , state NOL carryforwards begin to expire in 2031. As of December 31, ~~2023~~ **2024** , we had federal and state research and development tax credit carryforwards of $ ~~1~~ **5** . ~~6~~ **4** million and $ 2. 0 million, respectively, which could be limited if we experience an " ownership change. " As of December 31, ~~2023~~ **2024** , our federal research and development tax credit carryforwards begin to expire in 2036, $ 0. 3 million of our state research and development tax credit carryforwards can be carried forward indefinitely, and the remaining $ 1. 7 million of our state research and development tax credit carryforwards expires beginning in 2036. The reduction of the corporate tax rate under the Tax Cuts and Jobs Act of 2017 (the" TCJA"), may cause a reduction in the economic benefit of our NOL carryforwards and other deferred tax assets available to us. Under the TCJA, federal NOLs generated after December 31, 2017 will not be subject to expiration but will not be permitted to be carried back. In addition, under the TCJA, the amount of post- 2017 NOLs that we are permitted to deduct in any taxable year is limited to 80 % of our taxable income in such year, where taxable income is determined without regard to the NOL deduction itself. 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 second amended and restated certificate of incorporation and ~~second~~ **third** 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. Some of these provisions include: • a board of directors divided into three classes serving staggered three- year terms, such that not all members of the board will be elected at one time; • a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders; • a requirement that special meetings of stockholders be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office; • advance notice requirements for stockholder proposals and nominations for election to our board of directors; • a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two- thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors; • a requirement of approval of not less than two- thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and • the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock. 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 second amended and restated certificate of incorporation and ~~second~~ **third** 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 ~~second~~ **third** amended and restated bylaws designate specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us. Pursuant to our ~~second~~ **third** amended and restated bylaws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for state law claims for (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, or other employees to us or our stockholders; (3) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law or our certificate of incorporation or bylaws; (4) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; or (5) any action asserting a claim governed by the internal affairs doctrine, or the Delaware Forum Provision. The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Our ~~second~~ **third** amended and restated bylaws will further provide that unless we consent in writing to the selection of an alternative forum, the U. S. District Court for the District of Delaware will be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or the Federal Forum Provision, as the Company is incorporated in the State of Delaware. In addition, our ~~second~~ **third** amended and restated bylaws will provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and consented to the Delaware Forum Provision and the Federal Forum Provision; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the U. S. federal securities laws and the rules and regulations thereunder. The Delaware Forum Provision and

the Federal Forum Provision in our ~~second~~ **third** amended and restated bylaws may impose additional litigation costs on stockholders in pursuing any such claims. Additionally, these forum selection clauses may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage the filing of lawsuits against us and our directors, officers and employees, even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are " facially valid " under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the U. S. District Court for the District of Delaware may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders. If we fail to establish and maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed. Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time- consuming effort that needs to be re- evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. **If we fail to adequately staff our accounting and finance function to address the additional demands that are applicable to us as a public company, including the requirements of the Sarbanes- Oxley Act of 2002, or fail to maintain adequate internal control over financial reporting, it could prevent our management from concluding our internal control over financial reporting is effective and impair our ability to prevent material misstatements in our financial statements, which could cause our business to suffer. As a large accelerated filer, we are subject to additional internal control requirements of the Sarbanes- Oxley Act of 2002.** Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes, and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm our stock price. If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline. The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. In the event one or more of the analysts who cover us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.