

Risk Factors Comparison 2025-02-20 to 2024-02-27 Form: 10-K

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Careful consideration should be given to the following risk factors, in addition to the other information set forth in this Annual Report on Form 10-K and in other documents that we file with the Securities and Exchange Commission, or the SEC, in evaluating the Company and our business. Investing in our common stock involves a high degree of risk. If any of the following risks and uncertainties actually occurs, our business, prospects, financial condition and results of operations could be materially and adversely affected. The risks described below are not intended to be exhaustive and are not the only risks facing the company. New risk factors can emerge from time to time, and it is not possible to predict the impact that any factor or combination of factors may have on our business, prospects, financial condition and results of operations. Summary of company-specific material risk factors We have included a summary of the material risks that we believe are specific to SpringWorks. The summary does not include all material risks associated with our business and is not a conclusive ranking or prioritization of our risk factors. Further, placement of certain of these risks in the summary section as opposed to others does not constitute guidance that the risk factors included in the summary are the only material risks to consider when considering an investment in our securities. We believe that all risk factors presented in this Annual Report on Form 10-K are important to an understanding of our company and should be given careful consideration. In addition, the summary of company-specific material risks does not include the appropriate level of detail necessary to fully understand these risks, and the corresponding risk factors that follow provide essential detail and context necessary to fully understand and appreciate these company-specific risks associated with our business. Risks related to our research and development and commercialization • Our business depends heavily on our ability to successfully commercialize OGSIVEO **and GOMEKLI** in the United States and in other jurisdictions where we may obtain marketing approval, including Europe. There is no assurance that our commercialization efforts with respect to OGSIVEO **or GOMEKLI** will be successful or that we will be able to generate revenues at the levels or on the timing we expect, or at levels or on the timing necessary to support our goals. • We have limited experience as a commercial company and the sales, marketing, and distribution of OGSIVEO **, GOMEKLI**, or any future approved products may be unsuccessful or less successful than anticipated. • Our business is highly dependent on the successful commercialization of OGSIVEO and **GOMEKLI and** development of our current product candidates ~~, including mirdametinib~~. If we are unable to successfully commercialize OGSIVEO **or GOMEKLI** or successfully complete clinical development of, obtain regulatory approval for, or commercialize, our product candidates, or if we experience delays in doing so, our business will be materially harmed. • We were not involved in the early development of our lead ~~product~~ **products candidates** or in the development of third-party agents being developed in combination with our product candidates; therefore, we are dependent on third parties having accurately generated, collected, interpreted and reported data from certain preclinical and clinical trials for our **products and** product candidates. • If our clinical trials fail to replicate positive results from earlier preclinical studies or clinical trials conducted by us or third parties, we may be unable to successfully develop, obtain regulatory approval for or commercialize our product candidates. • Interim “ topline ” and preliminary data from our clinical trials that we announce or publish from time to time may change as more data become available, are not necessarily predictive of the final results of the completed study or the results of other ongoing or future studies and are subject to audit and verification procedures that could result in material changes. • ~~Although we have successfully completed the DeFi trial and received approval for OGSIVEO for the treatment of adult patients with progressing desmoid tumors who require systemic treatment, we have limited experience completing registrational clinical trials, and we may be unable to do so for additional product candidates we may develop.~~ • We expect to develop nirogacestat and mirdametinib, and potentially future product candidates, in combination with other therapies, and safety or supply issues with combination use products may delay or prevent development and approval of such product candidates. • If we encounter difficulties enrolling patients in any of our clinical trials, our clinical development activities could be delayed or otherwise adversely affected. • The target patient populations of OGSIVEO for the treatment of desmoid tumors and ~~mirdametinib~~ **GOMEKLI** for the treatment of NF1- PN are small and have not been definitively determined, and if our estimates of the number of treatable patients is lower than expected, our potential revenues from sales of OGSIVEO or of **GOMEKLI** ~~mirdametinib, if approved~~, and our ability to achieve profitability would be compromised. • Even if our product candidates receive marketing approval, they may fail to achieve market acceptance by physicians, patients, third-party payers, or others in the medical community necessary for commercial success. Risks related to our reliance on third parties • We rely on third parties to conduct certain aspects of our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval for, or commercialize, any potential product candidates. • Because we rely on third-party manufacturing and supply partners, our supply of preclinical and clinical development materials and commercial product may become limited or interrupted or may not be of satisfactory quantity or quality, which could delay, prevent or impair our development or commercialization efforts. • Despite ~~entering~~ **having entered** into commercial manufacturing and supply agreements related to the supply of ~~nirogacestat~~'s active pharmaceutical ingredient and finished drug product **for both nirogacestat and mirdametinib**, we have limited experience manufacturing on a commercial scale, and we have not yet entered into commercial supply arrangements with respect to our **other** product candidates, and we rely on third parties to produce and process quantities of our ~~first~~-FDA- approved ~~product~~ **products**, OGSIVEO **and GOMEKLI**, and we expect to rely on third parties to produce and process commercial quantities of OGSIVEO **and GOMEKLI** and our product candidates, if approved. • We are dependent on a small number of suppliers for some of the materials used to manufacture our product candidates, and on a limited number

of qualified active ingredient manufacturers for the commercial supply of OGSIVEO, **GOMEKLI** and each of our ~~lead~~ **other** product candidates. • Our existing and future collaborations are important to our business. If we are unable to maintain our existing collaborations or enter into new collaborations, or if these collaborations are not successful, our business could be adversely affected. In addition, our collaborators have broad discretion in many aspects of their performance of collaboration activities and they may take actions with which we do not agree. Risks related to our intellectual property • We depend on intellectual property licensed from third parties, including from Pfizer ~~Inc., or Pfizer,~~ for our lead product candidates, and termination of any of these licenses could result in the loss of significant rights, which would harm our business. • If we fail to comply with our obligations under our patent licenses with third parties, we could lose license rights that are important to our business. Risks related to government regulation • We have been granted Orphan Drug ~~Designation~~ **designation** for nirogacestat and mirdametinib and may seek Orphan Drug ~~Designation~~ **designation** for other product candidates, but we may be unable to obtain or maintain such designation, or the benefits associated with such designation, including the potential for market exclusivity, which may negatively impact our financial performance. • A portion of our manufacturing of our lead ~~product~~ **products candidates** takes place in China, with additional capacity sourced from India, through third- party manufacturers. A significant disruption in the operation of those manufacturers, a trade war or political unrest could materially adversely affect our business, financial condition and results of operations. • **The U. S. Congress, the Trump administration, or any new administration may make substantial changes to fiscal, tax, and other federal policies that may adversely affect our business.** Risks related to managing our business and operations • We will need to grow the size of our organization, and we may experience difficulties in managing this growth. • We are still developing the internal research capabilities required to independently discover new product candidates, and we plan to execute our growth strategy, in part by identifying and in-licensing or acquiring additional product candidates that have been discovered and initially developed by others. We may not be successful in executing our growth strategy or such growth strategy may not deliver the anticipated results. • Our current operations are concentrated in two locations, and we or the third parties upon whom we depend may be adversely affected by natural disasters, including those that may be related to climate change, or other unforeseeable or uncontrollable events, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster. Risks related to our financial position and need for additional capital • We have incurred significant net losses since our inception and anticipate that we will **continue to incur net losses until we reach profitability, which we currently anticipate to be in the future first half of 2026. We may not be able to reach profitability in the first half of 2026 if we cannot continue to effectively commercialize OGSIVEO or effectively commercialize GOMEKLI.** • We have a limited operating history, which may make it difficult to evaluate our prospects and likelihood of success. • We may require additional capital to fund our operations and if we fail to obtain necessary capital, we will not be able to complete the development and commercialization of our product candidates. • Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. Risks related to our common stock • We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock. • Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval. • Anti- takeover provisions under our charter documents and Delaware law could delay or prevent a change of control which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management. • Our bylaws designate certain specified courts as the sole and exclusive forums for certain disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees. Company- specific material risk factors ~~To date, we have not generated substantial revenue from the sale of products.~~ In November 2023, OGSIVEO (nirogacestat) was approved by the FDA for the treatment of adult patients with progressing desmoid tumors who require systemic treatment, **and in February 2025, GOMEKLI (mirdametinib) was approved by the FDA for the treatment of adult and pediatric patients two years of age and older with neurofibromatosis type 1, or NF1, who have symptomatic plexiform neurofibromas, or PN, not amenable to complete resection.** Our business currently depends heavily on our ability to successfully commercialize OGSIVEO **and GOMEKLI** in the United States and in other jurisdictions where we may obtain marketing approval, including Europe. We may never be able to successfully commercialize our ~~product~~ **products** or meet our expectations with respect to revenues. **We have limited commercialization experience with OGSIVEO and we are only now commencing our commercialization of GOMEKLI.** We have never marketed, sold, or distributed for commercial use any ~~pharmaceutical product~~ **other products than OGSIVEO, nor have with respect to which we only recently began marketed, sold or distributed for commercial sales** ~~use any product in any other market outside of the United States.~~ There is no guarantee that the infrastructure, systems, processes, policies, relationships, and materials we have built for the launch and commercialization of OGSIVEO **or GOMEKLI** in the United States, or that we ~~may have begun~~ **build building** in Europe, will be sufficient for us to achieve success at the levels we expect. We may encounter issues and challenges in commercializing OGSIVEO **and GOMEKLI** and generating substantial revenues. We may also encounter challenges related to reimbursement of OGSIVEO **or GOMEKLI**, including potential limitations in the scope, breadth, availability, or amount of reimbursement covering OGSIVEO **or GOMEKLI, respectively.** Similarly, healthcare settings or patients may determine that the financial burdens of treatment are not acceptable. We may face other limitations or issues related to the price of OGSIVEO **or GOMEKLI.** Our results may also be negatively impacted if we have not adequately sized our field teams or our physician segmentation and targeting strategy is inadequate or if we encounter deficiencies or inefficiencies in our infrastructure or processes. Other factors that may hinder our ability to successfully commercialize OGSIVEO, **GOMEKLI**, or any of our future approved drugs, and generate substantial revenues, include: • the acceptance of OGSIVEO **and GOMEKLI** by patients and the medical community; • the ability of our third- party manufacturer (s) to manufacture commercial supplies of OGSIVEO **and GOMEKLI** at acceptable costs, to remain in good standing with regulatory agencies, and to maintain commercially viable

