Risk Factors Comparison 2024-02-22 to 2023-02-23 Form: 10-K

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Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report on Form 10- K, including our consolidated financial statements and the related notes and ~~“~~ **"** Management' s Discussion and Analysis of Financial Condition and Results of Operations, ~~”~~ **"** before deciding whether to invest in our common stock. We believe the risks described below include risks that are material to us as well as other risks that may adversely affect our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also materially harm our business, financial condition, results of operations and growth prospects and could result in a complete loss of your investment. Consequently, you should not consider the following to be a complete discussion of all potential risks or uncertainties. Risks Related to Our Product Candidates Risks Related to Clinical Development We have never successfully completed any **large- scale, pivotal** clinical trials, and we may be unable to do so for any product candidates we develop. We have not yet demonstrated our ability to successfully complete any ~~clinical trials, including~~ large- scale, pivotal clinical trials, obtain regulatory approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. We have three product candidates ~~, RLY- 4008, RLY- 2608 and GDC- 1971 (formerly known as RLY- 1971),~~ in clinical development. We may not be able to file INDs for any of our other product candidates on the timelines we expect, if at all. For example, we may experience manufacturing delays or delays with IND- enabling studies. Moreover, we cannot be sure that once we have submitted an IND, the FDA will allow further clinical trials to begin, or that, once begun, issues will not arise that require us to suspend or terminate clinical trials. The FDA or other regulatory authorities may impose a clinical hold before or after a trial begins for a number of reasons outlined in FDA regulations, including if the FDA believes the study drug raises a significant risk of illness or injury. If the FDA imposes a clinical hold, trials may not commence or recommence without FDA authorization and then only under terms authorized by the FDA. Accordingly, the submission of an IND does not mean the FDA will allow clinical trials to begin and, if and when clinical trials do commence under an active IND, issues may arise that require suspension or termination of such trials. Further, commencing each of these clinical trials is subject to finalizing the trial design based on discussions with the FDA and other regulatory authorities. Any guidance we receive from the FDA or other regulatory authorities is subject to change. Regulatory authorities could change their position, including, on the acceptability of our trial designs or the clinical endpoints selected, which may require us to complete additional clinical trials or impose stricter approval conditions than we currently expect. Successful completion of our clinical trials is a prerequisite to submitting a new drug application, or NDA, to the FDA and a Marketing Authorization Application, or MAA, to the EMA for each product candidate and, consequently, the ultimate approval and commercial marketing of each product candidate. **We have ongoing** ~~Our RLY- 4008 and RLY- 2608~~ first- in- human clinical trials ~~are ongoing~~ , but we do not know whether any of our future clinical trials will begin on time or be completed on schedule, if at all. If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may: • be delayed in obtaining marketing approval for our product candidates; • not obtain marketing approval at all; • obtain approval for indications or patient populations that are not as broad as intended or desired; • be subject to post- marketing requirements; or • have the product removed from the market after obtaining marketing approval. Clinical product development involves a lengthy and expensive process, with an uncertain outcome. 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 the required clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. 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. 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 and other nonclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates. Our preclinical and other nonclinical studies and future clinical trials may not be successful. From time to time, we may publish interim, top- line or preliminary 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 more participants enroll and as data mature. Preliminary or top- line data also remain subject to cleaning and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates. We may experience delays in completing our preclinical studies and initiating or completing clinical trials, and we may experience numerous unforeseen events during, or as a result of, any future clinical trials that we could conduct that could delay or prevent our ability to receive marketing approval or commercialize our product

candidates, including: • regulators or institutional review boards, or IRBs, or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site; • we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites; • existing clinical trial sites may drop out of the clinical trial, which may require that we add new clinical trial sites or investigators; • clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional nonclinical studies or clinical trials or we may decide to abandon product development programs; • the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials 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 or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol; • we may elect to, or regulators or IRBs or ethics committees may require us or our investigators to, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements 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; • we may not be able to adequately project the timing and quantity of our product candidates or other materials necessary to conduct clinical trials of our product candidates or the supply or quality of these materials may be insufficient or inadequate; and • our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs or ethics committees to suspend or terminate the clinical trials, or reports may arise from nonclinical studies or clinical testing of other therapies that raise safety or efficacy concerns about our product candidates. We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions at which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or other regulatory authorities. Such authorities may impose a suspension or termination or clinical hold due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or clinical trial site by the FDA or other regulatory authorities, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA may disagree with our clinical trial design or our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials. Our product development costs will also increase if we experience delays in preclinical studies, clinical trials or regulatory approvals. We do not know whether any of our future clinical trials will begin as planned, or whether any of our current or future clinical trials will need to be restructured or will be completed on schedule, if at all. Significant preclinical study or clinical trial delays ~~, including those caused by the ongoing COVID- 19 pandemic,~~ also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. Any delays in our preclinical or current or future clinical development programs may harm our business, financial condition and prospects significantly. If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. In particular, because we will be deploying our drug discovery platform across a broad target space, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. In addition, some of our competitors have ongoing clinical trials for product candidates that treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates ~~. Furthermore, our ability to enroll patients may be significantly delayed by developments in connection with the ongoing COVID- 19 pandemic, including increased severity or additional variant outbreaks thereof, which are highly uncertain, and we cannot predict the extent and scope of such delays at this point~~ . In addition to the competitive clinical trial environment, the eligibility criteria of our planned clinical trials will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure to assure their cancer is either severe enough or not too advanced to include them in a study. Additionally, the process of finding 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 candidates under study, the availability and efficacy of competing therapies and clinical trials, the proximity and availability of clinical trial sites for prospective patients, 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. We have engaged and may continue to engage third parties to develop companion diagnostics for use in our clinical trials, but such third parties may not be successful in developing such companion diagnostics, furthering the difficulty in identifying patients with the targeted genetic mutations for our clinical trials. Further, if we are required to develop companion diagnostics and are unable to include patients with the targeted genetic mutations, this could compromise our ability to seek participation in the FDA' s expedited review and development programs, including Breakthrough Therapy Designation and Fast Track Designation, or otherwise to seek to accelerate clinical development and regulatory timelines. The FDA has indicated that if we continue RLY- ~~4008 and RLY-~~ 2608 **and lirafugratinib** in a specific biomarker- defined population, a companion diagnostic device will be required to ensure their safe and effective use. Although we have engaged Foundation Medicine, Inc. to develop its FoundationOne ® CDx as a companion diagnostic for **lirafugratinib** ~~RLY- 4008~~ , if any of our current or future third- party

companion diagnostic partners is unable or unwilling to obtain or maintain regulatory approval for a companion diagnostic for any of our product candidates, regulatory approval for such product candidates, if obtained at all, may be delayed. Clinical trial enrollment may be affected by other factors including: • the severity of the disease under investigation; • the eligibility criteria for the clinical trial in question; • the availability of an appropriate genomic screening test; • the perceived risks and benefits of the product candidate under study; • the **resources and** efforts **required** to facilitate timely enrollment in clinical trials; • the availability of approved products that treat the same indications as our product candidates; • the patient referral practices of physicians; • the ability to monitor patients adequately during and after treatment; • the proximity and availability of clinical trial sites for prospective patients; and • factors we may not be able to control that may limit patients, principal investigators or staff or clinical site availability, such as uncertain geopolitical conditions or current or future pandemics ~~(e. g., complications due to the current conflict between Russia and Ukraine or the ongoing COVID- 19 pandemic)~~ . Positive data from preclinical or early clinical studies of our product candidates are not necessarily predictive of the results of later clinical studies and any future clinical trials of our product candidates. If we cannot replicate the positive data from our preclinical or early clinical studies of our product candidates in our future clinical trials, we will be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates. Any positive data from our preclinical or early clinical studies of our product candidates may not necessarily be predictive of the results of later clinical studies and any future clinical trials of our product candidates. Similarly, even if we are able to complete our planned preclinical and clinical studies or any future clinical trials of our product candidates according to our current development timeline, the positive data from such preclinical or early clinical studies and clinical trials of our product candidates may not be replicated in subsequent nonclinical studies or clinical trial results. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late- stage clinical trials after achieving positive results in early- stage development and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical and other nonclinical findings made while clinical trials were underway, or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Moreover, preclinical, other nonclinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA, EMA or other regulatory authority approval. Our current or future clinical trials or those of our future collaborators may reveal significant adverse events not seen in our preclinical or other nonclinical studies or early clinical data and may result in a safety profile that would inhibit regulatory approval or market acceptance of any of our product candidates. Before obtaining regulatory approvals for the commercial sale of any products, we must demonstrate through lengthy, complex and expensive preclinical or other nonclinical studies and clinical trials that our product candidates are both safe and effective for use in each target indication. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical or other nonclinical studies and early clinical trials of our product candidates may not be predictive of the results of later- stage clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical trials. Product candidates in later stages of clinical trials also may fail to show the desired safety and efficacy profile despite having progressed through preclinical or other nonclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that commence clinical trials are never approved as products and there can be no assurance that any of our current or future clinical trials will ultimately be successful or support further clinical development of any of our product candidates. We may develop future product candidates, in combination with one or more cancer therapies. The uncertainty resulting from the use of our product candidates in combination with other cancer therapies may make it difficult to accurately predict side effects in future clinical trials. As is the case with many treatments for cancer and rare diseases, it is likely that there may be side effects associated with the use of our product candidates. If significant adverse events or other side effects are observed in any of our current or future clinical trials, we may have difficulty recruiting patients to our clinical trials, patients may drop out of our clinical trials, or we may be required to abandon the clinical trials or our development efforts of one or more product candidates altogether. We, the FDA or other applicable regulatory authorities, or an IRB may suspend or terminate clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early- stage clinical trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the product from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance of the approved product due to its tolerability versus other therapies. Any of these developments could materially harm our business, financial condition and prospects. Although we intend to explore other therapeutic opportunities, in addition to the product candidates that we are currently developing, we may fail to identify viable new product candidates for clinical development for a number of reasons. If we fail to identify additional potential product candidates, our business could be materially harmed. Research programs to pursue the development of our existing and planned product candidates for additional indications and to identify new product candidates and disease targets require substantial technical, financial and human resources whether or not they are ultimately successful. For example, pursuant to the DESRES Agreement, we collaborate with D. E. Shaw Research to develop various protein models and make predictions as to how molecules might move, with subsequent validation efforts in our and our CROs' labs. There can be no assurance that we will find potential additional targets using this approach, that any such targets will be tractable, or that such clinical validations will be successful. Our research programs may initially show promise in identifying potential indications and / or product candidates, yet fail to yield results for clinical development for a number of reasons, including: • the research methodology used may not be successful in identifying potential indications and / or product

candidates; • potential product candidates may, after further study, be shown to have harmful adverse effects or other characteristics that indicate they are unlikely to be effective products; or • it may take greater human and financial resources than we will possess to identify additional therapeutic opportunities for our product candidates or to develop suitable potential product candidates through internal research programs, thereby limiting our ability to develop, diversify and expand our product portfolio. Because we have limited financial and human resources, we intend to initially focus on research programs and product candidates for a limited set of indications. As a result, we may forgo or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Accordingly, there can be no assurance that we will ever be able to identify additional therapeutic opportunities for our product candidates or to develop suitable potential product candidates through internal research programs or in collaboration with third parties, which could materially adversely affect our future growth and prospects. We may focus our efforts and resources on potential product candidates or other potential programs that ultimately prove to be unsuccessful. We intend to develop our current product candidates and potentially future product candidates, in combination with other therapies, which exposes us to additional risks. We intend to develop our current product candidates, and may develop future product candidates, for use in combination with one or more currently approved cancer therapies. Even if any product candidate we develop was to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to bear the risks that the FDA or similar regulatory authorities could revoke approval of the therapy used in combination with our product candidates or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies. Combination therapies are commonly used for the treatment of cancer, and we would be subject to similar risks if we develop any of our product candidates for use in combination with other drugs or for indications other than cancer. This could result in our own products being removed from the market or being less successful commercially. We may also evaluate our current product candidates or any other future product candidates in combination with one or more other cancer therapies that have not yet been approved for marketing by the FDA or similar regulatory authorities. We will not be able to market and sell any of our product candidates we develop in combination with any such unapproved cancer therapies that do not ultimately obtain marketing approval. Pursuant to the Genentech Agreement, Genentech ~~will~~ **has** ~~assume~~ **assumed** the development of **migoprotafib** ~~GDC-1971~~, including ~~developing GDC-1971~~ in combination with **other compounds** ~~Genentech's KRAS G12C program and in combination with atezolizumab, its PD-L1 antibody~~. See ~~"~~ **"** Business – Our Collaborations – ~~Key~~ License Agreements and Strategic Collaborations – Collaboration and License Agreement with Genentech. ~~"~~ **"** If the FDA or similar regulatory authorities do not approve these other drugs or revoke their approval of, or if safety, efficacy, manufacturing, or supply issues arise with, the drugs we choose to evaluate in combination with our current product candidates or any product candidate we develop, we may be unable to obtain approval of or market any of the product candidates we develop. Our product candidates utilize a novel mechanism of action and novel binding locations, which may result in greater research and development expenses, regulatory issues that could delay or prevent approval, or discovery of unknown or unanticipated adverse effects. Our product candidates utilize novel mechanisms of action and novel binding locations, which may result in greater research and development expenses, regulatory issues that could delay or prevent approval, or discovery of unknown or unanticipated adverse effects. Our Dynamo platform uses advanced computational models in tight integration with our medicinal chemistry, structural biology, enzymology and biophysics capabilities to predict and design the compounds that will achieve the most desirable characteristics, including potency, selectivity, bioavailability, and drug- like properties. A disruption in any of these capabilities may have significant adverse effects in our abilities to expand our Dynamo platform, and we cannot predict whether we will continue to have access to these capabilities in the future to support our Dynamo platform. In addition, there can be no assurance that we will be able to rapidly identify, design and synthesize the necessary compounds or that these or other problems related to the development of this novel mechanism will not arise in the future, which may cause significant delays, or we raise problems we may not be able to resolve. Regulatory approval of novel product candidates such as ours can be more expensive, riskier and take longer than for other, more well- known or extensively studied pharmaceutical or biopharmaceutical product candidates due to our and regulatory agencies' lack of experience with them. The novelty of our mechanism of action may lengthen the regulatory review process, require us to conduct additional studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post- approval limitations or restrictions. The novel mechanism of action also means that fewer people are trained in or experienced with product candidates of this type, which may make it more difficult to find, hire and retain personnel for research, development and manufacturing positions. Because our inhibitors utilize a novel mechanism of action that has not been the subject of extensive study compared to more well- known product candidates, there is also an increased risk that we may discover previously unknown or unanticipated adverse effects during our preclinical or other nonclinical studies and clinical trials. Any such events could adversely impact our business prospects, financial condition and results of operations. We are conducting, or have filed clinical trial applications to conduct, clinical trials for our product candidates outside the United States, and the FDA and similar foreign regulatory authorities may not accept data from such trials. We are conducting, or have filed clinical trial applications to conduct, additional clinical trials outside the United States, including Australia, the United Kingdom, Europe and Asia and may conduct, or file clinical trial applications to conduct, additional clinical trials in other foreign jurisdictions in the future. The acceptance of trial data from clinical trials conducted outside the United States by the FDA may be subject to certain conditions. In cases where data from clinical trials conducted outside the United States are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; (ii) the trials were performed by clinical investigators of recognized competence and (iii) the data may be considered valid without the need for an on- site inspection by the FDA or, if the FDA considers such