manufacturing processes that are, to the extent required, compliant with cGMP regulations; • our ability to remain compliant with laws and regulations that apply to us and our commercial activities; • FDA- mandated package insert requirements and successful completion of any related FDA post- marketing requirements; • the actual market size for OGSIVEO **or GOMEKLI, respectively**, which may be different than expected; • the length of time that patients who are prescribed our drug remain on treatment; • our ability to obtain marketing approval for OGSIVEO **and GOMEKLI** in Europe; • the sufficiency of our drug supply to meet commercial and clinical demands which could be negatively impacted if our projections regarding the potential number of patients are inaccurate, we are subject to unanticipated regulatory requirements, or our current drug supply is destroyed, or negatively impacted at our manufacturing sites, storage sites, or in transit; • our ability to effectively compete with other therapies that may emerge for desmoid tumors; and • our ability to maintain, enforce, and defend third party challenges to our intellectual property rights in and to OGSIVEO **and GOMEKLI**. Any of these issues could impair our ability to successfully commercialize our product or to generate substantial revenues or profits or to meet our expectations with respect to the amount or timing of revenues or profits. Any issues or hurdles related to our commercialization efforts may materially adversely affect our business, results of operations, financial condition, and prospects. There is no guarantee that we will be successful in our ~~launch or~~ commercialization efforts with respect to OGSIVEO **or our launch or commercialization efforts with respect to GOMEKLI**. We may also experience significant fluctuations in sales of OGSIVEO **or GOMEKLI** from period to period and, ultimately, we may never generate sufficient revenues from OGSIVEO **and GOMEKLI** to reach or maintain profitability or sustain our anticipated levels of operations. Any inability on our part to successfully commercialize OGSIVEO **or GOMEKLI** in the United States, and any other international markets where it may subsequently be approved, including Europe, or any significant delay, could have a material adverse impact on our ability to execute upon our business strategy. We ~~recently began commercializing~~ **commercialization of our first product, OGSIVEO, in November 2023 and have just commenced** the United States **commercial launch of GOMEKLI in February 2025**. As a company, we had no prior experience commercializing a product. The success of our commercialization efforts for **OGSIVEO-GOMEKLI** and any future approved products is difficult to predict and subject to the effective execution of our business plan, including, among other things, the continued development of our internal sales, marketing, and distribution capabilities and our ability to navigate the significant expenses and risks involved with the development and management of such capabilities. For example, we have **expanded** ~~completed hiring~~ in areas to support commercialization, including in sales management, sales representatives, marketing, access and reimbursement, sales support, and distribution. There are significant expenses and risks involved with establishing our own sales, marketing, and distribution capabilities, including our ability to hire, retain, and appropriately incentivize qualified individuals, provide adequate training to sales and marketing personnel, and effectively manage geographically dispersed sales and marketing teams to generate sufficient demand. Any failure or delay in the development of these capabilities could delay or negatively affect the success of our commercialization efforts and our business. For example, the commercialization of OGSIVEO **and GOMEKLI** may not develop as planned or anticipated, which may require us to, among others, adjust or amend our business plan and incur significant expenses. Further, given our lack of experience commercializing products, we do not have a track record of successfully executing on the commercialization of an approved product. If we are unsuccessful in accomplishing our objectives and executing on our business plan, or if the commercialization of OGSIVEO **and GOMEKLI** or any future approved products does not develop as planned, we may require significant additional capital and financial resources, we may not become profitable, and we may not be able to compete against more established companies in our industry. Our future success and ability to generate revenue from our product candidates is dependent on our ability to successfully develop, obtain regulatory approval for and commercialize one or more product candidates. We currently have ~~one two product~~ **products** approved for commercial sale and a portfolio of product candidates in various stages of development. Our product candidates that are in earlier stages of development and will require substantial additional investment for preclinical development, clinical development, regulatory review and approval in one or more jurisdictions. In November 2023, the FDA approved OGSIVEO (nirogacestat) for the treatment of adult patients with progressing desmoid tumors who require systemic treatment. **In February 2025, We are exploring nirogacestat in additional indications and in combination with other -- the therapies and also advancing FDA approved GOMEKLI (mirdametinib,) for the treatment of adults an and investigational MEK inhibitor, in pediatric and adult patients two years of age and older with neurofibromatosis type 1 --associated, or NF1, who have symptomatic plexiform neurofibromas, or (NF1-PN). In November 2023, not amenable to complete resection. We are also exploring nirogacestat and we announced positive topline results from the pivotal Phase 2b ReNeu trial evaluating mirdametinib in additional indications for NF1-PN.** If nirogacestat **or mirdametinib** for additional indications, ~~mirdametinib~~ or any of our other product candidates encounter safety or efficacy problems, development delays or regulatory issues or other problems, our development plans and ability to obtain regulatory approval for, or commercialize, additional indications or product candidates would be significantly harmed. We may not have the financial resources to continue the development of, or to modify existing or enter into new collaborations for, a product candidate if we experience any issues that delay or prevent regulatory approval of, or our ability to commercialize, our product candidates, including: • our inability to demonstrate to the satisfaction of the FDA, or comparable foreign regulatory authorities that our product candidates are safe and effective; • our ability to establish commercial manufacturing processes and product supply arrangements; • insufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials; • negative or inconclusive results from our preclinical studies, clinical trials or the clinical trials of others for product candidates similar to ours, leading to a decision or requirement to conduct additional preclinical studies or clinical trials or abandon a program; • product- related adverse events experienced by subjects in our clinical trials or by individuals using drugs or therapeutic biologics similar to our product candidates; • delays in submitting an IND or comparable foreign applications, or delays or failure in obtaining the necessary approvals from regulators to commence a clinical trial or a suspension or termination of a clinical trial once commenced; • conditions imposed by the FDA, EMA, or comparable foreign

regulatory authorities regarding the scope or design of our clinical trials; • poor effectiveness of our product candidates during clinical trials; • better than expected performance of control arms, such as placebo groups, which could lead to negative or inconclusive results from our clinical trials; • delays in enrolling subjects in clinical trials; • high drop- out rates of subjects from clinical trials; • inadequate supply or quality of product candidates or other materials necessary for the conduct of our clinical trials; • greater than anticipated clinical trial or manufacturing costs; • unfavorable FDA, EMA, or comparable regulatory authority inspection and review of a clinical trial site; • failure of our third- party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all; • delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our therapies in particular; or varying interpretations of data by the FDA, EMA, and comparable foreign regulatory authorities. We had no involvement with or control over the initial preclinical and clinical development of any of our lead ~~product-products candidates~~ or third- party agents being developed in combination with our product candidates. We are dependent on third parties having conducted their research and development in accordance with the applicable protocols and legal, regulatory and scientific standards; having accurately reported the results of all preclinical studies and clinical trials conducted with respect to such **products and** product candidates; and having correctly collected and interpreted the data from these trials. If these activities were not compliant, accurate or correct, the clinical development, regulatory approval or commercialization of our **products and** product candidates will be adversely affected. Our preclinical studies or early clinical trials of our product candidates, whether conducted by us or third parties, may not necessarily be predictive of the results of later clinical trials that we conduct. Similarly, even if we are able to complete our planned clinical trials of our product candidates, positive results from such clinical trials may not be replicated in our subsequent preclinical studies or clinical trials. 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 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 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 comparable foreign regulatory authority approval. Furthermore, the approval policies or regulations of the FDA, EMA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval, which may lead to the FDA, EMA or comparable foreign regulatory authorities delaying, limiting or denying approval of our product candidates. From time to time, we may publicly disclose interim topline or preliminary data from our clinical trials ~~, such as the positive topline results from pediatric and adult patients in the ReNeu trial, our Phase 2b clinical trial of mirdametinib announced in November 2023.~~ Interim updates are based on a preliminary analysis of then- available data, and the data and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, any topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Interim topline or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim topline or preliminary data should be viewed with caution until the final data are available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. As a result, interim data may not be predictive of the final results of the same study or the results of ongoing or future studies. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly. Furthermore, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is typically selected from a more extensive amount of available information. You or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product, product candidate or our business. If the interim topline or preliminary data that we report differ from late, final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, the product candidate being studied or any of our other product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects. We ~~will need to successfully complete registrational clinical trials in order to obtain the approval of the FDA, EMA or comparable foreign regulatory authorities to market any product candidates.~~ Carrying out clinical trials, including later- stage registrational clinical trials, is a complicated process. Although we completed the DeFi trial, which supported the approval of OGSIVEO for the treatment of adult patients with progressing desmoid tumors who require systemic treatment by the FDA in November 2023, as an organization, we have limited experience completing registrational clinical trials. We will need to continue to build and expand our clinical development and regulatory capabilities, and we may be unable to recruit and train qualified personnel. We also expect to continue to rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval of or commercialize any potential product candidates. Consequently, we may be unable to successfully and

~~efficiently execute and complete necessary clinical trials in a way that leads to an NDA submission and approval of any other product candidates. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approval of any product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing our product candidates.~~ We intend to develop nirogacestat and mirdametinib, and likely other future product candidates, in combination with one or more other approved or unapproved rational therapies to treat cancer or other diseases. For example, we are currently evaluating ~~mirdametinib in combination with lifirafenib, BeiGene Ltd.'s, or BeiGene's, RAF dimer inhibitor, and~~ nirogacestat in combination with several BCMA- directed therapies across modalities through our collaborations with industry leaders developing such therapies. We will not be able to market and sell nirogacestat, mirdametinib or any product candidate we develop in combination with an unapproved rational therapy to treat cancer for a combination indication if that unapproved cancer therapy does not ultimately obtain marketing approval either alone or in combination with our product. In addition, unapproved cancer therapies face the same risks described herein elsewhere with respect to our product candidates currently in development and clinical trials, including the potential for serious adverse effects, delay in the clinical trials and lack of FDA approval. Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA, EMA or comparable foreign regulatory authorities outside of the United States could revoke approval of the therapy used in combination with our product or that safety, efficacy, manufacturing or supply issues could arise with any of those existing therapies. If the therapies we use in combination with our product candidates are replaced as the standard of care for the indications we choose for any of our product candidates, the FDA, EMA or comparable foreign regulatory authorities may require us to conduct additional clinical trials. The occurrence of any of these risks could result in our own products, if approved, being removed from the market or being less successful commercially. If the FDA, EMA or comparable foreign regulatory authorities do not approve these other drugs or revoke their approval of, or if safety, efficacy, quality, manufacturing or supply issues arise with, the drugs we choose to evaluate in combination with our product candidate we develop, we may be unable to obtain approval of or market such combination therapy. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons, including: • the patient eligibility and exclusion criteria defined in the protocol; • the size of the patient population required for analysis of the clinical trial's primary endpoints; • the proximity of patients to clinical trial sites; • the design of the clinical trial; • our ability to recruit clinical trial investigators with the appropriate competencies and experience, and the ability of these investigators to identify and enroll suitable patients; • perception of the safety profile of our product candidates; • our ability to obtain and maintain patient consents; and • the risk that patients enrolled in clinical trials will drop out of the trials before completion. **We** ~~For example, we are developing mirdametinib for the treatment of NF1-PN, which is a rare disease with a small patient population. As a result, although we have completed enrollment in our ReNeu trial, we~~ may encounter difficulties enrolling subjects in our ~~other~~ clinical trials for our product candidates due, in part, to the small size of rare disease patient populations. In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a clinical trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site. In addition, ~~in the case of mirdametinib,~~ we may face difficulty with enrollment due to physician or patient perception of an adverse tolerability profile. Delays in patient enrollment may result in increased costs or may affect the timing or outcome of our clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our product candidates. Our estimates of both the number of patients who have the diseases we are targeting, as well as the subset of patients with these diseases in a position to receive our product candidates, if approved, are based on our beliefs and estimates, and these estimates may prove to be incorrect. These estimates have been derived from a variety of sources, including scientific literature, input from physicians that treat patients with the diseases we are targeting, patient foundations and secondary market research databases. Further, new studies may change the estimated incidence or prevalence of these diseases, and any regulatory approvals that we may receive for a product candidate may include limitations for use or contraindications that decrease the addressable patient population. Accordingly, the target patient populations may turn out to be lower than expected, in which case the potential revenues from sales of our product candidates, if approved, would be lower than expected. Notwithstanding the marketing approval of OGSIVEO, **GOMEKLI**, and any other product candidates, such products may fail to gain sufficient market acceptance by physicians, patients, third-party payers, and others in the medical community. If OGSIVEO, **GOMEKLI**, or our other product candidates do not achieve an adequate level of acceptance, we may not generate adequate product revenue or become profitable. The degree of market acceptance will depend on a number of factors, including but not limited to: • the safety, efficacy, risk- benefit profile, and potential advantages compared to alternative or existing treatments, which physicians may perceive to be adequately effective for some or all patients; • the prevalence and severity of any side effects and the difficulty of, or costs associated with, resolving such side effects; • the content of the approved product label, including any limitations or warnings contained in the labeling approved by FDA or other applicable foreign regulatory authorities; • any restrictions on the use of our products; • the effectiveness of our sales and marketing efforts; • the strength of our marketing and distribution support; • our ability to offer our products for sale at competitive prices; and • the convenience and ease of administration compared to alternative treatments. We cannot assure you that OGSIVEO, **GOMEKLI**, or our current or future product candidates, if approved, will achieve market acceptance among physicians, patients, third- party payers, or others in the medical community necessary for commercial success. Any failure by OGSIVEO, **GOMEKLI**, or such other product candidates that obtain regulatory approval to achieve

market acceptance or commercial success would harm our results of operations. We depend upon third parties to conduct certain aspects of our preclinical studies and depend on third parties, including independent investigators, to conduct our clinical trials under agreements with universities, medical institutions, contract research organizations, or CROs, strategic partners and others. We expect to negotiate budgets and contracts with such third parties, which may result in delays to our development timelines and increased costs. We commenced operations in August 2017, and we continue to build our infrastructure and hire personnel necessary to execute our operational plans. We rely especially heavily on third parties over the course of our clinical trials, and, as a result, may have limited control over the clinical investigators and limited visibility into their day- to- day activities, including with respect to their compliance with the approved clinical protocol. 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 third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with good clinical practice, or GCP, requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of clinical trial sponsors, clinical investigators and clinical trial sites. If we or any of these third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to suspend or terminate these trials or perform additional preclinical studies or clinical trials before approving our marketing applications. We cannot be certain that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with GCP requirements. In addition, our clinical trials must be conducted with product produced under current good manufacturing practice, or cGMP, requirements and may require a large number of patients. Our failure or any failure by these third parties to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be adversely affected if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws. Any third parties conducting aspects of our preclinical studies or our clinical trials will not be our employees and, except for remedies that may be available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our preclinical studies and clinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the preclinical or clinical data they obtain is compromised due to the failure to adhere to our protocols or regulatory requirements or for other reasons, our development timelines, including clinical development timelines, may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed or precluded entirely. If any of our relationships with these third- party contract research organizations, or CROs, or others terminate, we may not be able to enter into arrangements with alternative CROs or other third parties or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management' s time and focus. In addition, there is a natural transition period when a new CRO begins work. As a result, delays may occur, which can materially impact our ability to meet our desired development timelines. Though we carefully manage our relationships with our CROs, investigators and other third parties, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects. We rely on third- party contract manufacturers to manufacture all of our preclinical and clinical trial product supplies. We do not own manufacturing facilities for producing any product supplies. There can be no assurance that our preclinical and clinical development product supplies will not be limited, interrupted, of satisfactory quality or continue to be available at acceptable prices. In particular, any replacement of our manufacturers could require significant effort and expertise because there may be a limited number of qualified replacements. The manufacturing process for a product candidate is subject to FDA, EMA and comparable foreign regulatory authority review. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as cGMPs. In the event that any of our manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In either scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills or technology to another third party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third- party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget. Furthermore, a manufacturer may possess technology related to the manufacture of our product candidate that such manufacturer owns independently. This would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another manufacturer manufacture our product candidates. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies

between our prior clinical supply 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. Our or a third party's failure to execute on our manufacturing requirements and comply with cGMP could adversely affect our business in a number of ways, including: • an inability to initiate or continue clinical trials of product candidates under development; • delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates; • loss of the cooperation of an existing or future collaborator; • subjecting third- party manufacturing facilities to additional inspections by regulatory authorities; • requirements to cease distribution or to recall batches of our product candidates; and • in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products. In addition, we contract with packaging providers with the appropriate expertise, facilities and scale to meet our needs. Failure to maintain cGMP can result in a contractor receiving FDA sanctions, which can impact our ability to operate or lead to delays in clinical development programs. We believe that our current packaging contractors operate in accordance with cGMP, but we can give no assurance that FDA, EMA or comparable foreign regulatory authorities will not conclude that a lack of compliance exists. In addition, any delay in contracting for packaging services, or failure of the contract manufacturer to perform the services as needed, may delay clinical trials, registration and launches, which could negatively affect our business. If our current third- party contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers and we may be unable to replace them on a timely basis or at all. 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. Our product candidates and any drugs that we may develop may compete with other product candidates and drugs for access to manufacturing facilities. There is no assurance we would be able to enter into similar commercial arrangements with other manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. ~~Despite entering into commercial manufacturing and supply agreements related to the supply of nirogacestat's active pharmaceutical ingredient and finished drug product, we have limited experience manufacturing on a commercial scale, and we have not yet entered into commercial supply arrangements with respect to our product candidates, and we rely on third parties to produce and process quantities of our first FDA- approved product, OGSIVEO, and we expect to rely on third parties to produce and process commercial quantities of OGSIVEO and our product candidates, if approved.~~ We expect to continue to rely on third- party manufacturers for our commercial requirements of OGSIVEO and **GOMEKLI, and** if we receive regulatory approval for other product candidates. We have only limited manufacturing and supply agreements in place with respect to our product candidates. Although we have agreements for the commercial supply of ~~nirogacestat's~~ active pharmaceutical ingredient and finished products **for nirogacestat and mirdametinib**, our supply arrangements for our other product candidates are limited to non- commercial, development- stage manufacturing and supply. As a result, we do not yet have long- term supply arrangements with respect to such other product candidates. To the extent that we enter into future manufacturing arrangements with third parties for commercial supply of our product candidates, if approved, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. Any performance failure on the part of our existing or future third- party manufacturers could delay clinical development, marketing approval, or commercial supply, including with respect to nirogacestat. If our current suppliers, or future third- party manufacturers, cannot perform as agreed, or if such contract manufacturers choose to terminate their agreements with us, we will be required to replace such manufacturers. We may incur added costs, delays, and difficulties in identifying and qualifying any such replacement manufacturer or in reaching an agreement with any such alternative manufacturers. We will also need to verify, such as through a manufacturing comparability study, that any new supplier will produce our product candidate or product according to the specifications previously submitted to the FDA, EMA or another comparable regulatory authority. In addition, changes in suppliers 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 supplier. The delays associated with the verification of a new supplier or comparability of new manufacturing processes could negatively affect our ability to develop product candidates or commercialize our product in a timely manner or within budget. The facilities used by our contract manufacturers to manufacture our product candidates must also be approved by the FDA, EMA or comparable foreign regulatory authorities following inspections that will be conducted after we submit an application to the FDA, EMA or comparable foreign regulatory authorities. We do not directly control the manufacturing process of, and will be completely dependent on, our contract manufacturing partners for compliance with cGMP requirements for 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, EMA or comparable foreign regulatory authorities, they will not be able to secure and / or maintain regulatory approval for their manufacturing facilities. In addition, we have no direct control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, EMA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any 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. **We are dependent on a small number of suppliers for some of the materials used to manufacture our product candidates, and on a limited number of qualified active ingredient manufacturers for the commercial supply of OGSIVEO, GOMEKLI and each of our lead product candidates.** We currently depend on a small number of suppliers for some of the materials used in, and processes required to develop, our product candidates. We cannot ensure that these suppliers or service providers will remain in business or have sufficient capacity or supply to meet our needs, or that they will not be purchased by one of our competitors or another company that is not interested in continuing to work with us. Our use of a small number of suppliers exposes us to

several risks, including disruptions in supply, price increases or late deliveries. There are, in general, relatively few alternative sources of supply for substitute materials. Our current vendors may be unable or unwilling to meet our future demands for our clinical trials or commercial sale. Finding suitable replacement suppliers, materials and processes could take a substantial amount of time and it may be difficult to establish replacement suppliers who meet regulatory requirements. Any disruption or delay in supply could compromise our ability to pursue development and eventual commercialization of our product candidates. An important part of our strategy is to evaluate and, as deemed appropriate, extend our current, or enter into additional, partnerships in the future, including potentially with major biopharmaceutical companies. We have limited capabilities for product development and are currently in the process of building our preclinical research and development and commercial capabilities. Accordingly, we have entered into collaborations with other companies to provide us with important technologies in order to more fully develop our product candidates and we may enter into collaborations with other companies to provide us with important technologies or funding for our programs. Any current or future collaborations we may extend or enter into may pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs or license arrangements based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as a strategic transaction that may divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, 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;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products and product candidates if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- for collaborations involving combination therapies that have not yet been tested together, treatment- emergent adverse events may be unforeseen and may negatively impact the monotherapy development of our product candidates;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- collaborators may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;
- collaborators 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 such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might 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;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated by the collaborator, and, if terminated, we could lose license rights to the applicable product candidates or could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Additionally, under our various collaboration agreements with industry leading BCMA- directed therapy developers, the combination of nivolumab and the BCMA- directed therapy of each such developer is being evaluated in relapsed or refractory MM patients. Under these existing collaboration arrangements, upon completion of the relevant clinical trials, we and our collaboration partners will have the opportunity to negotiate in good faith to provide for the expansion of the respective clinical collaboration and the potential establishment of a commercial relationship. However, our partners have no obligation to continue development of the combination products, regardless of the applicable clinical trial results. We also jointly formed MapKure, LLC, or MapKure, with BeiGene for the development of brimrafenib, and although we contribute to clinical development and other operational activities and have representation on MapKure' s board of directors and joint steering committee, we do not control the development process. MapKure may pursue a development plan that differs from our expectations, which may or may not be successful. If our collaborations do not result in the successful discovery, development and commercialization of product candidates, or if one of our collaborators elects not to enter into collaboration agreements to pursue future development, we may not receive any future funding or milestone or royalty payments under such collaborations. Risks relating to product development, regulatory approval and commercialization described in this report may also apply to the activities of our collaborators. Additionally, if one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected. Furthermore, we face significant competition in seeking appropriate partners for our product candidates and the negotiation process is time- consuming and complex. In order for us to successfully partner our product candidates, potential partners must view our product candidates as economically valuable in markets they determine to be attractive in light of the terms that we are seeking and other available products for licensing by other companies. In addition, there have been a significant number of recent business combinations among large biopharmaceutical companies that have resulted in a reduced number of potential future collaborators. Our ability to 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. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay 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 planning, 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 expertise or capital, which may not be available to us on acceptable terms, or at all. If we fail to enter into collaborations or do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates, bring them to market and generate revenue from sales of drugs or continue to develop our technology, and our business may be materially and adversely affected. Even if we are successful in our efforts to establish new strategic partnerships, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such strategic partnerships if, for example, development or approval of a product candidate is delayed or sales of an approved product are disappointing. Any delay in entering into new strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market. We depend on intellectual property licensed from third parties, including from Pfizer for our lead product candidates, and termination of any of these licenses could result in the loss of significant rights, which would harm our business. We are dependent on patents, know-how and proprietary technology, both our own and licensed from others. Any termination of a product license could result in the loss of significant rights and would cause material adverse harm to our ability to commercialize our product candidates. Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including: • the scope of rights granted under the license agreement and other interpretation-related issues; • whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement; • our right to sublicense patent and other rights to third parties under collaborative development relationships; • our diligence obligations with respect to the use of licensed technology in relation to our development and commercialization of our product candidates and what activities satisfy those diligence obligations; and • the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners. If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. We are generally also subject to all of the same risks with respect to protection of intellectual property that we own, as we are for intellectual property that we license, which are described below. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize products could materially suffer. We are a party to license agreements pursuant to which we in-license key patents for our product candidates. At the time we began our operations in August 2017, we entered into four license agreements with Pfizer, three of which remain in effect, including a license agreement for each of our lead product candidates, nirogacestat and mirdametinib, both of which agreements were amended and restated in 2019. In addition, in 2021, we entered into a license for our TEAD inhibitor program with Katholieke Universiteit Leuven and the Flanders Institute for Biotechnology, as well as an in-license licensed for a portfolio of novel epidermal growth factor receptor-small molecule inhibitors/activators of protein phosphatase 2a, or PP2A, complexes with Rappta Therapeutics Oy the Dana-Farber Cancer Institute. Each of our existing licenses imposes various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, our licensors may have the right to terminate the license, in which event we would not be able to develop or market the products covered by such licensed intellectual property. While we assigned the Pfizer license agreement covering our FAAH inhibitor program in connection with the sale of that program to Jazz Pharmaceuticals Ireland Limited, or Jazz, in October 2020, there can be no assurance that Jazz will comply with the terms of such license, which could result in its termination and our inability to recover that asset as a remedy for a potential material breach of Jazz's obligations to us in connection with such sale. We may have limited control over the maintenance and prosecution of these in-licensed rights, activities or any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that such activities by these licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the intellectual property rights or defend certain of the intellectual property that is licensed to us. It is possible that the licensors' infringement proceeding or defense activities may be less vigorous than they would have been had we conducted them ourselves. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs and therapeutic biologics for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug or therapeutic biologic as an orphan drug if it is a drug or therapeutic biologic 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 greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug or therapeutic biologic will be recovered from sales in the United States. In the United States, Orphan Drug Designation designates a party to financial incentives such as opportunities for grant funding toward clinical trial costs, tax advantages and user-fee waivers. Such a designation, however, may be revoked by the FDA in certain circumstances, such as if the agency finds that the applicant's request for designation request omitted material information required under the Orphan Drug Act and its implementing regulations. If a product that has Orphan Drug Designation designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including a full NDA, or Biologics License Application, or BLA, to market the same product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity. In January 2024, the FDA granted Orphan Exclusivity to nirogacestat for the treatment of desmoid tumors and in September 2019, the European Commission, or EC, granted nirogacestat Orphan Drug Designation designation for the treatment of soft tissue sarcoma. In October 2018, the FDA granted Orphan Drug Designation designation to mirdametinib for the treatment of NF1 and in July 2019 the EC European Commission granted mirdametinib