an inspection to be necessary, the FDA is able to validate the data through an on- site inspection or other appropriate means. Additionally, the FDA' s clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any similar foreign regulatory authority will accept data from clinical trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any similar foreign regulatory authority does not accept such data, it would result in the need for additional clinical trials, which would be costly and time- consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction. Risks Related to Obtaining Regulatory Approvals If we are not able to obtain, or if delays occur 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 regulatory agencies in the United States and by similar authorities in other countries. Before we can commercialize any of our product candidates, we must obtain marketing approval. Currently, all of our product candidates are in development, and we have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. It is possible that our product candidates, including any product candidates we may seek to develop in the future, will never obtain regulatory approval. We have only limited experience in filing and supporting the applications necessary to gain regulatory approvals and expect to rely on third- party CROs and / or regulatory consultants to assist us in this process. Securing regulatory approval requires the submission of extensive nonclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate' s safety and efficacy. 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. 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. In addition, regulatory authorities may find fault with our manufacturing process or facilities or that of third- party contract manufacturers. We may also face greater than expected difficulty in manufacturing our product candidates. The process of obtaining regulatory approvals, both in the United States and abroad, is expensive and often takes many years. If the FDA or a similar foreign regulatory authority requires that we perform additional nonclinical studies or clinical trials, approval, if obtained at all, may be delayed. The length of such a delay varies 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 NDA, a 510 (k) or other premarket approval application, or PMA, or equivalent application types, may cause delays in the approval or rejection of an application. The FDA and similar authorities in other countries 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 nonclinical, 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 similar foreign regulatory authorities may disagree with or change their position regarding the design or implementation of our clinical trials; • we may not be able to enroll a sufficient number of patients in our clinical studies; • we may be unable to demonstrate to the satisfaction of the FDA or similar 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 similar 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 similar foreign regulatory authorities may disagree with our interpretation of data from nonclinical studies or clinical trials; • the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere; • the FDA or similar foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes or facilities of third- party manufacturers with which we contract for clinical and commercial supplies; and • the approval policies or regulations of the FDA or similar foreign regulatory authorities may significantly change such that our clinical data are insufficient for approval. Even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, thereby narrowing the commercial potential of the product candidate. In addition, regulatory authorities may grant approval contingent on the performance of costly post- marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates. If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired. Risks Related to Commercialization The incidence and prevalence for target patient populations of our product candidates have not been established with precision. If the market opportunities for our product candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability will be adversely affected, possibly materially. ~~In 2022, we completed enrollment of a Phase 1a dose escalation study of GDC- 1971 as a monotherapy in patients with advanced or metastatic solid tumors, and pursuant to the Genentech Agreement entered into in December 2020, future development for GDC- 1971, including the potential to conduct multiple combination studies, is governed by a joint development team between us and Genentech. Genentech initiated the cohort of GDC- 1971 in combination with GDC- 6036, its~~

~~KRAS G12C inhibitor, in a Phase 1b trial in July 2021, and a Phase 1b trial of GDC- 1971 in combination with atezolizumab, its PD- L1 antibody, in August 2022. We estimate there are approximately 37, 000 patients annually in the United States with advanced lung cancer or colorectal cancer who might benefit from a combination of GDC- 1971 with another targeted inhibitor. In the future, if GDC- 1971 advances to earlier lines of combination treatment for lung cancer or colorectal cancer, we believe it could be applied in the treatment of approximately 69, 000 patients annually in the United States. The subset of patients with KRAS G12C mutations in lung cancer and colorectal cancer who could potentially benefit from the combination of GDC- 1971 with GDC- 6036 is approximately 17, 000 to 32, 000 annually in the United States. We are also evaluating the safety and tolerability of RLY- 4008 in a first- in- human clinical trial initiated in September 2020 in patients with advanced or metastatic FGFR2- altered solid tumors with a single arm, potentially registration- enabling cohort for FGFRi treatment- naïve FGFR2- fusion CCA. We believe FGFR2- mediated cancers affect approximately 11, 000 late- line patients annually in the United States. In the future, if RLY- 4008 advances to earlier lines of treatment, we believe it could potentially address approximately 35, 000 patients annually in the United States. These numbers reflect the inclusion of patients with additional FGFR2 gene fusions and rearrangements that result from truncation of the protein at exon 18 based on recently published research suggesting that patients with these truncations should be considered for FGFR- targeted therapies. In December 2021, we dosed the first patient in a first- in- human clinical trial for RLY- 2608, the first known allosteric, pan- mutant (H1047X, E542X and E545X) and isoform- selective PI3Kα inhibitor in clinical development. We believe RLY- 2608 has the potential to address approximately 50, 000 to 156, 000 patients per year in the United States, one of the largest patient populations for a precision oncology medicine.~~ Our projections of both the number of people who have ~~these~~ -- **the** diseases **our product candidates are targeting**, as well as the subset of people with ~~these~~ **such** ~~diseases~~ - **disease** who have the potential to benefit from treatment with **any of** ~~RLY- 4008, RLY- 2608 or~~ **our** ~~GDC- 1971, or our other~~ product candidates, are based on estimates. The total addressable market opportunity will ultimately depend upon, among other things, the diagnosis criteria included in the final label, and, if our product candidates are approved for sale for these indications, acceptance by the medical community and patient access, product pricing and reimbursement. The number of patients with cancers and solid tumors may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our products, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business. We may not be successful in our efforts to identify additional product candidates. Due to our limited resources and access to capital, we must prioritize development of certain product candidates **. For example** , ~~which~~ **we recently deprioritized RLY- 5836 in order to focus our resources on advancing RLY- 2608. These and other prioritization decisions** may prove to be the wrong choice and may adversely affect our business. We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do. The development and commercialization of new products in the biopharmaceutical and related industries is highly competitive. We compete in the segments of the pharmaceutical, biotechnology, and other related markets that address computationally focused structure- based drug design in cancer and genetic diseases. There are other companies focusing on structure- based drug design to develop therapies in the fields of cancer and other diseases. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. These companies include divisions of large pharmaceutical companies and biotechnology companies of various sizes. We face competition with respect to our current product candidates, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Any product candidates that we successfully develop and commercialize will compete with currently approved therapies and new therapies that may become available in the future from segments of the pharmaceutical, biotechnology and other related markets that pursue precision medicines. Key product features that would affect our ability to effectively compete with other therapeutics include the efficacy, safety and convenience of our products. We believe principal competitive factors to our business include, among other things, the accuracy of our computations and predictions, ability to integrate computational and experimental capabilities, ability to successfully transition research programs into clinical development, ability to raise capital, and the scalability of the platform, pipeline, and business. Many of the companies that we compete against or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or earlier stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. In addition, we cannot predict whether our current competitive advantages, such as our ability to leverage our Dynamo platform and our ~~relationship~~ **relationships** with **external collaborators** ~~D. E. Shaw Research~~, will remain in place in the future. If these or other barriers to entry do not remain in place, other companies may be able to more directly or effectively compete with us. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we or our collaborators may develop. Our competitors also may obtain FDA or other 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 or our collaborators are able to enter the market. 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. The insurance coverage and reimbursement status of newly- approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for any of our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue. In the United States 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 healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments. Sales of these or other product candidates that we may identify will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third- party payors. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. **See" Business – Governmental Regulation – Insurance coverage and reimbursement."** There is also significant uncertainty related to the insurance coverage and reimbursement of newly approved products and coverage may be more limited than the purposes for which the medicine is approved by the FDA or similar foreign regulatory authorities. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U. S. Department of Health and Human Services. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. Factors payors consider in determining reimbursement are based on whether the product is (i) a covered benefit under its health plan; (ii) safe, effective and medically necessary; (iii) appropriate for the specific patient; (iv) cost- effective; and (v) neither experimental nor investigational. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Increasingly, third- party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price, or ASP, and best price. Penalties may apply in some cases when such metrics are not submitted accurately and in a timely manner. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs. In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. A Member State may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, products launched in the EU do not follow price structures of the U. S. and generally prices tend to be significantly lower. Risks Related to Our Reliance on Third Parties Under the DESRES Agreement, as amended..... ability to enter into such transactions. We rely on third parties to conduct our ongoing clinical trials of **our product candidates** ~~RLY- 4008 and RLY- 2608~~ and expect to rely on third parties to conduct future clinical trials, as well as investigator- sponsored clinical trials of our product candidates. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed. We do not have the ability to independently conduct clinical trials. We rely and expect to continue to rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct or otherwise support clinical trials for our product candidates. We may also rely on academic and private non- academic institutions to conduct and sponsor clinical trials relating to our product candidates. We will not control the design or conduct of the investigator- sponsored trials, and it is possible that the FDA or non- U. S. regulatory authorities will not view these investigator- sponsored trials as providing adequate support for future clinical trials, whether controlled by us or third parties, for any one or more reasons, including elements of the design or execution of the trials or safety concerns or other trial results. Such arrangements will likely provide us certain information rights with respect to the investigator- sponsored trials, including access to and the ability to use and reference the data, including for our own regulatory filings, resulting from the investigator- sponsored trials. However, we would not have control over the timing and reporting of the data from investigator- sponsored trials, nor would we own the data from the investigator- sponsored trials. If we are unable to confirm or replicate the results from the investigator- sponsored trials or if negative results are obtained, we would likely be further delayed or prevented from advancing further clinical development of our product candidates. Further, if investigators or institutions breach their obligations with respect to the clinical

development of our product candidates, or if the data prove to be inadequate compared to the first- hand knowledge we might have gained had the investigator- sponsored trials been sponsored and conducted by us, then our ability to design and conduct any future clinical trials ourselves may be adversely affected. We rely and expect to continue to rely heavily on these parties for execution of clinical trials for our product candidates and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on CROs will not relieve us of our regulatory responsibilities. For any violations of laws and regulations during the conduct of our clinical trials, we could be subject to warning letters or enforcement action that may include civil penalties up to and including criminal prosecution. We, our principal investigators and our CROs are required to comply with regulations, including Good Clinical Practices, or GCPs, for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and similar foreign regulatory authorities for any products in clinical development, including the EMA and the **MHRA** ~~Medicines and Healthcare Products Regulatory Agency~~ . These regulatory authorities enforce GCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we, our principal investigators or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or similar foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, these regulatory authorities will determine that any of our future clinical trials will comply with GCPs. In addition, our clinical trials must be conducted with product candidates produced under current Good Manufacturing Practice, or cGMP, regulations. Our failure or the failure of our principal investigators or CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government- sponsored database, ClinicalTrials. gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. Although we designed our first- in- human clinical trials of **our lead product candidates** ~~RLY- 4008, RLY- 2608 and GDC- 1971,~~ and intend to design the future clinical trials for **any** ~~the~~ **other** product candidates that we develop, we expect that CROs will conduct all of our clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, are outside of our direct control. Our reliance on third parties to conduct future clinical trials also results in less direct control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may: • have staffing difficulties; • fail to comply with contractual obligations; • experience regulatory compliance issues; • undergo changes in priorities or become financially distressed; or • form relationships with other entities, some of which may be our competitors. These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. If the principal investigators or CROs do not perform clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our product candidates may be delayed, we may not be able to obtain regulatory approval and commercialize our product candidates, or our development program may be materially and irreversibly harmed. If we are unable to rely on clinical data collected by our principal investigators or CROs, we could be required to repeat, extend the duration of, or increase the size of any clinical trials we conduct and this could significantly delay commercialization and require significantly greater expenditures. If any of our relationships with these third- party principal investigators or CROs terminate, we may not be able to enter into arrangements with alternative CROs. If principal investigators or CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any clinical trials such principal investigators or CROs are associated with may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, we believe that our financial results and the commercial prospects for our product candidates in the subject indication would be harmed, our costs could increase and our ability to generate revenue could be delayed. We contract with third parties for the manufacture of our product candidates for preclinical development, clinical testing, and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. We do not currently own or operate, nor do we have any plans to establish in the future, any manufacturing facilities or personnel. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical development and clinical testing, as well as for the commercial manufacture of our products if any of our product candidates receive marketing approval. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. The facilities used by our contract manufacturers to manufacture our product candidates must be inspected by the FDA pursuant to pre- approval inspections that will be conducted after we submit our marketing applications to the FDA. We do not control the manufacturing process of, and will be completely dependent on, our contract manufacturers for compliance with cGMPs in connection with the manufacture of our product candidates. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to pass regulatory inspections and / or maintain regulatory compliance for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA

or a similar foreign regulatory authority finds deficiencies with or does not approve these facilities for the manufacture of our product candidates or if it finds deficiencies or withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Further, our failure, or the failure of our third- party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, if approved, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business and supplies of our product candidates. We may be unable to establish any agreements with third- party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third- party manufacturers, reliance on third- party manufacturers entails additional risks, including: • reliance on the third party for regulatory compliance and quality assurance; • the possible breach of the manufacturing agreement by the third party; • the possible misappropriation of our proprietary information, including our trade secrets and know- how; and • the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us. Our product candidates and any products that we may develop may compete with other product candidates and approved products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Due to capacity constraints at cGMP manufacturers ~~relating to the ongoing COVID- 19 pandemic~~ , we have been required to forecast the amount of clinical trial supply needed for our clinical trials further in advance than had typically been required, and there is limited flexibility to adjust our manufacturing needs as our clinical trials progress, which may lead to added costs or delays in our clinical trials. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We are also unable to predict how the **effects of** ongoing **geopolitical** ~~COVID- 19 pandemic or the current conflict~~ **conflicts** ~~between Russia and Ukraine~~ may affect our third- party manufacturers, including any potential disruptions to our global supply chain. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers, which we may not be able to do on reasonable terms, if at all, or manufacture the materials ourselves, for which we may not have the capabilities or resources. In either scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or product candidates may be unique or proprietary to the original contract manufacturing organization, or 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. Changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials. We may incur added costs and delays in identifying and qualifying any such replacement. Furthermore, a CMO may possess technology related to the manufacture of our product candidates that such CMO owns independently. This would increase our reliance on such CMO or require us to obtain a license from such CMO in order to have another CMO manufacture our product candidates. Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis. The third parties upon whom we rely for the supply of the active pharmaceutical ingredients, drug product and starting materials used in our product candidates are our sole source of supply, and the loss of any of these suppliers could significantly harm our business. The active pharmaceutical ingredients, or API, drug product and starting materials used in our product candidates are supplied to us primarily from single- source suppliers. Our ability to successfully develop our product candidates, and to ultimately supply our commercial products in quantities sufficient to meet the market demand, depends in part on our ability to obtain the API, drug product and starting materials for these products in accordance with regulatory requirements and in sufficient quantities for clinical testing and commercialization. We do not currently have arrangements in place for a redundant or second- source supply of any such API, drug product or starting materials in the event any of our current suppliers of such API, drug product or starting materials ceases its operations for any reason. If any of our third- party suppliers or manufacturers ceases its operations for any reason or is unable or unwilling to supply API, drug product or starting material in sufficient quantities, on the timelines necessary, or at acceptable prices, to meet our needs, it could impede, delay, limit or prevent our development efforts, which could harm our business, results of operations, financial condition and prospects. We are also unable to predict how changing global economic ~~or political~~ conditions **or ongoing geopolitical** ~~, such as the current conflict~~ **conflicts** ~~between Russia and Ukraine~~ and related global economic sanctions, or potential global health concerns ~~, such as the ongoing COVID- 19 pandemic,~~ will affect our third- party suppliers and manufacturers. Any negative impact of such matters on our third- party suppliers and manufacturers may also have an adverse impact on our results of operations or financial condition. For all of our product candidates, we intend to identify and qualify additional manufacturers to provide such API, drug product and starting materials prior to or after submission of an NDA to the FDA and / or an MAA to the EMA. We are not certain, however, that our single-source suppliers will be able to meet our demand for their products, either because of the nature of our agreements with those suppliers, our limited experience with those suppliers or our relative importance as a customer to those suppliers. It may be difficult for us to assess their ability to timely meet our demand in the future based on past performance. While our suppliers have generally met our demand for their products on a timely basis in the past, they may subordinate our needs in the future to their other customers. Establishing additional or replacement suppliers for the API, drug product and starting materials used in our product candidates, if required, may not be accomplished quickly. If we are able to find a replacement supplier, such replacement supplier would need to be qualified and may require additional regulatory inspection or approval, which could

result in further delay. While we seek to maintain adequate inventory of the API, drug product and starting materials used in our product candidates, any interruption or delay in the supply of components or materials, or our inability to obtain such API, drug product or starting materials from alternate sources at acceptable prices in a timely manner could impede, delay, limit or prevent our development efforts, which could harm our business, results of operations, financial condition and prospects. We have and may enter into other collaborations with third parties for the research, development, manufacture and commercialization of one or more of our programs or product candidates. If these collaborations are not successful, our business could be adversely affected. We have entered into and may enter into collaborations with third parties for one or more of our programs or product candidates, such as our Genentech Agreement to develop and commercialize **migoprotafib** ~~GDC- 1971~~ . If we enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that any future collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them. Any collaborations we have entered into or will enter into may pose risks, including the following: • Collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations; • Collaborators may not perform their obligations as expected; • The clinical trials conducted as part of these collaborations may not be successful; • Collaborators may not pursue development and / or commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities; • Collaborators may delay clinical trials, provide insufficient funding for clinical trials, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing; • We may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our stockholders about the status of such product candidates; • Collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours; • Product candidates developed in collaboration with us may be viewed by any collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates; • A collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of any such product candidate; • Disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development of any programs or product candidates, may cause delays or termination of the research, development, manufacture or commercialization of such programs or product candidates, may lead to additional responsibilities for us with respect to such programs or product candidates or may result in litigation or arbitration, any of which would be time- consuming and expensive; • Collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation. For example, Genentech has the first right to enforce or defend certain of our intellectual property rights under our collaboration, and although we may have the right to assume the enforcement and defense of such intellectual property rights if Genentech does not, our ability to do so may be compromised by Genentech' s actions; • Disputes may arise with respect to the ownership of intellectual property developed pursuant to our collaborations; • Collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and • Collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates. For example, Genentech may terminate its collaboration with us for convenience after a specified notice period. If our collaborations do not result in the successful development and commercialization of products, or if one of any future collaborators terminates its agreement with us, we may not receive any milestone or royalty payments under the collaboration. If we do not receive the payments we expect under these agreements, our development of product candidates could be delayed and we may need additional resources to develop our product candidates. All of the risks relating to product development, regulatory approval and commercialization summarized and described in this report also apply to the activities of our collaborators. In addition, if any collaborator terminates its agreement with us, we may find it more difficult to attract new collaborators and our reputation among the business and financial communities could be adversely affected. We may seek to establish additional collaborations, and, if we are not able to establish them on commercially reasonable terms, or at all, we may have to alter our development and commercialization plans. Our product development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with additional pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator' s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator' s evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. The terms of any additional collaborations

or other arrangements that we may establish may not be favorable to us. We may also be restricted under collaboration agreements from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time- consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue. Under the DESRES Agreement,D.E.Shaw Research controls the rights to its technology,we control the rights to certain compounds,and we jointly own with D.E.Shaw Research any other work product created by D.E.Shaw Research and us.Any work product we jointly own with D.E.Shaw Research and any other information that we or D.E.Shaw Research share is subject to a non- exclusive cross- license between us and D.E.Shaw Research,subject to certain exceptions.In some instances,D.E.Shaw Research is required to assign to us some of the work product created by D.E.Shaw Research.Disputes may arise between us and D.E.Shaw Research,as well as any future potential collaborators,regarding intellectual property subject to the DESRES Agreement.If disputes over intellectual property that we co- own or we own individually prevent or impair our ability to maintain our current collaboration arrangements on acceptable terms,or undermine our ability to successfully control the intellectual property necessary to protect our product candidates,we may be unable to successfully develop and commercialize the affected product candidates.Uncertainties or disagreements around our rights under any such intellectual property may undermine our ability to partner our programs with third parties. We may be required to pay certain milestones and royalties under our license or collaboration agreements with third- party licensors or collaborators, which may adversely affect the overall profitability of any products that we may seek to commercialize. Under our current and future license or collaboration agreements, including our DESRES Agreement, we may be required to pay milestones, royalties and other payments based on our revenues, including revenues from product sales, and these milestones and royalty payments could adversely affect the overall profitability of any products that we may seek to commercialize. In order to maintain our rights under these agreements, we may need to meet certain specified milestones in the development of our product candidates. Further, our licensors (or their licensors), licensees or other strategic collaborators may dispute the terms, including amounts, that we are required to pay under the respective license or collaboration agreements. If these claims result in a material increase in the amounts that we are required to pay to our licensors or collaborators, or in the event of a claim of breach of the license, our ability to research, develop and obtain approval of product candidates or to commercialize our products could be significantly impaired. Risks Related to Our Financial Position and Ability to Raise Additional Capital Risks Related to Our Operating History We are a biopharmaceutical company with a limited operating history. We are a biopharmaceutical company with a limited operating history and have incurred net losses in each year since our inception. Our net losses were $ **342. 0 million, $** 290. 5 million, **and** $ 363. 9 ~~million, and $ 52. 4~~ million for the years ended December 31, **2023,** 2022, **and** 2021 ~~, and 2020~~ , respectively. We had an accumulated deficit of $ 1. ~~1~~ **4** billion as of December 31, ~~2022~~ **2023** . Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We commenced operations in May 2015. Since inception, we have focused substantially all of our efforts and financial resources on developing our Dynamo drug discovery platform and initial product candidates. We have no products approved for commercial sale and therefore have never generated any revenue from product sales, and we do not expect to in the foreseeable future. We have not obtained regulatory approvals for any of our product candidates and there is no assurance that we will obtain approvals in the future. We expect to continue to incur significant expenses and operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital. We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect our research and development expenses to significantly increase in connection with the commencement and continuation of clinical trials of our product candidates. In addition, if we obtain marketing approval for our product candidates, we will incur significant sales, marketing and outsourced- manufacturing expenses. We will also continue to incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis. The amount of our future losses is uncertain and our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline. Our quarterly and annual operating results may fluctuate significantly in the future due to a variety of factors, many of which are outside of our control and may be difficult to predict, including the following: • the timing and success or failure of clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners; • our ability to successfully recruit and retain subjects for clinical trials, and any delays caused by difficulties in such efforts; • our ability to obtain marketing approval for our product candidates, and the timing and scope of any such approvals we may receive; • the timing and cost of, and level of investment in, research and development activities relating to our product candidates, which may change from time to time; • the cost of manufacturing our product candidates, which may vary depending

on the quantity of production and the terms of our agreements with manufacturers; • our ability to attract, hire and retain qualified personnel; • expenditures that we will or may incur to develop additional product candidates; • the level of demand for our product candidates should they receive approval, which may vary significantly; • the risk / benefit profile, cost and reimbursement policies with respect to our product candidates, if approved, and existing and potential future therapeutics that compete with our product candidates; • the changing and volatile U. S. and global economic environments **or** ~~, including as a result of the~~ ongoing ~~COVID- 19 pandemic, or unstable political~~ **geopolitical** ~~conditions, such as the current conflict~~ **conflicts** ~~between Russia and Ukraine~~ ; and • future accounting pronouncements or changes in our accounting policies. The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period- to- period basis may not be meaningful. This variability and unpredictability could also result in our failing to meet the expectations of industry or securities analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide. We have no products approved for commercial sale and we have not generated any revenue from product sales. Our ability to become profitable depends upon our ability to generate revenue. To date, we have no products approved for commercial sale, we have not generated any revenue from our product sales and we do not expect to generate any revenue from the sale of products in the near future. We do not expect to generate significant revenue unless and until we obtain marketing approval of, and begin to sell one or more of our product candidates. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to: • successfully complete preclinical studies; • successfully enroll subjects in, and complete, clinical trials; • have our IND applications go into effect for our planned clinical trials or future clinical trials; • receive regulatory approvals from applicable regulatory authorities; • initiate and successfully complete all safety studies required to obtain U. S. and foreign marketing approval for our product candidates; • establish commercial manufacturing capabilities or make arrangements with third- party manufacturers for clinical supply and commercial manufacturing; • obtain and maintain patent and trade secret protection or regulatory exclusivity for our product candidates; • launch commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others; • obtain and maintain acceptance of the product candidates, if and when approved, by patients, the medical community and third-party payors; • effectively compete with other therapies; • obtain and maintain healthcare coverage and adequate reimbursement; • enforce and defend intellectual property rights and claims; • take precautionary measures to help minimize the risk of **any future pandemics or outbreaks similar to** COVID- 19 ~~or any future pandemics or similar outbreaks~~ to our employees; and • maintain a continued acceptable safety profile of the product candidates following approval. If we do not achieve one or more of these factors in a timely manner or at all, we may experience significant delays in our commercialization efforts or we may be unable to successfully commercialize our product candidates at all, which would materially harm our business and prospects. In addition, if we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations. Risks Related to Raising Additional Capital We will need to raise substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate some of our product development programs or commercialization efforts. The development of pharmaceutical products is capital- intensive. We **have ongoing** ~~are continuing our~~ clinical trials ~~of our lead product candidates, RLY- 4008~~ and **we are** ~~RLY- 2608, and~~ advancing our other product candidates through preclinical development. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate clinical trials of, and seek marketing approval for, our product candidates. In addition, depending on the status of regulatory approval or, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. We may also need to raise additional funds sooner if we choose to pursue additional indications and / or geographies for our product candidates or otherwise expand more rapidly than we presently anticipate. Furthermore, we continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or fail to do so on attractive terms, we would be forced to delay, reduce or eliminate certain of our research and development programs or future commercialization efforts. We expect that our existing cash and cash equivalents and investments will be sufficient to fund our operations through at least the next 12 months. Our future capital requirements will depend on and could increase significantly as a result of many factors, including: • the impact of any business interruptions to our operations, including the timing and enrollment of patients in our planned clinical trials, or to those of our manufacturers, suppliers, or other vendors, resulting from **any** ~~the ongoing COVID- 19 pandemic or similar~~ public health crisis or **ongoing** ~~the changing political~~ **geopolitical** ~~conditions such as the current conflict~~ **conflicts** ~~between Russia and Ukraine~~ and related global economic sanctions; • the scope, progress, results and costs of our current and future clinical trials of **our lead product candidates** ~~RLY- 4008 and RLY- 2608~~ and additional preclinical research of our other programs; • the scope, progress, results and costs of drug discovery, preclinical research and clinical trials for our other product candidates; • the number of future product candidates that we pursue and their development requirements; • the costs, timing and outcome of regulatory review of our product candidates; • our ability to establish and maintain collaborations on favorable terms, if at all; • the success of any existing or future collaborations that we may enter into with third parties; • the extent to which we acquire or invest in businesses, products and technologies, including entering into licensing or collaboration arrangements for product candidates, such as our collaboration with Genentech; • the achievement of milestones or occurrence of other developments that trigger payments under any existing or future collaboration agreements, if any; • the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under any existing or future collaboration agreements, if any; • the costs and timing of future commercialization activities, including **drug** sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing

approval, to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of any collaborator that we may have at such time; • the amount of revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval; • the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property- related claims; • our headcount growth and associated costs as we expand our business operations and our research and development activities; and • the costs of operating as a public company. Identifying potential product candidates and conducting preclinical development testing and clinical trials is a time- consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Any additional fundraising efforts may divert our management from their day- to- day activities, which may adversely affect our ability to develop and commercialize our product candidates. Disruptions in the financial markets may make equity and debt financing more difficult to obtain, and may have a material adverse effect on our ability to meet our fundraising needs. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborators or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidate or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations. Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of private and public equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, the ownership interest of our stockholders will be diluted, and the terms of those securities may include liquidation or other preferences that materially adversely affect their rights as a common stockholder. We may offer and sell up to an aggregate amount of $ 300. 0 million of our common stock from time to time in ~~“~~ **"** at the market ~~”~~ **"** offerings pursuant to the sales agreement, or the Sales Agreement, with Cowen and Company, LLC, subject to the limitations thereof. As of December 31, ~~2022~~ **2023** , ~~no~~ **we have sold 3, 026, 072** shares of common stock ~~have been sold~~ under the Sales Agreement. Debt financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our intellectual property, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Risks Related to ~~COVID- 19~~ **Public Health Matters** and the Global Economy ~~The ongoing~~ **Any future pandemic, epidemic, or outbreak of an infectious disease similar to the** COVID- 19 pandemic ~~has impacted our business and any future pandemic, epidemic, or outbreak of an infectious disease~~ could ~~similarly~~ affect our business and our financial results and could cause ~~further~~ disruption to the development of our product candidates. Public health crises such as pandemics or similar outbreaks could adversely impact our business. ~~The~~ **A public health crisis similar to the** COVID- 19 pandemic **could adversely impact** ~~continues to evolve as new variants of COVID- 19 have been identified and spread, which has led to various responses and public health safety measures. The extent to which the ongoing COVID- 19 pandemic may continue to affect our operations or those of our third- party partners, including~~ our preclinical ~~or~~ **,** other nonclinical ~~studies~~ or clinical trial operations ~~, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the severity and duration of additional variant outbreaks (including acceleration of the spread of more transmissible variants of COVID- 19 in the areas in which the we or our third party partners conduct operations), plateauing or stagnant vaccination and booster vaccination rates in geographies where we or our third party partners conduct operations, and the actions to contain COVID- 19 or treat its impact, among others. The continued spread of COVID- 19 globally could adversely impact our preclinical, other nonclinical or clinical trial operations~~ in the United States, ~~including~~ **and we may experience delays in initiating,** ~~our~~ - **or** ~~ability~~ **fail** to **initiate,** ~~obtain slots for~~ IND- enabling studies ~~and~~ **,** ~~recruit~~ **recruiting** and ~~retain~~ **retaining** patients ~~and~~ **,** principal investigators and site staff **for** ~~who, as healthcare providers, may have heightened exposure to COVID- 19 if infection rates substantially increase. For example, similar to other biopharmaceutical companies, we may experience delays in initiating IND- enabling studies, enrolling~~ our clinical trials, ~~or~~ dosing of patients in our clinical trials as well as in activating new trial sites, and protocol deviations. **The** ~~COVID- 19 may also affect employees of third- party CROs located in affected geographies that we rely upon to carry out our clinical trials. In addition, if any patients~~

~~enrolled in our clinical trials are infected with COVID- 19, they may not be able to complete these trials. Any~~ negative impact ~~COVID- 19 has to~~ **of any such public health crisis on** patient enrollment or treatment or the execution of our product candidates could cause costly delays to clinical trial activities, which could adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, and have a material adverse effect on our financial results. **Any unforeseen disruptions arising from a public** ~~Additionally, timely enrollment in ongoing and planned future clinical trials is dependent upon clinical trial sites which could be adversely affected by global~~ health ~~matters~~ **crisis, including potential shutdowns or disruptions of businesses and government agencies** , such as **the SEC** ~~pandemics. We conduct clinical trials for~~ **or FDA** ~~our product candidates in geographies which continue to be affected by COVID- 19. Some factors from the ongoing COVID- 19 pandemic that will delay or otherwise adversely affect enrollment in the clinical trials of our product candidates~~ , ~~as well as our business generally, include: • the potential diversion of healthcare resources away from the conduct of clinical trials to focus on pandemic concerns, including the attention of physicians serving as our clinical trial investigators, hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials; • limitations on travel that~~ could ~~interrupt key trial and business activities, such as clinical trial site initiations and monitoring, domestic and international travel by employees, contractors or patients to clinical trial sites, including any government- imposed travel restrictions or quarantines that will impact the ability or willingness of patients, employees or contractors to travel to our clinical trial sites or secure visas or entry permissions, a loss of face- to- face meetings and other interactions with potential partners, any of which could delay or adversely impact the conduct or progress of our clinical trials; • the potential negative effect on the operations of our third- party manufacturers, suppliers or other collaboration partners, including issues due to worker shortages, supply chain disruptions such as delays in procurement of manufacturing equipment and any related parts, facilities and production suspensions and a sudden increase in demand for certain goods and services, such as medical services and supplies; • interruption in global shipping affecting the transport of clinical trial materials, such as patient samples, investigational drug product and conditioning drugs and other supplies used in our clinical trials; and • business disruptions caused by potential workplace, laboratory and office closures and an increased reliance on employees working from home, disruptions to or delays in ongoing laboratory experiments and operations, staffing shortages, travel limitations or mass transit disruptions, any of which could adversely impact our business operations or delay necessary interactions with local regulators, ethics committees and other important agencies and contractors. We cannot presently predict the scope and severity of the planned and potential shutdowns or disruptions of businesses and government agencies, such as the SEC or FDA. These and other factors arising from the ongoing COVID- 19 pandemic could worsen as the pandemic continues to evolve. Any of these factors, and other factors related to any unforeseen disruptions, have had and could continue to~~ have a material adverse effect on our business and our results of operation and financial condition. Further, uncertainty around these and related issues could lead to adverse effects on the economy of the United States and other economies, which could impact our ability to raise the necessary capital needed to develop and commercialize our product candidates. Global economic and political conditions, including ~~the~~ economic uncertainty tied to ~~inflation and rising~~ interest rates ~~as well as political~~ **, credit and financial market instability, and** uncertainty ~~relating~~ **related** to ~~Russia and Ukraine~~ **ongoing geopolitical conflicts** , are difficult to mitigate and could pose challenges to our growth and profitability and could adversely affect our business, financial condition or results of operations. Unstable market and economic conditions may have adverse consequences on our business, financial condition or results of operations. The global economy, in particular the credit and financial markets, has recently experienced significant volatility and disruptions, including diminished liquidity and credit availability, volatility in commodity prices, declines in consumer confidence and economic growth, and supply chain interruptions. Other factors, including rising interest rates and record inflation, may also increase the general cost of doing business **. In 2023, the closures of Silicon Valley Bank and Signature Bank and their placement into receivership with the Federal Deposit Insurance Corporation, or FDIC, created bank- specific and broader financial institution liquidity risk and concerns. Although the Department of the Treasury, the Federal Reserve, and the FDIC jointly released a statement that depositors at Silicon Valley Bank and Signature Bank would have access to their funds, even those in excess of the standard FDIC insurance limits, under a systemic risk exception, future adverse developments with respect to specific financial institutions or the broader financial services industry may lead to market- wide liquidity shortages, impair the ability of companies to access near- term working capital needs, and create additional market and economic uncertainty. There can be no assurance that future credit and financial market instability and a deterioration in confidence in economic conditions will not occur** . Continued economic uncertainty caused by these and other factors, including political instability, conflicts or crises **, at the global level or** involving individual countries or regions ~~, such as the current conflict between Russia and Ukraine,~~ and any associated economic sanctions, could result in a variety of risks to our business, including difficulty in enrolling participants in our clinical trials, difficulty in forecasting our financial results and managing inventory levels, increases in our business costs, which in turn affect our ability to develop our current and future product candidates, and negatively impacting our ability to raise additional capital when needed on acceptable terms, if at all. In addition, political developments impacting government spending and international trade, including changes in trade agreements, potential government shutdowns and trade disputes and tariffs, such as the ongoing trade dispute between the United States and China, may negatively impact markets and cause weaker macroeconomic conditions. These global economic and political factors have also strained and could continue to strain certain of our suppliers and manufacturers, possibly resulting in supply disruptions or increased raw material or manufacturing costs, or adversely impacting their ability to manufacture clinical trial materials for our product candidates. Any of the foregoing could harm our business and prospects and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our operations. Risks Related to Protecting Our Intellectual Property If we are unable to adequately protect our proprietary technology or obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology

and products similar or identical to ours, and our ability to successfully commercialize our technology and products will be impaired. Our commercial success will depend in part on our ability to obtain and maintain proprietary or intellectual property protection in the United States and other countries for our product candidates, and our core technologies, including our novel target discovery technology and our proprietary compound library and other know- how. We seek to protect our proprietary and intellectual property position by, among other methods, filing patent applications in the United States and abroad related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know- how and continuing technological innovation to develop and maintain our proprietary and intellectual property position. Other than our U. S. patent relating to **migoprotafib (** RLY- 1971 ~~(~~**,** now referred to as GDC- 1971) composition of matter **and our U. S. patent relating to lirafugratinib (RLY- 4008) composition of matter** , we do not own or in- license any issued patents relating to our platform or our lead product candidates under clinical development. Pursuant to the Genentech Agreement, we have granted an exclusive, worldwide, royalty- bearing license to Genentech, with the right to sublicense, develop and commercialize **migoprotafib** ~~GDC- 1971~~ and any other SHP2 inhibitors developed under the Genentech Agreement. Genentech has the first right, but not the obligation, to file, prosecute and maintain any patents licensed to it, as well as to enforce infringement of or defend claims against such patents that relate to **migoprotafib** ~~GDC- 1971~~ or other SHP2 inhibitors. See ~~“~~ **"** Risks Related to Our Reliance on Third Parties — We have and may enter into **other** collaborations with third parties for the research, development, manufacture and commercialization of one or more of our programs or product candidates. If these collaborations are not successful, our business could be adversely affected. ~~”~~ **"** for a discussion of risks related to the protection of our intellectual property rights under our collaborations. Most of the research and development for our programs has been performed under the DESRES Agreement. Under the DESRES Agreement, D. E. Shaw Research controls the rights to its technology (including its supercomputer and software, each of which are important aspects of our Dynamo platform), we control the rights to certain compounds, and we jointly own with D. E. Shaw Research any other work product created by D. E. Shaw Research and us. Subject to certain limits, we have the right to have the following work product assigned to us: the composition of matter, method of use, and method of manufacture of certain compounds directed to a Category 1 Target, as set forth in the DESRES Agreement. We have not yet designated all of the compounds for which we will have this right of assignment, and thus, we do not yet know the scope of exclusivity we will enjoy under our patent rights for our product candidates. After any work product is assigned to us, we will have the right to prepare, file, prosecute and maintain patents that cover such assigned work product. We also have the implicit right to defend patents that cover work product owned by us. To date, ~~much~~ **some** of the work product created under our agreement with D. E. Shaw Research has been created by D. E. Shaw Research and us, together, and is thus **initially** co- owned **. We have subsequently obtained sole ownership of certain intellectual property relating specifically to some of our clinical candidates (e. g. migoprotafib and lirafugratinib). By virtue of inventorship, we jointly own intellectual property rights pertaining to RLY- 2608, but retain the option to obtain sole ownership of intellectual property rights relating to it and other jointly owned PIK3CA inhibitors** . We have the first right to prepare, file, prosecute, maintain and defend patents that cover work product jointly created by D. E. Shaw Research and us. If we choose not to exercise those rights with respect to patents and patent applications that cover joint work product, D. E. Shaw Research will have the right to take over such activities, unless such rights are waived, as is the case for our co- owned SHP2 patent applications. The party that is preparing, filing, prosecuting and maintaining a patent that covers joint work product also has the right to enforce such patent against infringers. The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. The degree of patent protection we require to successfully commercialize our product candidates 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 of our pending patent applications will issue, or that any of our pending patent applications that mature into issued patents will include claims with a scope sufficient to protect our lead product candidates under clinical development ~~, RLY- 4008, RLY- 2608, GDC- 1971,~~ or our other product candidates. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally twenty 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. As a result, our owned patent portfolio and any patent portfolio we may license in the future may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing products similar or identical to our product candidates, including generic versions of such products. We have licensed patent rights, and in the future may license additional patent rights, to or from third parties. For example, we have licensed our patent rights to our SHP2 program to Genentech. These licensed patent rights may be valuable to our business, and we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology or medicines underlying such licenses. We cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. If any such licensors or licensees fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected. Other parties have developed technologies that may be related or competitive to our own, and such parties may have filed or may file patent applications, or may have received or may receive patents, claiming inventions that may overlap or conflict with those claimed in our own patent applications, with respect to either the same methods or formulations or the same subject matter, in either case that we may rely upon to dominate our patent position in the market. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases

not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights cannot be predicted with any certainty. In addition, the patent prosecution process is expensive and time- consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Further, with respect to most of the pending patent applications covering our product candidates, prosecution has yet to commence. Patent prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the U. S. Patent and Trademark Office, or USPTO, have been significantly narrowed by the time they issue, if at all. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Even if we acquire patent protection that we expect should enable us to maintain such competitive advantage, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. For example, we may be subject to a third- party submission of prior art to the USPTO challenging the priority of an invention claimed within one of our patents, which submissions may also be made prior to a patent' s issuance, precluding the granting of any of our pending patent applications. We may become involved in opposition, derivation, reexamination, inter parties review, post- grant review or interference proceedings challenging our patent rights or the patent rights of others from whom we have obtained licenses to such rights. Competitors may claim that they invented the inventions claimed in our issued patents or patent applications prior to us, or may file patent applications before we do. Competitors may also claim that we are infringing on their patents and that we therefore cannot practice our technology as claimed under our patents, if issued. Competitors may also contest our patents, if issued, by showing the patent examiner that the invention was not original, was not novel or was obvious. In litigation, a competitor could claim that our patents, if issued, are not valid for a number of reasons. If a court agrees, we would lose our rights to those challenged patents. In addition, we may in the future be subject to claims by our former employees or consultants asserting an ownership right in our patents or patent applications, as a result of the work they performed on our behalf. Although we generally require all of our employees, consultants and advisors and any other third parties who have access to our proprietary know- how, information or technology to assign or grant similar rights to their inventions to us, we cannot be certain that we have executed such agreements with all parties who may have contributed to our intellectual property, nor can we be certain that our agreements with such parties will be upheld in the face of a potential challenge, or that they will not be breached, for which we may not have an adequate remedy. With respect to intellectual property arising in the course of our collaboration with D. E. Shaw Research, disagreements between us and D. E. Shaw Research may impact our exclusive control of intellectual property important for protecting our product candidates and proprietary position. A loss of exclusivity, in whole or in part, could allow others to compete with us and harm our business. An adverse determination in any such submission or proceeding may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, without payment to us, or could limit the duration of the patent protection covering our technology and product candidates. Such challenges may also result in our inability to manufacture or commercialize our product candidates without infringing third party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Even if they are unchallenged, our owned patent portfolio and any patent portfolio we may license in the future may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non- infringing manner. For example, a third party may develop a competitive product that provides benefits similar to one or more of our product candidates but that has a different composition that falls outside the scope of our patent protection. If the patent protection provided by the patents and patent applications we hold or 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. Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. 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. In addition, periodic maintenance fees on issued patents often must be paid to the USPTO and foreign patent agencies over the lifetime of the patent. While an unintentional lapse can in many 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. Non- compliance events that could result in abandonment or lapse of a patent or patent application 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. If we fail to maintain the patents and patent applications covering our products or procedures, we may not be able to stop a competitor from marketing products that are the same as or similar to our product candidates, which would have a material adverse effect on our business. Our failure to secure trademark registrations could adversely affect our business and our ability to market our products and product candidates. Our trademark applications in the United States and any other jurisdictions where we may file may not be allowed for registration, and our registered trademarks may not be maintained or enforced. During trademark