Orphan Drug Designation **designation** for the treatment of NF1. We may seek Orphan Drug Designations **designations** for nirogacestat and mirdametinib for other indications or for our other product candidates. There can be no assurances that we will be able to obtain such designations. Even if we obtain Orphan Drug Designation **designation** for any of our future product candidates in specific indications, we may not be the first to obtain marketing approval of nirogacestat, mirdametinib or any other such product candidates for the orphan- designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan- designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we obtain orphan drug exclusivity in the United States for a product, that exclusivity may not effectively protect the product from competition because different drugs or therapeutic biologics with different active moieties can be approved for the same condition. Even after an orphan product is approved, the FDA can subsequently approve the same drug or therapeutic biologic with the same active moiety for the same condition if the FDA concludes that the later drug or therapeutic biologic is safer, more effective or makes a major contribution to patient care. In ~~Europe~~ **the EU**, we could be prevented from marketing our products if a similar medicinal product is granted Orphan Drug Designation **designation** for the same indications that we are pursuing **and obtains a marketing authorization before us**. Once **an orphan medicinal product is** authorized, with a limited number of exceptions, neither the competent authorities of the EU member states, the EMA or the ~~EC~~ **European Commission** are permitted to accept applications or grant marketing authorization for ~~other~~ similar medicinal products **to such orphan product** with the same therapeutic indication. Marketing authorization could ~~also~~, **however**, be granted to a similar medicinal product with the same orphan indication if the latter product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. ~~⊖~~ **We have exclusive licenses under the Nirogacestat License Agreement to patent rights in the United States and numerous foreign jurisdictions relating to nirogacestat**. ~~S.~~ **In addition, we have developed and exclusively own a portfolio of granted and pending patents covering in the United States and foreign jurisdictions. In the United States, we have numerous issued patents protecting nirogacestat as a composition of matter with the latest expiring in 2043. We have a statutory expiration date** ~~exclusive licenses under the Mirdametinib License Agreement to patent rights~~ **in 2025, U** ~~the United States and numerous foreign jurisdictions relating to mirdametinib~~. ~~S.~~ **In addition, we have developed and exclusively own a portfolio of granted and pending patents that cover the drug substance, including polymorphic forms of nirogacestat** ~~expire in 2039, U~~ **the United States and foreign jurisdictions**. ~~S.~~ **In the United States, we have several issued patents protecting mirdametinib** that cover pharmaceutical compositions ~~expire in 2042, and a U. S. patent that covers methods of treating desmoid tumors expires in 2043, in each case, not including patent term adjustment or any regulatory extensions, with foreign counterparts pending. U. S. patents that cover polymorphic forms of mirdametinib, including the latest expiring form that is currently in clinical development, expire in 2041~~ **2044**, a U. S. patent that covers pharmaceutical compositions ~~expires in 2041, and U. S. patents directed to methods of treatment expire in 2041 and 2043, in each case not including any regulatory extensions, with foreign counterparts pending.~~ Notwithstanding ~~the~~ expected patent life, if orphan drug exclusivity does not protect these products from competition, our business and financial condition could be materially adversely affected. Orphan Drug Designation **designation** neither shortens the development time or regulatory review time of a drug or therapeutic biologic nor gives the drug or therapeutic biologic any advantage in the regulatory review or approval process. In addition, while we may seek Orphan Drug Designation **designation** for our future product candidates, we may never receive such designations. We currently contract manufacturing operations to third parties, and commercial quantities of OGSIVEO **and GOMEKLI** and clinical quantities of our product candidates are manufactured by these third parties outside the United States, including in China, with additional capacity sourced from India. We expect to continue to use such third- party manufacturers for such product candidates. Any disruption in production or inability of our manufacturers in those countries to produce adequate quantities to meet our needs, whether as a result of a natural disaster or other causes, could impair our ability to operate our business on a day- to- day basis and to continue our development of our product candidates. Furthermore, since certain of these manufacturers are located in China, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the policies of the United States or Chinese governments, political unrest or unstable economic conditions in China. For example, a trade war could lead to tariffs on the chemical intermediates we use that are manufactured in China. Any of these matters could materially and adversely affect our business and results of operations. Legislative proposals have been **previously** introduced that, if enacted, would limit government contracting or renewals, loans, or grants with certain biotechnology service providers in China which, if extended more broadly to industry members, could create supply interruptions and require identification of new suppliers. Any recall of the manufacturing lots or similar action regarding our product candidates used in clinical trials could delay the trials or detract from the integrity of the trial data and its potential use in future regulatory filings. In addition, manufacturing interruptions or failure to comply with regulatory requirements by any of these manufacturers could significantly delay clinical development of potential products and reduce third- party or clinical researcher interest and support of proposed trials. These interruptions or failures could also impede commercialization of our product candidates and impair our competitive position. Further, we may be exposed to fluctuations in the value of the local currencies in China and India. Future appreciation of the local currencies could increase our costs. In addition, our labor costs could continue to rise as wage rates increase due to increased demand for skilled laborers and the availability of skilled labor declines in such countries. **In 2017, the U. S. Congress and the Trump administration made substantial changes to U. S. policies, which included comprehensive corporate and individual tax reform. In addition, the Trump administration called for significant changes to U. S. trade, healthcare, immigration and government regulatory policy. With the transition to the Biden administration in early 2021, changes to U. S. policy occurred and since the start of the Trump Administration in 2025, U. S. policy changes have been implemented at a rapid pace and additional changes are likely.**

Changes to U. S. policy implemented by the U. S. Congress, the Trump administration or any new administration have impacted and may in the future impact, among other things, the U. S. and global economy, international trade relations, unemployment, immigration, healthcare, taxation, the U. S. regulatory environment, inflation and other areas. Although we cannot predict the impact, if any, of these changes to our business, they could adversely affect our business. Until we know what policy changes are made, whether those policy changes are challenged and subsequently upheld by the court system and how those changes impact our business and the business of our competitors over the long term, we will not know if, overall, we will benefit from them or be negatively affected by them. As of December 31, 2023-2024, we had 305

368 full-time employees. As our clinical development and commercialization plans and strategies develop, we expect we will need additional managerial, clinical, manufacturing, medical, regulatory, sales, marketing, financial, legal and other personnel. Future growth would impose significant added responsibilities on members of management, including: • recruiting, integrating, retaining and motivating additional employees; • managing our development efforts effectively, including the clinical, manufacturing and quality review process for our product candidates, while complying with our contractual obligations to contractors, collaboration partners and other third parties; and • improving our operational, financial and management controls, reporting systems and procedures. Our future financial performance and our ability to commercialize our product candidates, if approved, will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities. We currently rely, and for the foreseeable future will continue to rely, in substantial part on third parties, including independent organizations, advisors and consultants, to provide certain services to support and perform our operations. There can be no assurance that the services of these third parties will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality, accuracy or quantity of the services provided is compromised for any reason, our clinical trials may be delayed or terminated, and we may not be able to obtain, or may be substantially delayed in obtaining, regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other suitable outside contractors and consultants on economically reasonable terms, or at all. If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully execute the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our development and commercialization goals. While we are currently building out internal discovery and preclinical research and development capabilities, there can be no assurance that we will successfully achieve the capacity to independently discover and initially develop new product candidates. We also plan to source new product candidates, including those that may be complementary to our existing product candidates, by in-licensing or acquiring them from other companies, academic institutions or other asset originators. If we are unable to identify, in-license or acquire and integrate product candidates, our ability to pursue our growth strategy would be limited. Research programs and business development efforts to identify new product candidates require substantial technical, financial and human resources, and we currently have limited internal drug discovery and preclinical research and development capabilities. In-licensing and acquiring product candidates or development programs often requires significant payments and expenses and may consume valuable resources. We will need to devote a substantial amount of time and personnel to develop and commercialize any in-licensed or acquired technology or product candidate, in addition to doing so for our existing product candidates. Our business development efforts or acquisition or licensing attempts may fail to yield additional complementary or successful product candidates for clinical development and commercialization for a number of reasons, including the following: • our identification or business development methodology or search criteria and process may be unsuccessful in identifying potential product candidates with a high probability of success for development progression; • we may not be able or willing to assemble sufficient resources or expertise to identify and in-license or acquire additional product candidates; • for product candidates we seek to in-license or acquire, we may not be able to agree to acceptable terms with the licensor or owner of those product candidates; • any product candidates that we do in-license or acquire may not succeed in preclinical studies or clinical trials; • we may not succeed in formulation or process development of such in-licensed or acquired product candidates; • such in-licensed or acquired product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unlikely to receive regulatory approval or be unmarketable if approved; • competitors may develop alternatives that render such in-licensed product candidates obsolete or less attractive; • in-licensed or acquired product candidates may be covered by third parties' patents or other exclusive rights that we may not be able to access; • in-licensed or acquired product candidates that we develop may not allow us to best make use of our expertise and our development and commercial infrastructure as currently expected; • the market for a product candidate that we in-license or acquire may change during the course of our development of the product candidate so that such product candidate may become unreasonable to continue to develop; • a product candidate that we in-license or acquire may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and • a product candidate that we in-license or acquire may not be accepted as safe and effective by patients, the medical community or third-party payors. If any of these events occur, we may not be successful in executing our growth strategy or our growth strategy may not deliver the anticipated results. Our current headquarters are located in Stamford, Connecticut. Our development operations are currently located at two facilities in Durham and Research Triangle Park, North Carolina. We currently outsource our manufacturing operations to third parties, and clinical and commercial quantities of our approved product products and product candidates are manufactured by these third parties outside the United States, including in Canada, China, France, Germany and India. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, 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 manufacturing facilities of our third-party contract manufacturers, 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. Earthquakes or other natural disasters 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 or our development operations, that damaged critical infrastructure, such as the manufacturing facilities of our third- party contract manufacturers, 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. Disaster recovery and business continuity plans 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 approach, 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 you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities, or the manufacturing facilities of our third- party contract manufacturers, 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. We have incurred significant net losses in each reporting period since our inception. To date, we have financed our operations principally through equity financings. We have derived license and collaboration revenue from the nonrefundable upfront payment we received under the Jazz asset purchase and license agreement and limited deferred revenue from the non- exclusive license and collaboration agreement with GlaxoSmithKline. In November 2023, the FDA approved OGSIVEO (nirogacestat) for the treatment of adult patients with desmoid tumors **and in February 2025, the FDA approved GOMEKLI (mirdametinib) for the treatment of adult and pediatric patients two years of age and older with NF1 who have symptomatic PN not amenable to complete resection**. In December 2023, we began to generate revenue from sales of OGSIVEO in the United States **and in February 2025, we began to generate revenue from sales of GOMEKLI in the United States**. We continue to incur significant research and development and selling, general and administrative expenses related to our ongoing operations, including expenses incurred in connection with the commercialization of OGSIVEO **and the launch and commercialization of GOMEKLI**. As a result, we are not profitable and have incurred losses in each annual period since our inception. Our net losses were \$ ~~325-258~~ .1 million, \$ **325.1 million and \$ 277.4 million and \$ 173.9 million** for the fiscal years ended December 31, ~~2023-2024~~, December 31, ~~2022-2023~~ and December 31, ~~2021-2022~~, respectively. As of December 31, ~~2023-2024~~ and December 31, ~~2022-2023~~, we had an accumulated deficit of \$ **1.2 billion and \$ 895.0 million and \$ 569.9 million**, respectively. We expect to continue to incur **net losses in the near future, and we expect to continue to incur** significant ~~losses expenses~~ for the foreseeable future ~~, and we expect these losses to increase~~ as we continue our research and development of, seek regulatory approvals for, and prepare for commercialization of, our product candidates, including our lead product candidates, nirogacestat and mirdametinib, and any future product candidates. We anticipate that our expenses will increase substantially if, and as, we: • launch, promote and support commercialization of OGSIVEO **and GOMEKLI**; • advance the development of our other product candidates, including nirogacestat and mirdametinib, through late- stage clinical trials, including registrational clinical trials and potentially for other indications; • advance our development programs for our other product candidates through clinical development and into later- stage clinical development; • seek marketing approvals for any product candidates that successfully complete clinical trials; • invest in or in- license other technologies or product candidates for further preclinical and clinical development; • hire additional personnel, including clinical, quality control, scientific, medical, business development and finance personnel, and continue to build our infrastructure; • expand our operational, financial and management systems and increase personnel, including personnel to support our clinical development, manufacturing and commercialization efforts and our operations as a public company; • maintain, expand and protect our intellectual property portfolio; and • establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval and intend to commercialize on our own or jointly with third parties. To become and remain profitable, we or any potential future collaborators must develop and eventually commercialize products with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials, obtaining marketing approval for product candidates, manufacturing, obtaining reimbursement approval, marketing and selling products for which we may obtain marketing approval and satisfying any post-marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate revenue that is significant or large enough to achieve profitability. If we do **not continue to effectively commercialize OGSIVEO or effectively commercialize GOMEKLI, we will not be able to execute our business plan and may not be able to achieve profitability**. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations **. Additionally, our revenues, market share and / or other indicators of market acceptance of OGSIVEO or GOMEKLI do not meet the expectations of investors or public market analysts, the market price of our common stock would likely decline**. A decline in the value of our company also could cause stockholders to lose all or part of their investment. Even if we succeed in commercializing our product candidates, we will continue to incur substantial research and development and other expenditures to develop, register and market additional product candidates. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. We are a commercial- stage biopharmaceutical company with a limited operating history. We were formed in August 2017 and our

operations to date have been focused on preparing and executing our clinical trials for our product candidates, building our infrastructure, raising capital and executing partnerships. Consequently, we have limited operations upon which to evaluate our business, and predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing drug products. Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate activity or an acceptable safety profile, gain regulatory approval, secure market access and reimbursement and become commercially viable. Although we received FDA approval for OGSIVEO for the treatment of adult patients with progressing desmoid tumors who require systemic treatment **in November 2023, this is our first** and **recently received FDA approval of GOMEKLI for the treatment of adult and pediatric patients two years of age and older with NF1 who have symptomatic PN not amenable to complete resection, these are our only product products** approved for commercial sale, and we have not yet generated significant revenue from product sales to date. In addition, as a business with a limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors and risks frequently experienced by early-stage biopharmaceutical companies in rapidly evolving fields, or other known or unknown factors and risks that may be infrequent or unique. In addition, we are transitioning from a company with a development focus to a company supporting commercial activities and may not be successful in such a transition. Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts of cash to launch, promote and support commercialization of OGSIVEO, **support the launch and commercialization of GOMEKLI,** to conduct further research and development and clinical trials of our product candidates, to seek regulatory approvals for our product candidates and to launch and commercialize any additional products for which we receive regulatory approval. As of December 31, ~~2023~~ **2024**, we had \$ ~~662-461~~ **6-9** million in cash, cash equivalents and marketable securities. Based on our current operating plan, we believe that our cash, cash equivalents and marketable securities will be sufficient to fund our operating expenses and capital expenditure requirements for at least the next 12 months from the date of issuance of this Annual Report. However, our future capital requirements and the period for which our existing resources will support our operations may vary significantly from what we expect, and we will in any event require additional capital in order to complete clinical development and obtain regulatory approval of our product candidates, **particularly if our expectation to achieve profitability in the first half of 2026 is incorrect**. Our monthly spending levels will vary based on new and ongoing development and corporate activities. Because the length of time and activities associated with development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. Our future funding requirements will depend on many factors, including, but not limited to: • costs to launch, promote and support commercialization of OGSIVEO **and GOMEKLI**; • the initiation, progress, timing, costs and results of clinical trials for our product candidates; including any unforeseen costs we may incur as a result of clinical trial delays due to ongoing global and regional conflicts, or other causes; • the clinical and preclinical development and manufacturing plans we establish for these product candidates; • the number and characteristics of product candidates that we develop or in-license; • the cost of identifying and evaluating potential product candidates for acquisition or license, including the cost of preclinical activities or clinical activities; • the terms of any collaboration or licensing agreements we may choose to enter into; • the outcome, timing and cost of meeting regulatory requirements established by the FDA, the EMA, and other comparable foreign regulatory authorities; • the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights; • the cost of defending intellectual property disputes, including patent infringement actions brought by third parties against us or our product candidates; • the effect of competing technological and market developments; • the cost and timing of completion of commercial-scale outsourced manufacturing activities; • the establishment of sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval in regions where we choose to commercialize our products on our own or jointly with third parties; and • the degree of commercial success achieved following the successful completion of development and regulatory approval activities for a product candidate. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates or one or more of our other research and development initiatives. Any of the foregoing events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline. We do not have any committed external source of funds or other support for our development efforts, and we cannot be certain that additional funding will be available on acceptable terms, or at all. Until we can generate sufficient product or royalty revenue to finance our cash requirements, which we may never do, we expect to finance our future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing or distribution arrangements. If we raise additional funds through public or private equity offerings, the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. Further, to the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, existing stockholder ownership interest may be diluted. In addition, any debt financing may subject us to fixed payment obligations and covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish certain valuable rights to our product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us. We also could be required to seek commercial or development partners for our lead products or any future product candidate at an earlier stage than otherwise would be desirable or relinquish our rights to product candidates or technologies that we otherwise would seek to develop or commercialize ourselves. We currently anticipate that we will retain future earnings for the development, operation and

expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Furthermore, future debt or other financing arrangements may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited to the appreciation of their stock. Our executive officers, directors and their affiliates and holders of more than 5 % of our common stock beneficially hold, in the aggregate, as of December 31, ~~2023~~ **2024**, approximately ~~36-38~~ **8-0** % of our outstanding voting stock. Therefore, these stockholders will have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that stockholders may feel are in their best interest as one of our stockholders. Our amended and restated certificate of incorporation, or the certificate of incorporation, and amended and restated bylaws, as further amended, or 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 stockholders be called only by the chairman of the board of directors, the chief executive officer or by a majority of the total number of authorized directors; • advance notice requirements for stockholder proposals and nominations for election to our board of directors; • a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two- thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors; and • a requirement of approval of not less than two- thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and the authority of the board of directors to issue convertible preferred stock on terms determined by the board of directors without stockholder approval and which convertible 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 Corporation 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 stockholders to elect directors of their choosing or cause us to take other corporate actions they 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 provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware, or the Chancery Court, will be the sole and exclusive forum for state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim pursuant to any provision of the General Corporation Law of the State of Delaware, our certificate of incorporation or our bylaws, (iv) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws, or (v) any action asserting a claim governed by the internal affairs doctrine, or the Delaware Forum Provision. The Delaware Forum Provision does not apply to any causes of action arising under the Securities Act of 1933, as amended, or the Securities Act, or the Securities Exchange Act of 1934, as amended, or the Exchange Act. Our bylaws further provide that, unless we consent in writing to the selection of an alternative forum, the U. S. District Court for the District of Connecticut will be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act or the Federal Forum Provision. 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 foregoing 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. The Delaware Forum Provision and the Federal Forum Provision may impose additional litigation costs on stockholders in pursuing the claims identified above, particularly if the stockholders do not reside in or near the State of Delaware or the State of Connecticut. Additionally, the Delaware Forum Provision and the Federal Forum Provision may limit a stockholder’ s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits. 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 in an action, we may incur additional costs associated with resolving such an action. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Chancery Court or the U. S. District Court for the District of Connecticut 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. General risk factors Risks related to research and development and the biopharmaceutical industry Clinical development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates. To obtain the requisite regulatory approvals to commercialize any product candidate, we must demonstrate through extensive preclinical studies and clinical trials that such product candidate is safe and effective in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain.