registration proceedings, we may receive rejections. Although we are given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in corresponding foreign agencies, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our applications and / or registrations, and our applications and / or registrations may not survive such proceedings. Failure to secure such trademark registrations in the United States and in foreign jurisdictions could adversely affect our business and our ability to market our products and product candidates. If we are unable to protect the confidentiality of our trade secrets, our business and competitive position may be harmed. In addition to the protection afforded by patents, we rely upon unpatented trade secret protection, unpatented know- how and continuing technological innovation to develop and maintain our competitive position. With respect to the building of our proprietary compound library, we consider trade secrets and know- how to be our primary intellectual property. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our collaborators, scientific advisors, employees and consultants, and invention assignment agreements with our consultants and employees. We may not be able to prevent the unauthorized disclosure or use of our technical know- how or other trade secrets by the parties to these agreements, however, despite the existence generally of confidentiality agreements and other contractual restrictions. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result. Enforcing a claim that a third party illegally obtained and is using our trade secrets, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Our trade secrets could otherwise become known or be independently discovered by our competitors. Competitors could purchase our product candidates and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If our trade secrets are not adequately protected so as to protect our market against competitors' products, our competitive position could be adversely affected, as could our business. Risks Related to Intellectual Property Litigation Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and frequent litigation regarding patents and other intellectual property rights. We may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates and technology, including interference proceedings before the USPTO. Our competitors or other third parties may assert infringement claims against us, alleging that our products or technologies are covered by their patents. Given the vast number of patents in our field of technology, we cannot be certain that we do not infringe existing patents or that we will not infringe patents that may be granted in the future. Many companies have filed, and continue to file, patent applications related to SHP2 inhibitors, FGFR2 inhibitors ~~,~~ **and** PI3K inhibitors ~~, CDK2 inhibitors and ERα degraders~~ . Some of these patent applications have already been allowed or issued, and others may issue in the future. Since these areas are competitive and of strong interest to pharmaceutical and biotechnology companies, there will likely be additional patent applications filed and additional patents granted in the future, as well as additional research and development programs expected in the future. Furthermore, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our product candidates, or the practice of our technology. If a patent holder believes our product or product candidate infringes on its patent, the patent holder may sue us even if we have received patent protection for our technology. Moreover, we may face patent infringement claims from non- practicing entities that have no relevant product revenue and against whom our owned patent portfolio and any patent portfolio we may license in the future may thus have no deterrent effect. If we are found to infringe a third party' s intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our product candidates and technology. We may choose to obtain a license, even in the absence of an action or finding of infringement. In either case, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain such a license, it could be granted on non- exclusive terms, thereby providing our competitors and other third parties access to the same technologies licensed to us. Without such a license, we could be forced, including by court order, to cease developing and commercializing the infringing technology or product candidates. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed such third- party patent rights. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. If we lose a foreign patent lawsuit, alleging our infringement of a competitor' s patents, we could be prevented from marketing our products in one or more foreign countries, which would have a materially adverse effect on our business. We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of our competitors or are in breach of non- competition or non- solicitation agreements with our competitors. We could in the future be subject to claims that we or our employees have inadvertently or otherwise used or disclosed alleged trade secrets or other proprietary information of former employers or competitors. Although we try to ensure that our employees and consultants do not use the intellectual

property, proprietary information, know- how or trade secrets of others in their work for us, we may in the future be subject to claims that we caused an employee to breach the terms of his or her non- competition or non- solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and could be a distraction to management. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our product candidates, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. An inability to incorporate such technologies or features would have a material adverse effect on our business, and may prevent us from successfully commercializing our product candidates. In addition, we may lose valuable intellectual property rights or personnel as a result of such claims. Moreover, any such litigation or the threat thereof may adversely affect our ability to hire employees or contract with independent sales representatives. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our product candidates, which would have an adverse effect on our business, results of operations and financial condition. We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time consuming and unsuccessful. Competitors and other third parties may infringe, misappropriate or otherwise violate our patents and other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims. A court may disagree with our allegations, however, and may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the third- party technology in question. Further, such third parties could counterclaim that we infringe their intellectual property or that a patent we have asserted against them is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims challenging the validity, enforceability or scope of asserted patents are commonplace. In addition, third parties may initiate legal proceedings against us to assert such challenges to our intellectual property rights. The outcome of any such proceeding is generally unpredictable. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non- enablement. Patents may be unenforceable if someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. It is possible that prior art of which we and the patent examiner were unaware during prosecution exists, which could render any patents that may issue invalid. Moreover, it is also possible that prior art may exist that we are aware of but do not believe is relevant to our future patents, should they issue, but that could nevertheless be determined to render our patents invalid. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. If a defendant were to prevail on a legal assertion of invalidity or unenforceability of our patents covering one of our product candidates, we would lose at least part, and perhaps all, of the patent protection covering such product candidate. Competing products may also be sold in other countries in which our patent coverage might not exist or be as strong. Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities. Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. 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 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. 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 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 greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating or from successfully challenging our intellectual property rights. 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. Risks Related to Enforcement of Our Intellectual Property Rights We may not be able to effectively enforce our intellectual property rights throughout the world. Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, the patent laws of some foreign countries do not afford intellectual property protection to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States. 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, if our ability to enforce our patents to stop infringing activities is inadequate. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial

costs and divert our efforts and resources from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in the major markets for our product candidates, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. If we do not obtain patent term extension and data exclusivity for any 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 product candidates we may develop, one or more of our U. S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, or Hatch- Waxman Amendments. The Hatch- Waxman Amendments permit a patent extension term 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 term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations and prospects could be materially harmed. Risks Related to Third Party Intellectual Property We may need to license certain intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms. A third party may hold intellectual property, including patent rights, that are important or necessary to the development of our products. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties on commercially reasonable terms, or our business could be harmed, possibly materially. Although we believe that licenses to these patents are available from these third parties on commercially reasonable terms, if we were not able to obtain a license, or were not able to obtain a license on commercially reasonable terms, our business could be harmed, possibly materially. If we fail to comply with our obligations in the agreements under which we collaborate with or license intellectual property rights from third parties, or otherwise experience disruptions to our business relationships with our collaborators or licensors, we could lose rights that are important to our business. We expect our future license agreements will impose various development, diligence, commercialization, and other obligations on us in order to maintain the licenses. In spite of our efforts, a future licensor might conclude that we have materially breached our obligations under such license agreements and seek to terminate the license agreements, thereby removing or limiting our ability to develop and commercialize products and technology covered by these license agreements. If these in- licenses are terminated, or if the underlying patent rights licensed thereunder fail to provide the intended exclusivity, 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. Moreover, disputes may arise regarding intellectual property subject to a licensing agreement, including: • the scope of rights granted under the license agreement and other interpretation-related issues; • the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement; • the sublicensing of patent and other rights under our collaborative development relationships; • our diligence obligations under the license agreement and what activities satisfy those diligence obligations; • the inventorship and ownership of inventions and know- how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and • the priority of invention of patented technology. The agreements under which we may license intellectual property or technology from third parties may be 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. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our licensing arrangements on commercially 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. These and similar issues may arise with respect to our collaboration agreements, such as our DESRES Agreement, as amended. ~~Our~~ **While we primarily rely on our own internal computational capabilities, we currently actively** ~~collaboration~~ **collaborate** with D. E. Shaw Research ~~is our key computational collaboration~~ **on two preclinical research programs** , and there can be no assurance that this collaboration will continue past the current term of the DESRES Agreement, on favorable terms or at all, or that at any time while the collaboration is in effect D. E. Shaw Research will provide any particular level of services or that the parties will operate under the agreement without disputes. These disputes may involve ownership or control of intellectual property rights, exclusivity obligations, diligence and payment obligations, for example. The DESRES Agreement imposes certain exclusivity obligations on us during the term of the agreement with respect to Category 2 targets, and certain exclusivity obligations on D. E. Shaw Research during and after the term of the agreement. While we have some degree of control over how we designate various targets under the DESRES Agreement, D. E. Shaw Research has some degree of control over such designations as well, and our exclusivity obligations limit or delay our ability to conduct research on selected targets with third parties. Under the DESRES Agreement, D..... partner our programs with third parties. In addition, the DESRES Agreement is complex and certain provisions may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could be adverse to us, for example by narrowing what we believe to be the scope of our rights to certain intellectual

property, or increasing what we believe to be our financial or other obligations under the DESRES Agreement, and any such outcome could have a material adverse effect on our business, financial condition, results of operations, and prospects. Risks Related to Intellectual Property Laws Changes to the patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our product candidates. As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Recent patent reform legislation in the United States and other countries, including the Leahy- Smith America Invents Act, or Leahy- Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy- Smith Act includes a number of significant changes to U. S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost- effective avenues for competitors to challenge the validity of patents. In addition, the Leahy- Smith Act has transformed the U. S. patent system into a "first to file" system. The first- to- file provisions, however, only became effective on March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy- Smith Act will have on the operation of our business. However, the Leahy- Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations and financial condition. The U. S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce rights in our proprietary technology. Depending on future actions by the U. S. Congress, the U. S. courts, the USPTO and the relevant law- making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce any patents that we may obtain in the future. Intellectual property rights do not necessarily address all potential threats. The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example: • others may be able to make products that are similar to our product candidates or utilize similar technology but that are not covered by the claims of the patents that we license or may own; • we or our licensors or collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or own now or in the future; • we or our licensors or collaborators, might not have been the first to file patent applications covering certain of our or their inventions; • others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights; • it is possible that our present or future pending patent applications (whether owned or licensed) will not lead to issued patents; • issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties; • our competitors or other third parties might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; • we may not develop additional proprietary technologies that are patentable; • the patents of others may harm our business; and • we may choose not to file a patent in order to maintain certain trade secrets or know- how, and a third party may subsequently file a patent covering such intellectual property. Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects. Risks Related to Government Regulation Risks Related to Regulatory Approval Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, and our product candidates **, if approved,** could be subject to post- market study requirements, marketing and labeling restrictions, and even recall or market withdrawal if unanticipated safety issues are discovered following approval, which may result in significant additional expense. If the FDA or a similar foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post- marketing information and reports, establishment registration and listing, as well as continued compliance with cGMPs and GCPs for any clinical trials that we conduct post- approval and applicable product tracking and tracing requirements. Additionally, under FDORA, sponsors of approved drugs must provide six months' notice to the FDA of any changes in marketing status, such as the withdrawal of a drug, and failure to do so could result in the FDA placing the product on a list of discontinued products, which would revoke the product' s ability to be marketed. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post- marketing studies, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product. Later discovery of previously unknown problems with a product, 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 the product, withdrawal of the product from the market, or voluntary or mandatory product recalls; • clinical trial holds; • fines, warning letters or other regulatory enforcement action; • refusal by the FDA to approve pending applications or supplements to approved applications filed by us; • product seizure or detention, or refusal to permit the import or export of products; and • injunctions or the imposition of civil or criminal penalties. The FDA' s policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. 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, which would adversely affect our business, prospects and ability to