We may be unable to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful, and a clinical trial can fail at any stage of testing. Differences in trial design between early- stage clinical trials and later- stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their products. Additionally, we are conducting and plan to conduct some open- label trials, where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open- label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open- label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in those trials are aware when they are receiving treatment. Open- label clinical trials may be subject to a “ patient bias ” where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open- label clinical trials may be subject to an “ investigator bias ” where those assessing and reviewing the outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. Where a randomized, placebo- controlled clinical trial is designed to allow enrolled subjects to cross- over to the treatment arm, there may be a risk of inadvertent unblinding of subjects prior to cross- over, which may limit the clinical meaningfulness of those data and may require the conduct of additional clinical trials. As such, the results from an open- label trial may not be predictive of future clinical trial results with any of our product candidates for which we include an open- label clinical trial when studied in a controlled environment with a placebo or active control. Successful completion of clinical trials is a prerequisite to submitting an NDA to the FDA, a Marketing Authorisation ~~Authorisation~~ **Authorization** Application, or MAA, to the EMA and similar marketing applications to comparable foreign regulatory authorities for each product candidate and, consequently, the ultimate approval and commercial marketing of any product candidates. We do not know whether any of our ongoing or planned clinical trials, including trials for our combination therapies using nirogacestat ~~and mirdametinib~~, will be completed on schedule, if at all, or, in some cases, whether such clinical trials will begin. We may experience delays in initiating or completing clinical trials and preparing for regulatory submissions. We also 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 current product candidates or any future product candidates, including: • the potential impact that sanctions and other measures being imposed in response to the Russia- Ukraine conflict, or the global business disruption caused by the conflict, may have on revenue and supply chain; • regulators, 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 clinical trial sites and prospective CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites; • clinical trials of any product candidates may fail to show acceptable safety or efficacy, or produce negative or inconclusive results and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or we may decide to abandon product development programs; • the number of subjects required for clinical trials of any product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or subjects 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 or drop out of the trial, which may require that we add new clinical trial sites or investigators; • we may elect to, or regulators, IRBs or ethics committees may require, that we or our investigators suspend or terminate clinical research or trials for various reasons, including ~~non- noncompliance~~ **compliance** with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks; • the cost of clinical trials of any product candidates may be greater than we anticipate; • the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be inadequate to initiate or complete a given clinical trial; • our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators, IRBs or ethics committees to suspend or terminate the clinical trials; • reports from clinical testing of other therapies may raise safety or efficacy concerns about our product candidates; and • the FDA, EMA or comparable regulatory authorities may require us to submit additional data, such as long- term toxicology studies, or impose other requirements before permitting us to initiate a clinical trial. We could also encounter delays if a clinical trial is suspended or terminated by us, the IRBs of the institutions in which such clinical trials are being conducted, or the FDA, EMA or comparable regulatory authorities, or recommended for suspension or termination by the Data Safety Monitoring Board, or the DSMB, for such clinical trial. A suspension or termination may be imposed 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, EMA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product or treatment, failure to establish or achieve clinically meaningful trial endpoints, 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, EMA or comparable foreign regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials or may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials. Our costs will increase if we experience delays in clinical testing or marketing approvals. We do not know whether any of our clinical trials will begin as planned, will need to be reassigned or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates and may allow our competitors to bring

products to market before we do, potentially impairing our ability to successfully commercialize our product candidates and harming our business and results of operations. Any delays in our clinical development programs may harm our business, financial condition and results of operations significantly. The clinical trials sponsored by our partners with our product candidates in combination with our partners' therapies pose the same development risks. The successful development of biopharmaceuticals is highly uncertain. Successful development of biopharmaceuticals is highly uncertain and is dependent on numerous factors, many of which are beyond our control. Product candidates that appear promising in the early phases of development may fail to reach the market for several reasons including: • clinical trial results may show the product candidates to be less effective than expected (for example, a clinical trial could fail to meet its primary or key secondary endpoint (s)) or to have unacceptable side effects or toxicities; • failure to receive the necessary regulatory approvals or a delay in receiving such approvals. Among other things, such delays may be caused by patients who fail the trial screening process, slow enrollment in clinical trials, patients dropping out of trials, patients lost to follow-up; • length of time to achieve trial endpoints, additional time requirements for data analysis or NDA preparation, discussions with the FDA, an FDA request for additional preclinical or clinical data (such as long-term toxicology studies) or unexpected safety or manufacturing issues; • preclinical study results may show the product candidate to be less effective than desired or to have harmful side effects; • supply issues, manufacturing costs and formulation issues, including our inability to successfully combine our product candidates with other therapies; • post-marketing approval requirements; and • the proprietary rights of others and their competing products and technologies that may prevent our product candidates from being commercialized. The length of time necessary to complete clinical trials and to submit an application for marketing approval for a final decision by a regulatory authority varies significantly from one product candidate to the next and from one country to the next and may be difficult to predict. Even if we are successful in obtaining marketing approval, commercial success of any approved products will also depend in large part on the availability of coverage and adequate reimbursement from third-party payors, including government payors such as the Medicare and Medicaid programs, and managed care organizations in the United States or country specific governmental organizations in foreign countries, which may be affected by existing and future healthcare reform measures designed to reduce the cost of healthcare. Third-party payors could require us to conduct additional studies, including post-marketing studies related to the cost effectiveness of a product, to qualify for reimbursement, which could be costly and divert our resources. If government and other healthcare payors were not to provide coverage and adequate reimbursement for our products once approved, market acceptance and commercial success would be reduced. In addition, if any of our product candidates receive marketing approval, we will be subject to significant regulatory obligations regarding the submission of safety and other post-marketing information and reports and registration and will need to continue to comply (or ensure that our third-party providers comply) with cGMPs and GCPs for any clinical trials that we conduct post-approval. In addition, there is always the risk that we, a regulatory authority or a third party might identify previously unknown problems with a product post-approval, such as adverse events of unanticipated severity or frequency. Compliance with these requirements is costly, and any failure to comply or other issues with our product candidates post-approval could adversely affect our business, financial condition and results of operations. Due to our limited resources and access to additional capital, we must prioritize development of certain programs and product candidates; these decisions may prove to be wrong and may adversely affect our business. We may fail to identify and acquire, through purchase or license, viable new product candidates for clinical development for a number of reasons. If we fail to identify and acquire additional product candidates, our business could be materially harmed. Efforts to identify and pursue new product candidates and disease targets require substantial technical, financial and human resources, regardless of whether they are ultimately successful. We currently rely on third parties, including current and future collaborators, to perform all of our research and preclinical activities. Programs may initially show promise in preclinical studies, yet fail to yield positive results during clinical development for a number of reasons, including: • the methodology used may not be successful in identifying potential indications and / or product candidates; or • 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. Because we have limited financial and human resources, we intend to initially focus on programs and product candidates for a limited set of indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications with our existing product candidates that may later prove to have greater commercial potential or a greater likelihood of success. We may focus our efforts and resources on potential product candidates or other potential programs that ultimately prove to be unsuccessful. Our future clinical trials or those of our future collaborators may reveal significant adverse events not seen in prior preclinical studies or clinical trials and may result in a safety profile that could inhibit regulatory approval or market acceptance of any of our product candidates. If significant adverse events or other side effects are observed in any of our clinical trials, we may have difficulty recruiting patients to our clinical trials, patients may drop out of our trials or we may be required to abandon the trials or our development efforts of one or more product candidates altogether. ~~For example, a prior Phase 2 clinical trial of mirdametinib was terminated and enrollment in the Phase 2 portion of a Phase 1 / 2 clinical trial was halted as a result of adverse events observed at doses of mirdametinib of 15 mg twice daily, or BID, or above using both intermittent and continuous dosing schedules. These adverse events included ocular disorders (visual disturbances, blurred vision and retinal vein occlusion), nervous system disorders (confusion, slowed ideation, slurred speech and hallucinations), musculoskeletal and connective tissue disorders (general weakness and neck muscle weakness associated with mild and moderate elevations in creatine phosphokinase) and cardiac disorders (decreased left ventricular ejection fraction and congestive heart failure). Although these doses were significantly higher than the maximum allowable dose of 4 mg BID in our ongoing Phase 2b clinical trial of mirdametinib in NF1-PN, we plan to treat patients in this trial for a period of up to 24 months, which would be longer than any subjects have been treated with mirdametinib in prior trials. In our ongoing Phase 2b clinical trial, we may observe adverse events similar to those that were seen at higher doses of mirdametinib in prior clinical trials owing to the potentially increased duration of treatment, or other factors. In addition, this trial's enrollment includes pediatric NF1-PN patients. There is limited safety data of~~

~~mirdametinib in children under the age of 16 and it is possible that there may be unanticipated adverse events observed in this patient population.~~ If we elect or are required to delay, suspend or terminate any clinical trial of any product candidates that we develop, the commercial prospects of such product candidates will be harmed and our ability to generate product revenues from any of these product candidates will be delayed or eliminated. Serious adverse events or other adverse events, as well as tolerability issues, observed in clinical trials could hinder or prevent market acceptance of the product candidate at issue. We, the FDA, EMA or comparable foreign regulatory authorities or an IRB may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early- stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the product candidate from obtaining or maintaining marketing approval, restrictions could be imposed on the approval or an approved product could be subject to a boxed warning, which is the FDA's most prominent warning regarding safety concerns, and undesirable side effects may inhibit market acceptance of the approved product due to its tolerability versus other therapies. Increasing demand for compassionate use of our product candidates could negatively affect our reputation and harm our business. We are developing product candidates for the treatment of indications for which there are currently limited or no available therapeutic options. It is possible for individuals or groups to target companies with disruptive social media campaigns related to a request for access to unapproved drugs for patients with significant unmet medical need. If we experience a similar social media campaign regarding our decision to provide or not provide access to any of our current or future product candidates under an expanded access policy, our reputation may be negatively affected and our business may be harmed. Recent media attention to individual patients' expanded access requests has resulted in the introduction and enactment of legislation at the local and national level referred to as "Right to Try" laws, such as the federal Right to Try Act of 2017 signed into law on May 30, 2018, which are intended to allow patients access to unapproved therapies earlier than traditional expanded access programs. A possible consequence of both activism and legislation in this area may be the need for us to initiate an unanticipated expanded access program or to make our product candidates more widely available sooner than anticipated. In addition, some patients who receive access to drugs prior to their commercial approval through compassionate use, expanded access programs or right to try access have life- threatening illnesses and have exhausted all other available therapies. The risk for serious adverse events in this patient population is high, which could have a negative impact on the safety profile of our product candidates if we were to provide them to these patients, which could cause significant delays or an inability to successfully commercialize our product candidates, which could materially harm our business. If we were to provide patients with any of our product candidates under an expanded access program, we may in the future need to restructure or pause any compassionate use and / or expanded access programs for a variety of reasons, which could prompt adverse publicity or other disruptions related to current or potential participants in such programs. We face significant competition from other biopharmaceutical companies, and our operating results will suffer if we fail to compete effectively. The biopharmaceutical industry is characterized by intense competition and rapid innovation. Our competitors may be able to develop other compounds or drugs that are able to achieve similar or better results. Our potential competitors include major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies and universities and other research institutions. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations and well- established sales forces. Smaller or early- stage companies may also prove to be significant competitors, particularly as they develop novel approaches to treating disease indications that our product candidates are also focused on treating. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel therapeutics or to in- license novel therapeutics that could make the product candidates that we develop obsolete. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors, either alone or with collaboration partners, may succeed in developing, acquiring or licensing on an exclusive basis drug or biologic products that are more effective, safer, more easily commercialized or less costly than our product candidates or may develop proprietary technologies or secure patent protection that we may need for the development of our technologies and products. We believe the key competitive factors that will affect the development and commercial success of our product candidates are efficacy, safety, tolerability, reliability, convenience of use, price and reimbursement. Even if we obtain regulatory approval of our product candidates, the availability and price of our competitors' products could limit the demand and the price we are able to charge for our product candidates. We may not be able to implement our business plan if the acceptance of our product candidates is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to our product candidates, or if physicians switch to other new drug or biologic products or choose to reserve our product candidates for use in limited circumstances. Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay. As product candidates proceed through preclinical studies to late- stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing, including bridging or comparability testing to demonstrate the validity of clinical data obtained in clinical trials following manufacturing changes, FDA notification or FDA approval. ~~Because all prior~~ **For any product candidates we develop where earlier** clinical trials ~~of nirogacestat and mirdametinib~~ were conducted by third parties, we will need to perform analytical and other tests to demonstrate that any new drug product material is comparable in all respects, including potency, to the product used in such earlier clinical trials. There is no assurance that any

such product will pass the required comparability testing, that any other future third- party manufacturer that we engage will be successful in producing our product candidates or that any materials produced by any third- party manufacturer that we engage will have the same effect in patients that we have observed to date with respect to materials used in prior clinical trials. All of the above could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commence sales and generate revenue. **Although Moreover, we have limited experience manufacturing were successfully able to launch or our processing on a commercial scale first product, there is no guarantee and an attempt to launch a second product will be as successful and we** may not be able to **do so successfully launch GOMEKLI, for or** any of our product candidates if approved. We may make changes as we work to optimize our manufacturing processes, but we cannot be sure that even minor changes in our processes will result in therapies that are safe, effective and approved for commercial sale. If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates. We face an inherent risk of product liability as a result of testing our product candidates in clinical trials and face an even greater risk of product liability with the launch of our first approved **product products, OGSIVEO and GOMEKLI**. For example, we may be sued if OGSIVEO, **GOMEKLI** or any of our products or product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical trials, manufacturing, marketing or sale. Any such product liability claim may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of OGSIVEO, **GOMEKLI** or our product candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in: • inability to bring a product candidate to the market; • decreased demand for our products; • harm to our reputation; • withdrawal of clinical trial participants and inability to continue clinical trials; • initiation of investigations by regulators; • costs to defend the related litigation; • diversion of management' s time and our resources; • substantial monetary awards to clinical trial participants or patients who receive an approved product; • product recalls, withdrawals or labeling, marketing or promotional restrictions; • loss of revenue; • exhaustion of any available insurance and of our capital resources; • inability to commercialize any product candidate, if approved; and • a decline in our stock price. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with collaborators. Even if our agreements with any current or future corporate collaborators entitle us to indemnification against losses, that indemnification may not be available or adequate should any claim arise. Although we currently carry commercial product liability and clinical trial insurance, the amount of insurance coverage we carry may not be adequate, and, in the future, we may be unable to maintain this insurance coverage, or we may not be able to obtain additional or replacement insurance at a reasonable cost, if at all. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay those amounts. Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, defaults, or non- performance by financial institutions or transactional counterparties, could adversely affect the Company' s current and projected business operations and its financial condition and results of operations. Actual events involving limited liquidity, defaults, non- performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market- wide liquidity problems. For example, in 2023, the closures of Silicon Valley Bank, or SVB, and Signature Bank were placed into receivership with the Federal Deposit Insurance Corporation, or FDIC. Although a statement by the Department of the Treasury, the Federal Reserve, and the FDIC indicated that all depositors at Silicon Valley Bank and Signature Bank would have access to their funds, borrowers under credit agreements, letters of credit and certain other financial instruments with SVB, Signature Bank or any other financial institution that is placed into receivership by the FDIC may be unable to access undrawn amounts thereunder or obtain such access in a timely manner. If any of our counterparties to any such instruments were to be placed into receivership, we may be unable to access such funds. In addition, if any of our customers, suppliers or other parties with whom we conduct business are unable to access funds pursuant to such instruments or lending arrangements with such a financial institution, such parties' ability to pay their obligations to us or to enter into new commercial arrangements requiring additional payments to us could be adversely affected. Inflation and rapid increases in interest rates have led to a decline in the trading value of previously issued government securities with interest rates below current market interest rates. Although the U. S. Department of Treasury, FDIC and Federal Reserve Board have announced a program to provide up to \$ 25 billion of loans to financial institutions secured by certain of such government securities held by financial institutions to mitigate the risk of potential losses on the sale of such instruments, widespread demands for customer withdrawals or other liquidity needs of financial institutions for immediately liquidity may exceed the capacity of such program. Additionally, there is no guarantee that the U. S. Department of Treasury, FDIC and Federal Reserve Board will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions, or that they would do so in a timely fashion. Although we assess our banking and customer relationships as we believe necessary or appropriate, our access to funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect the Company, the financial institutions with which the Company may have credit agreements or arrangements directly, or the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in

the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. These factors could involve financial institutions or financial services industry companies with which the Company has financial or business relationships, but could also include factors involving financial markets or the financial services industry generally. The results of events or concerns that involve one or more of these factors could include a variety of material and adverse impacts on our current and projected business operations and our financial condition and results of operations. These could include, but may not be limited to, the following: • Delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets; or • Termination of cash management arrangements and / or delays in accessing or actual loss of funds subject to cash management arrangements. In addition, investor concerns regarding the U. S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our financial and / or contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity and our current and / or projected business operations and financial condition and results of operations. In addition, any further deterioration in the macroeconomic economy or financial services industry could lead to losses or defaults by our customers or suppliers, which in turn, could have a material adverse effect on our current and / or projected business operations and results of operations and financial condition. For example, a customer may fail to make payments when due, default under their agreements with us, become insolvent or declare bankruptcy, or a supplier may determine that it will no longer deal with us as a customer. In addition, a customer or supplier could be adversely affected by any of the liquidity or other risks that are described above as factors that could result in material adverse impacts on the Company, including but not limited to delayed access or loss of access to uninsured deposits or loss of the ability to draw on existing credit facilities involving a troubled or failed financial institution. Any customer or supplier bankruptcy or insolvency, or the failure of any customer to make payments when due, or any breach or default by a customer or supplier, or the loss of any significant supplier relationships, could result in material losses to the Company and may have a material adverse impact on our business. Risks related to intellectual property Our success depends in part on our ability to protect our intellectual property, and patent terms may be inadequate to protect our competitive position. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection. Our commercial success will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our proprietary technologies and our product candidates, their respective components, formulations, combination therapies, methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third- party challenges. Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing our product candidates is affected by the extent to which we have rights under valid and enforceable patents that cover these activities. If our patents expire, or we are unable to secure and maintain patent protection for any product or technology we develop, or if the scope of the patent protection secured is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to commercialize any product candidates we may develop may be adversely affected. Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U. S. non- provisional filing date. Various extensions such as patent term adjustments and / or extensions, may be available, but the life of a patent, and the protection it affords, is limited. **Our current composition We have exclusive licenses under the Nirogacestat License Agreement to patent rights in the United States and numerous foreign jurisdictions relating to nirogacestat. In addition, we have developed and exclusively own a portfolio of matter granted and pending patents covering in the United States and foreign jurisdictions. In the United States, we have numerous issued patents protecting nirogacestat with the latest expiring in 2043. We have exclusive licenses under the Mirdametinib License Agreement to patent rights in the United States and numerous foreign jurisdictions relating to mirdametinib . In addition, we were licensed from Pfizer we have developed and exclusively own a portfolio of granted and pending patents in connection the United States and foreign jurisdictions. In the United States, we have several issued patents protecting mirdametinib with the latest formation of our company. U. S. patents covering nirogacestat as a composition of matter have a statutory expiration --- expiring date in 2025, U. S. patents that cover the drug substance, including polymorphic forms of nirogacestat expire in 2039, U. S. patents that cover pharmaceutical compositions expire in 2042-2044 , and a U. S. patent that covers methods of treating desmoid tumors expires in 2043, in each case, not including patent term adjustment or any regulatory extensions, with foreign counterparts pending. U. S. patents that cover polymorphic forms of mirdametinib, including the form that is currently in clinical development expire in 2041, a U. S. patent that covers pharmaceutical compositions expires in 2041, and U. S. patents directed to methods of treatment expire in 2041 and 2043, in each case not including any regulatory extensions, with foreign counterparts pending.** Our earliest patents may expire before, or soon after, either product candidate achieves marketing approval in the United States or foreign jurisdictions. We also intend to rely on orphan drug exclusivity to market our lead products. Once the patent life has expired, we may be open to competition from competitive products, including generics. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. The expiration of the patents covering our lead product candidates, and our inability to secure additional patent protection, could also have a material adverse effect on our business, results of operations, financial condition and prospects. The patenting 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. In addition, we may not pursue or obtain patent protection in all relevant markets. 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 may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third parties and are reliant on our licensors or licensees. The strength of patents in the biopharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license now or in the future may fail to result in issued patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries. Even if the patents do successfully issue, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, the patents and patent applications covering our product candidates may not adequately protect our intellectual property or prevent others from designing around our claims. If the breadth or strength of protection provided by the patents we hold with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, there is no certainty that any patent application related to a product candidate was the first to be filed. Furthermore, for U. S. applications in which at least one claim is entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party or instituted by the U. S. Patent and Trademark Office, or USPTO, to determine who was the first to invent any of the subject matter covered by the patent claims of an application. We cannot be certain that we are the first to invent any inventions covered by a pending patent application and, if we are not, we could be subject to priority disputes. We may be required to disclaim part or all of the term of certain patents or all of the term of certain patent applications. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that if challenged, our patents would be declared by a court to be valid or enforceable or that even if found valid and enforceable, a competitor's technology or product would be found by a court to infringe our patents. We may analyze patents or patent applications of our competitors that we believe are relevant to our activities and consider that we are free to operate in relation to our product candidates, but our competitors may achieve issued claims, including in patents we consider to be unrelated, which block our efforts or may potentially result in our product candidates or our activities infringing such claims. The possibility exists that others will develop products which have the same effect as our products on an independent basis which do not infringe our patents or other intellectual property rights or will design around the claims of patents that we have had issued that cover our products. In addition, some of our patent applications and patents may cover inventions owned jointly by us and our collaborators. There can be no assurance that we and our collaborators will agree upon matters related to patent filing and prosecution strategy required to execute an effective patent strategy or that decisions made by our collaborators will be consistent with our goals for protecting our solely owned intellectual property. Recent or future patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. Under the enacted Leahy-Smith America Invents Act, or America Invents Act, enacted in 2013, the United States moved from a "first-to-invent" to a "first-to-file" system. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. The America Invents Act includes a number of other significant changes to U. S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a new post-grant review system. The effects of these changes are currently unclear as the USPTO only recently developed new regulations and procedures in connection with the America Invents Act and many of the substantive changes to patent law, including the "first-to-file" provisions, only became effective in March 2013. In addition, the courts have yet to address many of these provisions and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of any patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition. The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make or use compounds that are similar to the compositions of our product candidates but that are not covered by the claims of our patents;
- the active ingredients in our current product candidates will eventually become commercially available in generic drug products, and no patent protection may be available with regard to formulation or method of use;
- a company or its licensor, as the case may be, may fail to meet its obligations to the U. S. government in regard to any in-licensed patents and patent applications funded by U. S. government grants, leading to the loss of patent rights;
- such company or its licensors, as the case may be, might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- it is possible that a pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents, as the case may be, or parts of our or their patents;
- it is possible that others may circumvent our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;
- the laws of foreign countries may not protect our or our licensors', as the case may be, proprietary rights to the same extent as the laws of the United States;
- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our product candidates;
- our owned or in-licensed issued patents may not provide us with any competitive advantages, may be narrowed in scope, or be held invalid or unenforceable as a result of legal challenges by third parties;
- the inventors of owned or in-licensed patents or patent applications may become involved with competitors, develop products or processes which design

around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors; • it is possible that owned or in- licensed patents or patent applications omit individual (s) that should be listed as inventor (s) or include individual (s) that should not be listed as inventor (s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable; • we have engaged in scientific collaborations in the past, and will continue to do so in the future. Such collaborators may develop adjacent or competing products to ours that are outside the scope of our patents; • we may not develop additional proprietary technologies for which we can obtain patent protection; • it is possible that product candidates we develop may be covered by third parties' patents or other exclusive rights; or • the patents of others may have an adverse effect on our business. If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. In addition to patent protection, we rely heavily upon know- how and trade secret protection, as well as non- disclosure agreements and invention assignment agreements with our employees, consultants and third parties, to protect our confidential and proprietary information, especially where we do not believe patent protection is appropriate or obtainable. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using physical and technological security measures. Such measures may not, for example, in the case of misappropriation of a trade secret by an employee or third party with authorized access, provide adequate protection for our proprietary information. Our security measures may not prevent an employee or consultant from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time- consuming, and the outcome is unpredictable. In addition, trade secrets may be independently developed by others in a manner that could prevent legal recourse by us. If any of our confidential or proprietary information, such as our trade secrets, were to be disclosed or misappropriated, or if any such information was independently developed by a competitor, our competitive position could be harmed. In addition, courts outside the United States are sometimes less willing to protect trade secrets. If we choose to go to court to stop a third party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party' s relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary technology by third parties. Third- party claims of intellectual property infringement may prevent or delay our product discovery and development efforts. Our commercial success depends in part on our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation, inter partes review, post grant review, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our product candidates and / or proprietary technologies infringe their intellectual property rights. Numerous U. S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product candidates, technologies or methods. If a third party claims that we infringe its intellectual property rights, we may face a number of issues, including, but not limited to: • infringement and other intellectual property claims which, regardless of merit, may be expensive and time- consuming to litigate and may divert our management' s attention from our core business; • substantial damages for infringement, which we may have to pay if a court decides that the product candidate or technology at issue infringes on or violates the third party' s rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner' s attorneys' fees; • a court prohibiting us from developing, manufacturing, marketing or selling our product candidates, or from using our proprietary technologies, unless the third party licenses its product rights to us, which it is not required to do; • if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and / or grant cross- licenses to intellectual property rights for our products; and • redesigning our product candidates or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. Third parties may assert that we are employing their proprietary technology without authorization.