achieve or sustain profitability. The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off- label uses. If any of our product candidates are approved and we are found to have improperly promoted off-label uses of those products, we may become subject to significant liability. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about approved prescription drug products. In particular, while the FDA permits the dissemination of truthful and non- misleading information about an approved product, a manufacturer may not promote a product for uses that are not approved by the FDA. If 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 regulated products for off- label uses and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees, corporate integrity agreements or permanent injunctions under which specified promotional conduct must be changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition. European data collection is governed by restrictive regulations governing the processing and cross- border transfer of personal information and failure to comply with such requirements in jurisdictions where we may conduct clinical trials or enroll subjects in our ongoing or future clinical trials could have a material adverse effect on our business, financial condition or results of operations. In the event we decide to conduct clinical trials or continue to enroll subjects in our ongoing or future clinical trials, we may be subject to additional data collection restrictions. Privacy and data security have become significant issues in the U. S., Europe and in many other jurisdictions where we conduct or may in the future conduct our operations. The regulatory framework for the collection, use, safeguarding, sharing and transfer of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. For example, the collection, use, storage, disclosure, transfer, or other processing of personal data of individuals in the EEA, including personal health data, is subject to the GDPR. The GDPR is wide- ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, providing notice to the individuals to whom the personal data relates regarding data processing activities, implementing safeguards to protect the privacy and security of personal data, implementing processes to handle requests from individuals to exercise their data protection rights, maintaining records of our processing activities and to document data protection impact assessments where there is high risk processing, providing notification of data breaches in certain circumstances, and taking certain measures when engaging third- party processors or sub- processors. The GDPR focuses on accountability of data controllers (such as us) and requires us to put in place all technical and organizational measures (privacy by design and by default) to ensure that we meet our obligations. ~~It also increases substantially the penalties~~ **Penalties under** ~~to which we could be subject in~~ the **GDPR** ~~event of any non- compliance, including~~ **include** fines of up to € 10, 000, 000 or up to 2 % of our total worldwide annual turnover for certain comparatively minor offenses, or up to € 20, 000, 000 or up to 4 % of our total worldwide annual turnover for more serious offenses. ~~In addition~~ **EEA Member States have adopted implementing national laws to implement the GDPR which may partially deviate from the GDPR , and the competent authorities in the EEA Member States may interpret GDPR obligations slightly differently from country to country, so we do not expect to operate in a uniform legal landscape in the EU.** ~~further~~ **Further** to the UK' s exit from the EU on January 31, 2020, the ~~GDPR ceased to apply in the~~ UK ~~at the end of the transition period on December 31, 2020. However, as of January 1, 2021, the UK' s European Union (Withdrawal) Act 2018~~ incorporated the GDPR (as it existed on December 31, 2020 but subject to certain UK specific amendments) into UK law, referred to as the UK GDPR. The UK GDPR and the UK Data Protection Act 2018, or collectively, UK GDPR, set out the UK' s data protection regime, which is independent from but **currently still** aligned to the EU' s data protection regime. Non-compliance with the UK GDPR may result in monetary penalties of up to £ 17. 5 million or 4 % of worldwide revenue, whichever is higher. Although the UK is regarded as a third country under the EU' s GDPR, the ~~European Commission has now issued a decision recognizing the~~ UK **is recognized** as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EU to the UK remain unrestricted ~~. Like the EU GDPR~~ , **or** the UK **Adequacy Decision** ~~GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection~~ . ~~The~~ **Likewise, the** UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing. ~~Significantly~~ **The UK Government has introduced a Data Protection and Digital Information Bill , or UK Bill, into** the **UK legislative process. The aim of the UK Bill is to reform the UK' s data protection regime following Brexit. If passed, the final version of the UK Bill may have the effect of further altering the similarities between the UK and EEA data protection regime and threaten the UK Adequacy Decision from the European Commission, or EC. This may lead to additional compliance costs and could increase our overall risk. The respective provisions and enforcement of the EU GDPR and UK GDPR may further diverge in the future and create additional regulatory challenges and uncertainties. The** GDPR imposes strict rules on the transfer of personal data out of the EEA and UK to the U. S. or other regions that have not been deemed to offer ~~“~~ **"** adequate ~~”~~ **"** privacy protections. ~~In the past~~ **On June 4** , ~~companies in~~ **2021,** the **EC issued new forms of standard contractual clauses, or SCCs, for** ~~U. S. were able to rely upon the EU- U. S. UK- U. S. and the Swiss- U. S. Privacy Shield frameworks to legitimize~~ data transfers from **controllers or processors in the EEA (or otherwise subject to** the EU **GDPR)** ~~and the UK~~ to **controllers** ~~the U. S. In July 2020, the Court of Justice of the European Union,~~ or ~~CJEU, invalidated~~ **processors established outside the EEA (and not subject to** the EU **GDPR)** ~~- U. S. Privacy Shield on the grounds that the Privacy Shield failed to offer adequate protections to EU personal data transferred to the U. S~~ . The ~~CJEU also ruled that transfers made pursuant to the Standard Contractual Clauses, or SCCs, published by the European Commission, or EC, need to be assessed on a case- by- case basis to ensure the law in the recipient country provides “ essentially equivalent ” protections to safeguard the transferred personal data as the EU, and required businesses to adopt supplementary measures if such standard is not met. On June 4, 2021, the EC published new versions of the SCCs, which seek to address the issues identified by the CJEU and provide further details regarding the transfer assessments that the parties are required to conduct when implementing the~~

new SCCs **replace** ~~. However, there continue to be concerns about whether~~ the SCCs ~~and~~ **that were adopted previously under** ~~other~~ -- **the** ~~mechanisms will face additional challenges. While SCCs provide an alternative to our Privacy Shield certification for EU- U. S. data~~ **Data Protection Directive** ~~flows, the decision (and certain regulatory guidance issued in its wake) casts doubt on the legality of EU- U. S. data flows in general~~ . The UK is not subject to the EC' s new SCCs but has published its own ~~transfer mechanism~~ **standard clauses** , the International Data Transfer Agreement ~~or International Data Transfer Addendum, or IDTA~~ , which enables transfers from the UK. ~~The new IDTA or the UK addendum must be used for any new contract entered into after September 21, 2022 and implemented in existing contracts that incorporate the prior version of the SCCs by March 21, 2024. On March 25, 2022, the EC and the U. S. announced to have reached a political agreement on a new " Trans- Atlantic Data Privacy Framework ", which will replace the invalidated Privacy Shield and on December 13, 2022, the EC published a draft adequacy decision on the Trans- Atlantic Data Privacy Framework.~~ We will be required to implement these new safeguards ~~when~~ **in the event** these safeguards are used as ~~the~~ **our** basis for ~~transferring personal~~ **conducting restricted** data ~~out of~~ **transfers under** the ~~EEA~~ **EU GDPR** and ~~/ or~~ UK **GDPR** and doing so may require significant effort and cost. ~~EEA Member States have~~ **If relying on the SCCs or UK IDTA for data transfers, we may also be required to carry out transfer impact assessments to assess whether the recipient is subject to local laws which allow public authority access to personal data. In July 2023, the European Commission** adopted **its adequacy decision for** ~~implementing national laws to implement~~ the ~~GDPR~~ **EU- U. S. Data Privacy Framework, or the Framework, the successor of the EU- U. S. Privacy Shield framework,** which ~~may partially deviate~~ **the Court of Justice of the European Union invalidated in 2020. On the basis of the new adequacy decision, personal data can flow safely** from the ~~GDPR and the competent authorities in the EEA Member States may interpret GDPR obligations slightly differently from country to country, so that we do not expect to operate in a uniform legal landscape in the~~ EU **to U** . ~~In~~ **S. companies participating in the Framework, without having to put in place** ~~addition~~ **additional** ~~, the UK has announced plans to reform the country' s~~ data protection ~~legal~~ **safeguards. However, the long term validity of the** ~~framework~~ **Framework** ~~in its Data Reform Bill~~ , ~~but these have~~ **which has already** been ~~put on hold~~ **challenged in court, remains uncertain** . If we decide to conduct clinical trials or enroll subjects in our ongoing or future clinical trials in Europe and / or the UK, we are subject to the supervision of local data protection authorities in those jurisdictions where we are monitoring the behavior of individuals in the EEA or UK (i. e., undertaking clinical trials). If we are investigated by a European or UK data protection authority, we may face fines and other penalties. Any such investigation or charges by European or UK data protection authorities could have a negative effect on our business and on our ability to commercialize our products in the future, including with European, UK- based or multi- national pharmaceutical partners. In addition to European data protection requirements, we may be subject to various privacy laws in the United States at the state and federal level. In the United States, at the state level, for example, California Consumer Privacy Act (CCPA), which took effect on January 1, 2020, imposes sweeping privacy and security obligations on many companies doing business in California and provides for substantial fines for non- compliance and, in some cases, a private right of action to consumers who are victims of data breaches involving their unredacted or unencrypted personal information. While there is currently an exception for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact our business activities. The CCPA became enforceable as of July 1, 2020, but there continues to be uncertainty about how the law will be interpreted and enforced. Additionally, the California Privacy Rights Act (CPRA) became effective on January 1, 2023. The CPRA imposes additional obligations on companies covered by the legislation and significantly modifies the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also creates a new state agency that will be vested with authority to implement and enforce the CCPA and the CPRA. As of January 1, 2023, the privacy protections of the CPRA also apply to personal information of contacts collected in a business to business capacity and from employment applicants, employees and former employees. The effects of the CCPA and the CPRA are potentially significant and may require us to modify our data collection or processing practices and policies and to incur substantial costs and expenses in an effort to comply and increase our potential exposure to regulatory enforcement and / or litigation. Furthermore, four other states have enacted comprehensive consumer privacy laws and many others are considering proposals for such laws. The increasing number and complexity of regional, country and U. S. state data protection laws, and other changes in laws or regulations across the globe, especially those associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could lead to litigation or government investigations or enforcement actions and significant penalties against us and could have a material adverse effect on our business, financial condition or results of operations. 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. We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the United States 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. 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, similar 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 United States, including additional nonclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities

in other jurisdictions. In short, the foreign regulatory approval process involves all of the risks associated with FDA approval. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we may intend to charge for our products will also be subject to approval. If we are unable to successfully validate, develop and obtain regulatory approval for companion diagnostic tests for our product candidates that require or would commercially benefit from such tests, or experience significant delays in doing so, we 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 have engaged and may continue to engage third parties to develop or obtain access to in vitro companion diagnostic tests to identify patient subsets within a disease category who may derive selective and meaningful benefit from our product candidates. For example, we have engaged Foundation Medicine, Inc. to develop its FoundationOne ® CDx as a companion diagnostic for **lirafugratinib** ~~RLY- 4008~~ . The FDA has indicated that if we continue RLY- ~~4008 and RLY-~~2608 **and lirafugratinib** in a specific biomarker- defined population, a companion diagnostic device will be required to ensure their safe and effective use. Such companion diagnostics would be used during our clinical trials as well as in connection with the commercialization of our product candidates. To be successful, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. The FDA and similar foreign regulatory authorities regulate in vitro companion diagnostics as medical devices and, under that regulatory framework, will likely require the conduct of clinical trials to demonstrate the safety and effectiveness of any diagnostics we may develop, which we expect will require separate regulatory clearance or approval prior to commercialization. We rely and intend to continue to rely on third parties for the design, development and manufacture of companion diagnostic tests for our therapeutic product candidates that may require such tests. In connection with such current and future collaborative agreements, we will be dependent on the sustained cooperation and effort of our collaborators in developing and obtaining approval for these companion diagnostics. It may be necessary to resolve issues such as selectivity / specificity, analytical validation, reproducibility, or clinical validation of companion diagnostics during the development and regulatory approval processes. Moreover, even if data from preclinical studies and early clinical trials appear to support development of a companion diagnostic for a product candidate, data generated in later clinical trials may fail to support the analytical and clinical validation of the companion diagnostic. We and our current and future collaborators may encounter difficulties in developing, obtaining regulatory approval for, manufacturing and commercializing companion diagnostics similar to those we face with respect to our therapeutic 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 therapeutic product candidates, or experience delays in doing so, the development of these therapeutic product candidates may be adversely affected, these therapeutic product candidates may not obtain marketing approval, and we may not realize the full commercial potential of any of these therapeutics 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 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. Risks Related to Anti- bribery, Anti- corruption and Other Government Regulations Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain products outside of the United States and require us to develop and implement costly compliance programs. If we expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U. S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions. Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non- U. S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U. S. exchanges for violations of the FCPA' s accounting provisions. We are subject to certain U. S. and foreign anti- corruption, anti- money laundering, export control, sanctions, and other trade laws and regulations. We can face serious consequences for violations. Among other matters, U. S. and foreign anti- corruption, anti- money laundering, export control, sanctions, and other trade laws and regulations, which are collectively referred to as Trade Laws, prohibit

companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government- affiliated hospitals, universities, and other organizations. We also expect our non- U. S. activities to increase in time. We plan to engage third parties for clinical trials and / or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals and we can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities. Our relationships with customers and third- party payors will be subject to applicable anti- kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings. Although we do not currently have any products on the market, once we begin commercializing our product candidates, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and governments of foreign jurisdictions in which we conduct our business. Healthcare providers, physicians and third- party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third- party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our product candidates for which we obtain marketing approval. **See" Business –** ~~Restrictions under applicable federal and state healthcare laws and regulations, include the following: • the federal Anti- Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government~~ **Government** ~~healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act, or FCA, or federal civil money penalties; • the federal civil and criminal false claims and civil monetary penalties laws, including the FCA, imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to " cause " the submission of false or fraudulent claims. The FCA also permits a private individual acting as a " whistleblower " to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA; • the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti- Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation; • the federal physician payment transparency requirements, sometimes referred to as the " Sunshine Act " under the Affordable Care Act, require manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children' s Health Insurance Program to report to the Department of Health and Human Services information related to transfers of value made to physicians (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests of such physicians and their immediate family members. Effective January 1, 2022, these reporting obligations were extended to include transfers of value made to certain non- physician providers (physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists and anesthesiologist assistants, and certified- nurse midwives); • HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH and its implementing regulations~~ **Regulation –** ~~, including the Final Omnibus Rule published in January 2013, which impose obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their~~ **Other** ~~business associates that perform certain services involving the creation, maintenance, receipt, or other use or disclosure of individually identifiable health information, including mandatory contractual terms with business associates, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state and non- U. S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts; • federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs; • federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and • analogous state laws~~

~~and regulations, such as state anti- kickback and false claims laws may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non- governmental third- party payors, including private insurers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and / or the Pharmaceutical Research and Manufacturers of America' s Code on Interactions with~~ Healthcare ~~Professionals. Some state laws~~ **Laws** ~~require pharmaceutical companies to comply with the pharmaceutical industry' s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures~~ . **"** ~~State and foreign laws, including for example the EU GDPR, which became effective May 2018 also govern the privacy and security of health information and other personal information in some circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. There are ambiguities as to what is required to comply with these state and foreign requirements and if we fail to comply with an applicable state or foreign law requirement we could be subject to penalties. Further, many state laws governing the privacy and security of health information in certain circumstances, differ from each other in significant ways, thus complicating compliance efforts.~~ Ensuring that our future business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities to be conducted by our sales team, were to be found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, reputational harm, exclusion from government funded healthcare programs, such as Medicare and Medicaid, 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. Further, defending against any such actions can be costly and time consuming, and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment. If any of the above occur, our ability to operate our business and our results of operations could be adversely affected. Risks Related to Regulatory Review of Certain Drug Development Designations We may seek priority review designation for one or more of our product candidates, but we might not receive such designation, and even if we do, such designation may not lead to a faster regulatory review or approval process. If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. We may request priority review for our product candidates. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily result in an expedited regulatory review or approval process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six- month review cycle or at all. We have obtained orphan drug designation for one of our product candidates. We may seek orphan drug designation for certain of our other product candidates as well, and we may be unsuccessful or may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity. In January 2022, the FDA granted orphan drug designation to **lirafugratinib** ~~RLY- 4008~~ for the treatment of cholangiocarcinoma. As part of our business strategy, we may seek orphan drug designation for certain of our other product candidates as well, and we may be unsuccessful. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200, 000 individuals annually in the United States, or a patient population of 200, 000 or more in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the United States, 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. Similarly, in the EU, the European Commission, upon the recommendation of the EMA' s Committee for Orphan Medicinal Products, grants orphan ~~drug~~ designation **in respect** ~~to promote the development~~ of **a** ~~products~~ **product if it can be shown** that ~~are~~ **(1) it is** intended for the diagnosis, prevention or treatment of **a** life- threatening or chronically debilitating ~~conditions~~ **condition; (2) either (a) such condition** ~~affecting~~ **affects** ~~not~~ **no** more than ~~5~~ **five** in 10, 000 persons in the EU ~~and~~ **when the application is made,** ~~for~~ **or** ~~which~~ **(b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify the necessary investment in its development; and (3) there exists** no satisfactory method of diagnosis, prevention ~~,~~ or treatment ~~has been~~ **of such condition** authorized for marketing in the EU ~~(or~~ , **or** if **such** a method exists, the product ~~would~~ **will** be of ~~a~~ significant benefit to those affected by the condition ~~)~~ . **In** ~~Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life- threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the product in~~ the EU ~~would generate sufficient return to justify the necessary investment in developing the product. In the EU~~ , orphan ~~drug~~ designation entitles a party to financial incentives such as reduction of fees or fee waivers. In October 2022, the EMA adopted a positive opinion on the orphan ~~drug~~ designation application for **lirafugratinib** ~~RLY- 4008~~ for the treatment of biliary tract cancer. Generally, if a drug with an orphan drug

designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same drug and indication for that time period, except in limited circumstances. The applicable period is seven years in the United States and ten years in ~~Europe~~ **the EU**. The ~~European~~ **EU** exclusivity period can be reduced to six years if **, at the end of the fifth year, it is established that** a ~~drug~~ **product** no longer meets the criteria for orphan ~~drug~~ designation ~~or~~ **, including** if the ~~drug~~ **product** is sufficiently profitable so that market exclusivity is no longer justified. **The European Commission introduced a legislative proposal in April 2023 that, if implemented, could reduce the current ten- year marketing exclusivity period for certain orphan medicines to nine years (or five years for well- established use orphan medicines).** Even if we obtain orphan drug exclusivity for a drug, that exclusivity may not effectively protect the drug from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve a later drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan drug designation. Moreover, orphan drug exclusive marketing rights in the United States 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 quantity of the drug to meet the needs of patients with the rare disease or condition or if another drug with the same active moiety is determined to be safer, more effective, or represents a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. We have obtained orphan drug designation for one of our product candidates and while we may seek orphan drug designation for our other product candidates, we may never receive such designations. Even if we do receive such designations, there is no guarantee that we will enjoy the benefits of those designations. In addition, the FDA 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. Breakthrough therapy designation and fast track designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development, regulatory review or approval process, and each designation does not increase the likelihood that any of our product candidates will receive marketing approval in the United States. We may seek a breakthrough therapy designation for some of our product candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life- threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA may also be eligible for priority review and 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 a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. We may seek fast track designation for some of our product candidates. If a drug is intended for the treatment of a serious or life- threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for fast track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you 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. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA' s priority review procedures. We may seek approval of our product candidates, where applicable, under the FDA' s accelerated approval pathway. This pathway, even if granted for ~~our FGFR2 program or our PI3K program or~~ any ~~other~~ **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 our product candidates will receive marketing approval in the United States. We may seek accelerated approval of our ~~FGFR2 program or~~ **current and /** ~~our~~ **or** ~~PI3K program and for~~ future product candidates. A product may be eligible for accelerated approval if it treats a serious or life- threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. If granted, accelerated approval is usually contingent on the sponsor' s agreement to conduct, in a diligent manner, additional post- approval confirmatory studies to verify and describe the drug' s clinical benefit. Under FDORA, the FDA is permitted to require, as appropriate, that a post- approval confirmatory study or studies be underway prior to approval or within a specified time period after the date of approval for a product granted accelerated approval. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated

approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if such post- approval studies fail to verify the drug' s predicted clinical benefit. Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post- approval confirmatory study or submit timely reports to the agency on their progress. In addition, the FDA currently requires, unless otherwise informed by the agency, pre- approval of promotional materials for products receiving accelerated approval, which could adversely impact the timing of the commercial launch of the product. Thus, even if we do seek to utilize the accelerated approval pathway, we may not be able to obtain accelerated approval and, even if we do, we may not experience a faster development, regulatory review or approval process for that product. In addition, receiving accelerated approval does not assure that the product' s accelerated approval will eventually be converted to a traditional approval. Risks Related to Healthcare Legislative Reform The FDA, the EMA and other regulatory authorities may implement additional regulations or restrictions on the development and commercialization of our product candidates, and such changes can be difficult to predict. The FDA, the EMA and regulatory authorities in other countries have each expressed interest in further regulating biotechnology products. Agencies at both the federal and state level in the United States, as well as the U. S. Congressional committees and other governments or governing agencies, have also expressed interest in further regulating the biotechnology industry. Such action may delay or prevent commercialization of some or all of our product candidates. Adverse developments in clinical trials of products conducted by others may cause the FDA or other oversight bodies to change the requirements for approval of any of our product candidates. These regulatory review agencies and committees and the new requirements or guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post- approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory agencies and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all. Healthcare legislative reform measures may have a material adverse effect on our business and results of operations. The United States 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 current or future 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 United States, there have been~~ **See" Business – Governmental Regulation – Current** and **future** ~~continue to be a number of legislative initiatives to contain~~ healthcare **reform** ~~costs. For example, in March 2010, the Affordable Care Act, or the ACA, was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the United States pharmaceutical industry. The ACA, among other things, subjects biological products to potential competition by lower- cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50 % (increased to 70 % pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point- of- sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer' s outpatient drugs to be covered under Medicare Part D. Since then, the ACA risk adjustment program payment parameters have been updated annually. Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. On June 17, 2021, the U. S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court' s decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. On December 20, 2019, the Further Consolidated Appropriations Act (H. R. 1865) was signed into law, which repealed the so called " Cadillac " tax on certain high cost employer sponsored insurance plans, the health insurance provider tax, and the medical device excise tax. It is impossible to determine whether similar taxes could be instated in the future. The Bipartisan Budget Act of 2018 also amended the ACA, effective January 1, 2019, by increasing the point- of- sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the " donut hole. " Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $ 1. 2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the~~ legislation ~~' s automatic reduction to~~

several government programs. " This includes aggregate reductions of Medicare payments to providers up to 2 % per fiscal year, and, due to subsequent legislative amendments, will remain in effect through 2030 unless additional Congressional action is taken; however, pursuant to the CARES Act and subsequent legislation, these reductions were suspended from May 1, 2020 through March 31, 2022 due to the COVID- 19 pandemic. A 1 % payment reduction occurred from April 1, 2022 through June 30, 2022, and the 2 % payment reduction resumed on July 1, 2022. The American Taxpayer Relief Act of 2012 among other things, reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. On May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new product candidates that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its product candidates available to eligible patients as a result of the Right to Try Act. In May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy, a type of prior authorization, for Part B drugs beginning January 1, 2020. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. At a federal level, President Biden signed an Executive Order on July 9, 2021 affirming the administration' s policy to (i) support legislative reforms that would lower the prices of prescription drug and biologics, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and by supporting the development and market entry of lower- cost generic drugs and biosimilars; and (ii) support the enactment of a public health insurance option. Among other things, the Executive Order also directs the U. S. Department of Health and Human Services, or HHS, to provide a report on actions to combat excessive pricing of prescription drugs, enhance the domestic drug supply chain, reduce the price that the Federal government pays for drugs, and address price gouging in the industry; and directs the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, and the FDA' s implementing regulations. The FDA released such implementing regulations on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. On September 25, 2020, CMS stated drugs imported by states under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for " best price " or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. If implemented, importation of drugs from Canada may materially and adversely affect the price we receive for any of our product candidates. Further, on November 20, 2020, CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates would have been calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. However, on December 29, 2021, CMS rescinded the MFN rule. Additionally, on December 2, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point- of- sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed until January 1, 2026. This deadline was further pushed back to January 1, 2027 by the Bipartisan Safer Communities Act, and the Inflation Reduction Act of 2022 further delayed implementation of this rule to January 1, 2032. On August 16, 2022 the Inflation Reduction Act of 2022 was passed, which, among other things, allows for CMS to negotiate prices for certain single- source drugs and biologics reimbursed under Medicare Part B and Part D, beginning with ten high- cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. The legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated " maximum fair price " under the law or for taking price increases that exceed inflation. The legislation also caps Medicare beneficiaries' annual out- of- pocket drug expenses at $ 2, 000. The effect of the Inflation Reduction Act of 2022 on our business and the healthcare industry in general is not yet known. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our current or future product candidates or additional pricing pressures. In particular, any policy changes through CMS as well as local state Medicaid programs could have a significant impact on our business in light of the higher proportion of SCD patients that utilize Medicare and Medicaid programs to pay for treatments. **Moreover, increasing efforts by governmental and third- party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates.** Our revenue prospects could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition . There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare . We cannot predict

the initiatives that may be adopted in the future, including repeal, replacement or significant revisions to the ACA. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and / or impose price controls may adversely affect: • the demand for our current or future 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. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability. Recent federal legislation and actions by federal, state and local governments may permit reimportation of drugs from foreign countries into the United States, including foreign countries where the drugs are sold at lower prices than in the United States, which could materially adversely affect our operating results. We may face competition in the United States for our development candidates and investigational medicines, if approved, from therapies sourced from foreign countries that have placed price controls on pharmaceutical products. In the United States, the Medicare Modernization Act, or MMA, contains provisions that call for the promulgation of regulations that expand pharmacists' and wholesalers' ability to import cheaper versions of an approved drug and competing products from Canada, where there are government price controls. Further, the MMA provides that these changes to U. S. importation laws will not take effect, unless and until the Secretary of the HHS certifies that the changes will pose no additional risk to the public' s health and safety and will result in a significant reduction in the cost of products to consumers. On September 23, 2020, the Secretary of the HHS made such certification to Congress, and on October 1, 2020, FDA published a final rule that allows for the importation of certain prescription drugs from Canada. Under the final rule, States and Indian Tribes, and in certain future circumstances pharmacists and wholesalers, may submit importation program proposals to the FDA for review and authorization. On September 25, 2020, CMS stated drugs imported by States under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for " " best price " " or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. Separately, the FDA also issued a final guidance document outlining a pathway for manufacturers to obtain an additional National Drug Code, or NDC, for an FDA- approved drug that was originally intended to be marketed in a foreign country and that was authorized for sale in that foreign country. The market implications of the final rule and guidance are unknown at this time. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. Legislation or regulations allowing the reimportation of drugs, if enacted, could decrease the price we receive for any products that we may develop and adversely affect our future revenues and prospects for profitability. Risks Related to the Regulatory Agency Review Process Disruptions at the FDA, the SEC and other government agencies caused by funding shortages or global health concerns 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, global health concerns, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U. S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical government employees and stop critical activities. ~~Separately, in response to the ongoing COVID- 19 pandemic, since March 2020 when foreign and domestic inspections of facilities were largely placed on hold, the FDA has been working to resume pre- pandemic levels of inspection activities, including routine surveillance, bioresearch monitoring and pre- approval inspections. Should the FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be adequate, the agency has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. During the COVID- 19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA' s inability to complete required inspections for their applications. Regulatory authorities outside the U. S. may adopt similar restrictions or other policy measures in response to the ongoing COVID- 19 pandemic and may experience delays in their regulatory activities. Additionally, as of May 26, 2021, the FDA noted it is continuing to ensure timely reviews of applications for medical products during the ongoing COVID- 19 pandemic in line with its user fee performance goals. However, the FDA may not be able to continue its current pace and approval timelines could be extended, including where a pre- approval inspection or an inspection of clinical sites is required and due to the ongoing COVID- 19 pandemic and any travel restrictions, the FDA is unable to complete such required inspections during the review period.~~ If a prolonged government shutdown occurs, or if global health concerns ~~continue to~~ prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations. Risks Related to Employee Matters and Managing Growth Our future success depends on our ability to retain key executives and experienced scientists and to attract, retain and motivate qualified personnel. We are highly dependent on the research and development, clinical and business development expertise of

the principal members of our management, scientific and clinical team. Although we have entered into employment letter agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain ~~“~~ " key person ~~”~~ " insurance for any of our executives or other employees. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited. Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees, including temporary loss due to illness, could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel. In particular, we have experienced a very competitive hiring environment in Cambridge, Massachusetts, where we are headquartered. Many of the other pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high- quality candidates than what we have to offer. If we are unable to continue to attract and retain high- quality personnel, the rate and success with which we can discover and develop product candidates and our business will be limited. Our employees, principal investigators, CROs and consultants may engage in misconduct or other improper activities, including non- compliance with regulatory standards and requirements and insider trading. We are exposed to the risk that our employees, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and / or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of the FDA and other regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; healthcare fraud and abuse laws and regulations in the United States and abroad; or laws that require the reporting of financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self- dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical or other nonclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. 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 civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. Risks Related to Growth and Acquisitions We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations. As of December 31, ~~2022~~ **2023** , we had ~~327~~ **323** full- time employees. ~~We~~ **In the future, we** expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of pharmaceutical and clinical development, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations. We may acquire additional businesses or products, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction. Our acquisitions expose us to risks that could adversely affect our business, and we may not achieve the anticipated benefits of acquisitions of businesses or technologies. As

a part of our growth strategy, we may make selected acquisitions of complementary products and / or businesses, such as our acquisition of ZebiAI in April 2021. Any acquisition involves numerous risks and operational, financial, and managerial challenges, including the following, any of which could adversely affect our business, financial condition, or results of operations: • difficulties in integrating new operations, technologies, products, and personnel; • challenges maintaining uniform procedures, controls and policies with respect to our financial accounting systems; • lack of synergies or the inability to realize expected synergies and cost- savings; • underperformance of any acquired technology, product, or business relative to our expectations and the price we paid; • negative near- term impacts on financial results after an acquisition, including acquisition-related earnings charges; • the potential loss of key employees, customers, and strategic partners of acquired companies; • claims by terminated employees and shareholders of acquired companies or other third parties related to the transaction; • the assumption or incurrence of additional debt obligations or expenses, or use of substantial portions of our cash; • the issuance of equity securities to finance or as consideration for any acquisitions that dilute the ownership of our stockholders; • the issuance of equity securities to finance or as consideration for any acquisitions may not be an option if the price of our common stock is low or volatile which could preclude us from completing any such acquisitions; • any collaboration, strategic alliance and licensing arrangement may require us to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms that are not favorable to us; • diversion of management' s attention and company resources from existing operations of the business; • inconsistencies in standards, controls, procedures, and policies; • the impairment of intangible assets as a result of technological advancements, or worse- than- expected performance of acquired companies; • assumption of, or exposure to, historical liabilities of the acquired business, including unknown contingent or similar liabilities that are difficult to identify or accurately quantify; and • risks associated with acquiring intellectual property, including potential disputes regarding acquired companies' intellectual property. In addition, the successful integration of acquired businesses requires significant efforts and expense across all operational areas. There can be no assurance that any of the acquisitions we may make, including our acquisition of ZebiAI, will be successful or will be, or will remain, profitable. Our failure to successfully address the foregoing risks may prevent us from achieving the anticipated benefits from any acquisition in a reasonable time frame, or at all. Risks Related to Business Disruptions Our internal information technology systems, or those of our third- party collaborators and / or partners, may fail or suffer security breaches, loss or leakage of data and other disruptions, which could result in a material disruption of our development programs, compromise sensitive information related to our business or prevent us from accessing critical information, potentially exposing us to liability or otherwise adversely affecting our business. We are increasingly dependent upon information technology systems, infrastructure and data to operate our business. In the ordinary course of business, we collect, store and transmit confidential information (including but not limited to intellectual property, proprietary business information and personal information). It is critical that we do so in a secure manner to maintain the confidentiality ~~and~~ **,** integrity **, and availability** of such ~~confidential~~ information. We also have outsourced elements of our operations to third parties, and as a result we collaborate with a number of third- party CROs, vendors, and other contractors and consultants who have access to our confidential information. Given our limited operating history, we are still in the process of implementing our internal information technology security measures. Due to the size and complexity and the increasing amounts of confidential information that are maintained, our internal information technology systems and **infrastructure and** those of our third- party CROs, vendors and other contractors and consultants are potentially vulnerable to breakdown or other damage **,** ~~or interruption from~~ service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as **cyber- attacks or** security **compromises,** incidents **,** or breaches from inadvertent or intentional actions by our employees **, third- party CROs, vendors, contractors, consultants** and / or third parties with whom we do business, or from cyber- attacks **or security compromises, incidents, or breaches** by malicious third parties (including the deployment of harmful malware, ransomware, digital extortion, denial- of- service attacks, supply chain attacks, social engineering and **business email compromises, and** other means to affect service reliability and threaten the confidentiality, integrity ~~and~~ **,** availability **, and security** of **systems, infrastructure or** information), which may compromise our ~~system~~ **systems and** infrastructure or those of our partners **, third- party CROs, vendors, contractors, consultants and / or third parties with whom we do business,** or lead to data leakage **or compromise** . If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, similar events relating to the information technology systems of our third- party collaborators who we rely on for the manufacture of our product candidates and to conduct clinical trials could also have a material adverse effect on our business. The risk of a security breach or disruption, particularly through cyber- attacks or cyber intrusion, including by computer hackers, **insider threats,** foreign governments, and cyber terrorists, has generally increased as the frequency, persistence, intensity and sophistication of attempted attacks and intrusions from around the world have increased, including potentially in connection with the ~~current~~ **ongoing** conflict between Russia and Ukraine. We may not be able to anticipate all types of security threats, nor may we be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched and can originate from a wide variety of sources, including **insider threats and** outside groups such as external service providers, organized crime affiliates, terrorist organizations or hostile foreign governments or agencies **, or generated using artificial intelligence** . In addition, changes in how our employees work and access our systems **, which began** during the ~~ongoing~~ COVID- 19 pandemic **and continue today** , when part of our workforce is working remotely, could also lead to opportunities for bad actors to launch cyber- attacks or for employees to cause inadvertent **or intentional** security risks or incidents. The prevalent use of mobile devices also increases the risk of data security incidents. We are also subject to legal obligations concerning cyber security. For example, as a company ~~handing~~ **handling** employee information of individuals who reside in Massachusetts, we are required to comply with the Massachusetts Data Security Regulations (201 CMR 17. 00) **,** which

require the development and implementation of a Comprehensive Written Information Security Program and the maintenance of specific information security protections. While we have not **directly** experienced any material system failure, accident or security breach to date, we cannot guarantee that our data protection efforts and our investment in information technology will prevent significant breakdowns, data leakages, or breaches in **or compromises of** our systems **or those of third- party CROs, vendors, contractors, consultants and / or third parties with whom we do business. For example, in March 2023, we were notified that a third- party CMO with whom we collaborate had been subject to a ransomware attack. Based on information made available to us by the third party CMO, we do not believe the third- party CMO ransomware event has had a material impact on our business** . While we maintain liability insurance at levels that we believe are appropriate for our business, we cannot assure our investors that it will be sufficient in type or amount to cover us against all claims related to security compromises or breaches, cyberattacks and other related breaches. To the extent that any disruption or security **compromises, incident, or** breach were to result in a loss of, or damage to, our **systems, infrastructure,** data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed, the further development and commercialization of our product candidates or any future product candidates could be hindered or delayed, we could be required to expend significant amounts of money and other resources to repair **, remediate,** or replace our information systems or networks, the market perception of the effectiveness of our security measures could be harmed and our reputation and credibility could be damaged. Furthermore, any failure or perceived failure by us or any third-party collaborators, service providers, contractors or consultants to comply with our privacy, confidentiality, data security or similar obligations to third parties, or any data security incidents or other security compromises or breaches that result in the unauthorized access, use, acquisition, disclosure, release or transfer of **confidential or** sensitive information, including physician data, patient data, or any personally identifiable information, may result in governmental investigations, enforcement actions, regulatory fines, litigation or public statements against us, could cause third parties to lose trust in us or could result in claims by third parties asserting that we have breached our privacy, confidentiality, data security or similar obligations, any of which could have a material adverse effect on our reputation, business, financial condition or results of operations. Moreover, data security incidents and other security compromises and breaches can be difficult to detect, and any delay in identifying or remediating them may lead to increased harm. While we have implemented data security measures intended to protect our information technology systems and infrastructure, there can be no assurance that such measures will successfully prevent service interruptions or data security incidents or compromises, including security breaches. If we fail to comply with applicable 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 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. Compliance with applicable environmental, health and safety laws and regulations is expensive, and current or future environmental regulations may impair our business, prospects, financial condition or results of operations. Our current operations are located in Massachusetts; however, we rely on third parties, including those that are located outside the United States, and we or the third parties upon whom we depend may be adversely affected by natural disasters or other unplanned events and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster. Our current operations are located in Massachusetts. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, **geopolitical** ~~including any potential effects from the current global spread of COVID- 19, global~~ conflicts ~~such as the current conflict between Russia and Ukraine~~ , power shortage, telecommunication failure or other natural or man- made accidents or incidents that result in us being unable to fully utilize our facilities, or the facilities of our third- party contract manufacturers or CROs, may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our product candidates or interruption of our business operations. Natural disasters or pandemics ~~such as~~ **similar to** the ~~ongoing~~ COVID- 19 pandemic could ~~further~~ disrupt our operations and have a material and adverse effect on our business, financial condition, results of operations and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our research facilities or the facilities of our third- party contract manufacturers or CROs, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure our investors that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities or the facilities of our third- party contract manufacturers or CROs are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research

and development programs may be harmed. Any business interruption may have a material and adverse effect on our business, financial condition, results of operations and prospects. Risks Related to Our Common Stock Risks Related to Trading Our Common Stock The trading price of our common stock historically has been volatile, which may affect the price at which you could sell any shares of our common stock. Securities class action or other litigation involving our company or members of our management team could also substantially harm our business, financial condition and results of operations. The market price for our common stock historically has been volatile and could continue to be subject to wide fluctuations in response to various factors. Since shares of our common stock were sold in our initial public offering, or IPO, in July 2020 at a price of $ 20. 00 per share, our stock price has fluctuated significantly, ranging from an intraday low of $ ~~12~~ **5** . ~~65~~ **95** to an intraday high of $ 64. 37 through February ~~17~~ **16** , ~~2023~~ **2024** . This volatility may affect the price at which you could resell the common stock. Our stock price is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market and other factors, including the factors described below. The stock market in general and Nasdaq and the market for biopharmaceutical companies in particular, have experienced extreme volatility that has often been unrelated or disproportionate to the operating performance of these companies. The market price for our common stock may be influenced by many factors, including: • the success of competitive products or technologies; • results of clinical trials of our product candidates or those of our competitors; • regulatory or legal developments in the United States and other countries; • developments or disputes concerning patent applications, issued patents or other proprietary rights; • the recruitment or departure of key personnel; • the level of expenses related to any of our product candidates or clinical development programs; • the results of our efforts to discover, develop, acquire or in- license additional product candidates or products; • actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts; • sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares; • variations in our financial results or those of companies that are perceived to be similar to us; • changes in the structure of healthcare payment systems; • market conditions in the pharmaceutical and biotechnology sectors; • general economic, industry and market conditions; and • the other factors described in this ~~“~~ **"** Risk Factors ~~”~~ **"** section. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management’ s attention from other business concerns, which could seriously harm our business. An active trading market for our common stock may not be sustained. If an active market for our common stock does not continue, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or sell their shares at or above the prices at which they acquired their shares or sell their shares at the time they would like to sell. Any inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration. Risks Related to Dividends Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain. We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. General Risk Factors Risks Related to Insider Control Our executive officers, directors, principal stockholders and their affiliates exercise significant control over our company, which will limit your ability to influence corporate matters and could delay or prevent a change in corporate control. As of December 31, ~~2022~~ **2023** , the holdings of our executive officers, directors, principal stockholders and their affiliates, represented beneficial ownership, in the aggregate, of approximately ~~47~~ **54** . ~~2~~ **3** % of our outstanding common stock. As a result, these stockholders, if they act together, will be able to influence our management and affairs and control the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation, or sale of all or substantially all of our assets. These stockholders may have interests, with respect to their common stock, that are different from those of our public market investors and the concentration of voting power among these stockholders may have an adverse effect on the price of our common stock. In addition, this concentration of ownership might adversely affect the market price of our common stock by: • delaying, deferring or preventing a change of control of us; • impeding a merger, consolidation, takeover or other business combination involving us; or • discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us. Risks Related to Tax Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited. Under Section 382 of the Internal Revenue Code of 1986, as amended, or the IRC, if a corporation undergoes an ~~“~~ **"** ownership change ~~”~~ **"** (generally defined as a greater than 50 % change (by value) in the ownership of its equity over a three year period), the corporation’ s ability to use its pre- change net operating loss carryforwards and certain other pre- change tax attributes to offset its post- change income may be limited. We may experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As of December 31, ~~2022~~ **2023** , ~~,~~ we had federal net operating loss carryforwards of approximately $ ~~412~~ **498** . 0 million, and our ability to utilize those net operating loss carryforwards could be limited by an ~~“~~ **"** ownership change ~~”~~ **"** as described above. Comprehensive tax reform legislation could adversely affect our business and financial condition. The rules dealing with U. S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service, or IRS, and the U. S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many changes have been made and changes are likely to continue to occur in the future. Additional changes to U. S. federal income tax law are currently being contemplated, and future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. It cannot be predicted whether, when, in what form, or with what effective dates, new tax laws may be enacted, or regulations and rulings may be enacted, promulgated or issued under existing or new tax laws, which could result in an increase in our or our

stockholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law or in the interpretation thereof. You are urged to consult your tax advisor regarding the implications of potential changes in tax laws on an investment in our common stock. Risks Related to Operating as a Public Company We have incurred and will continue to incur increased costs as a result of operating as a public company, and our management has devoted and will continue to devote substantial time to compliance initiatives. As a public company, ~~and particularly since we are no longer an " emerging growth company, "~~ we have incurred and expect to incur significant legal, accounting and other expenses. In addition, the Sarbanes- Oxley Act of 2002 and rules subsequently implemented by the SEC and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will continue to increase our legal and financial compliance costs and will make some activities more time- consuming and costly. Pursuant to Section 404 of the Sarbanes- Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. **We** ~~Because we are no longer an emerging growth company, we~~ are required to include with our annual reports an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we have been and will continue to be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404 or that we will not be able to comply with the requirements of Section 404 in a timely manner. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. In addition, if we are not able to continue to meet these requirements, we may not be able to remain listed on Nasdaq. Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well- conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision- making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected. Risks Related to Our Charter and Bylaws Anti- takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management. Our fourth amended and restated certificate of incorporation, as amended, the Certificate of Incorporation, and our amended and restated bylaws, as amended, the 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 the stockholders may 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, and special meetings of stockholders may not be called by any other person or persons; • 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 (2 / 3) 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 a majority of all outstanding shares of our voting stock to amend any bylaws by stockholder action and not less than two- thirds (2 / 3) of all outstanding shares of our voting stock 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, 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 Certificate of Incorporation and 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 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 Bylaws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the sole and exclusive forum for any state law claims for (1) any derivative action or proceeding brought on our behalf; (2)

any action asserting a claim of or based on a breach of a fiduciary duty owed by any director, officer or other employee of ours to us or our stockholders; (3) any action asserting a claim pursuant to any provision of the Delaware General Corporation Law, our Certificate of Incorporation or our Bylaws; or (4) 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 Bylaws further provide that unless we consent in writing to the selection of an alternative forum, the United States District Court for the District of Massachusetts shall 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. In addition, our Bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock is 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 federal securities laws and the rules and regulations thereunder. We recognize that the Delaware Forum Provision and the Federal Forum Provision in our Bylaws may impose additional litigation costs on stockholders in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware or the Commonwealth of Massachusetts. Additionally, the forum selection clauses in our Bylaws 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 United States District Court for the District of Massachusetts 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. Risks Related to Securities Analysts If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline. The trading market for our common stock will rely in part on the research and reports that industry or securities analysts publish about us or our business. If one or more of the analysts covering our stock downgrade their evaluations of our stock or publishes inaccurate or unfavorable research about our business, the trading price of our stock may decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.