Generally, conducting clinical trials and other development activities in the United States is protected under the Safe Harbor exemption as set forth in 35 U. S. C. § 271. If any of our product candidates are approved by the FDA, third parties may then seek to enforce their patent by filing a patent infringement lawsuit against us. While we do not believe that any claims of such patent that could otherwise materially adversely affect commercialization of our product candidates, if approved, are valid and enforceable, we may be incorrect in this belief, or we may not be able to prove it in a litigation. In this regard, patents issued in the United States by law enjoy a presumption of validity that can be rebutted only with evidence that is “clear and convincing,” a heightened standard of proof. There may be third- party patents of which we are currently unaware with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third- party patents were held by a court of competent jurisdiction to cover the manufacturing process of our product candidates, constructs or molecules used in or formed during the manufacturing process, or any final product itself, the holders of any such patents may be able to block our ability to commercialize the product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third- party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third- party patent on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business. Even if we obtain a license, it may be non- exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, if the breadth or strength of protection provided by our patents and any patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we or our licensors may have to pay substantial damages, including treble damages and attorneys’ fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our product candidates, which could harm our business significantly. Third parties may assert that our employees, consultants, collaborators or partners have wrongfully used or disclosed confidential information or misappropriated trade secrets. As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at universities or other biopharmaceutical or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, and although we try to ensure that our employees and consultants do not use the proprietary information or know- how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace. We may not be successful in obtaining or maintaining necessary rights to develop any future product candidates on acceptable terms. Because our programs may involve additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in- license or use these proprietary rights. Our product candidates may also require specific formulations to work effectively and these rights may be held by others. We may develop products containing our compounds and pre- existing pharmaceutical compounds. We may be unable to acquire or in- license any compositions, methods of use, processes or other third- party intellectual property rights from third parties that we identify as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which could harm our business. We may need to cease use of the compositions or methods covered by such third- party intellectual property rights and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non- exclusive, thereby giving

our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. Additionally, we sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions may provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer. The licensing and acquisition of third-party intellectual property rights is a competitive area, and companies, which may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire. We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful. Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that one or more of our patents is not valid or is unenforceable or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly and could put any patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. We may choose to challenge the patentability of claims in a third party's U. S. patent by requesting that the USPTO review the patent claims in an ex-parte re-exam, inter partes review or post-grant review proceedings. These proceedings are expensive and may consume our time or other resources. We may choose to challenge a third party's patent in patent opposition proceedings in the European Patent Office, or EPO, or other foreign patent offices. The costs of these opposition proceedings could be substantial and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other foreign patent offices, then we may be exposed to litigation by a third party alleging that the patent may be infringed by our product candidates or proprietary technologies. In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and in many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by issued patents or any pending applications, or that we or, if applicable, a licensor were the first to invent the technology. Our competitors also may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Any such patent application may have priority over our patents or any patent applications, which could require us to obtain rights to issued patents covering such technologies. If another party has filed a U. S. patent application on inventions similar to those owned by or in-licensed to us, we or, in the case of in-licensed technology, the licensor may have to participate in an interference proceeding declared by the USPTO to determine priority of invention in the United States. If we or one of our licensors is a party to an interference proceeding involving a U. S. patent application on inventions owned by or in-licensed to us, we may incur substantial costs, divert management's time and expend other resources, even if we are successful. Interference proceedings provoked by third parties or brought by the USPTO may be necessary to determine the priority of inventions with respect to our patents or any patent applications or those of our licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Litigation or interference proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States. 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 such litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements. Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent application process and following the issuance of a patent. While an inadvertent 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 **non-compliance** can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. **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. In such an event, our

competitors might be able to enter the market, which would have a material adverse effect on our business. Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or the USPTO. If we or one of our licensing partners initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate, as applicable, is invalid and / or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and / or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re- examination, post grant review, and equivalent proceedings in foreign jurisdictions (e. g., opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and / or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates. Changes in patent law in the United States and in ex- U. S. jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products. As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity, and is therefore costly, time- consuming and inherently uncertain. In addition, the United States has recently enacted, and is currently implementing, wide- ranging patent reform legislation. Recent U. S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U. S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. We cannot predict how these decisions or any future decisions by the courts, the U. S. Congress or the USPTO may impact the value of our patents. Similarly, any adverse changes in the patent laws of other jurisdictions could have a material adverse effect on our business and financial condition. We may not be able to protect our intellectual property rights throughout the world. Filing, prosecuting and defending patents on product candidates in all countries throughout the world is expensive. While certain of our licensed patents, including patents covering our lead product candidates, have been issued in major markets and other countries, our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biopharmaceutical products, which could make it difficult for us or our licensors to stop the infringement of our patents or marketing of competing products against third parties in violation of our proprietary rights generally. The initiation of proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and any patent applications at risk of not issuing and could provoke third parties to assert claims against us or our licensors. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. If 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 Act 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. If our trademarks and trade names are not adequately protected, then we may not be able

to build name recognition in our markets of interest and our business may be adversely affected. Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected. The regulatory approval process for our product candidates in the United States, the European Union, and other jurisdictions is currently uncertain and will be lengthy, time- consuming and inherently unpredictable and we may experience significant delays in the clinical development and regulatory approval, if any, of our product candidates. The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products are subject to extensive regulation by the FDA in the United States, the EMA in the European Union, or EU, and comparable foreign regulatory authorities. We are not permitted to market any product in any jurisdiction until we receive marketing approval from the appropriate regulatory authority. ~~We have only submitted one NDA to the FDA, which was submitted in December 2022 for nirogacestat for the treatment of adults with progressing desmoid tumors requiring systemic treatment, and was granted regulatory approval on November 27, 2023. In addition, aside from the MAA we submitted to the EMA in February 2024 for nirogacestat for the treatment of adults with desmoid tumors, we have not otherwise submitted an MAA to the EMA or similar marketing application to comparable foreign regulatory authorities.~~ In the United States, an NDA must include extensive preclinical and clinical data and supporting information to establish that the product candidate is safe, pure and potent for each desired indication. An NDA must also include significant information regarding the chemistry, manufacturing and controls for the product, and the manufacturing facilities must complete a successful pre- approval inspection. The FDA may also require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The opinion of the Advisory Committee, although not binding, may have a significant impact on our ability to obtain approval of any product candidates that we develop based on the completed clinical trials. In addition, clinical trials can be delayed or terminated for a variety of reasons, including delays or failures related to: • obtaining regulatory authorization to begin a clinical trial, if applicable; • the availability of financial resources to begin and complete the planned trials; • reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites; • obtaining approval at each clinical trial site by an independent IRB or ethics committee; • recruiting suitable patients to participate in a clinical trial in a timely manner; • having patients complete a clinical trial or return for post- treatment follow- up; • clinical trial sites deviating from clinical trial protocol, not complying with GCP requirements or dropping out of a trial; • the availability of materials or manufacturing slots for the products needed for our clinical trials, as a result of the ongoing global and regional conflicts and resulting heightened economic sanctions from the United States, which could lead to delays in these trials; We could face higher costs or reduced availability of supplies, materials, components, or services for product candidates in the United States, the European Union, and other jurisdictions; • addressing any patient safety concerns that arise during the course of a clinical trial; • addressing any conflicts with new or existing laws or regulations; • adding new clinical trial sites; or • manufacturing qualified materials under cGMP regulations for use in clinical trials. Patient enrollment is a significant factor in the timing of clinical trials and is affected by many factors. Further, a clinical trial may be suspended or terminated by us, the IRBs for the institutions in which such clinical trials are being conducted, or the FDA, EMA or comparable foreign regulatory authorities, or recommended for suspension or termination by the DSMB for such clinical trial, 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 sites by the FDA, EMA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience termination of, or delays in the completion of, any clinical trial of our product candidates, the commercial prospects for our product candidates will be harmed, and our ability to generate product revenue will be delayed. In addition, any delays in completing any clinical trials will increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenue. The FDA, EMA or comparable foreign regulatory authorities may disagree with our regulatory plan for our product candidates. The general approach for FDA approval of a new drug is dispositive data from one or more well- controlled Phase 3 clinical trials of the product candidate in the relevant patient population. Phase 3 clinical trials typically involve a large number of patients, have significant costs and take years to complete. Our clinical trial results may not support approval of our product candidates. In addition, our product candidates could fail to receive regulatory approval, or regulatory approval could be delayed, for many reasons, including the following: • the FDA, EMA or comparable foreign regulatory authorities may disagree with the dosing regimen, design or implementation of our clinical trials; • we may be unable to demonstrate to the satisfaction of the FDA, EMA or comparable foreign regulatory authorities that our product candidates are safe and effective for any of their proposed indications; • the results of clinical trials may not meet the level of statistical significance required by the FDA, EMA or comparable foreign regulatory authorities for approval; • we may be unable to demonstrate that our product candidates' clinical and other benefits outweigh their safety risks; • the FDA, EMA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials; • the data collected from clinical trials of our product candidates may not be sufficient to the satisfaction of the FDA, EMA or comparable foreign regulatory authorities to support the submission of an NDA or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere; • the FDA, EMA or comparable foreign regulatory authorities may 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, EMA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data

insufficient for approval. We may seek regulatory approval of our product candidates based on an interim analysis conducted of a registrational trial, particularly if the interim analysis is statistically significant for the primary endpoint and the safety data demonstrate an acceptable safety and tolerability profile. The results of any such interim analysis would be discussed with the FDA at a pre- NDA meeting to assess the adequacy of the data to support the submission of an NDA; however, if the FDA does not agree that the interim analysis provides a sufficient basis for regulatory approval, we would not submit an NDA until the conclusion of such registrational trial. Breakthrough Therapy Designation or Fast Track Designation from the FDA may not actually lead to a faster development or regulatory review or approval process. The FDA has granted Fast Track Designation and Breakthrough Therapy Designation for nirugacestat for the treatment of adult patients with progressive, unresectable, recurrent or refractory desmoid tumors or deep fibromatosis, and has granted Fast Track Designation for mirdametinib for the treatment of patients at least two years of age with NF1- associated inoperable PN that are progressing or causing significant morbidity. We may seek Breakthrough Therapy Designation or Fast Track Designation for our other product candidates. If a product is intended for the treatment of a serious or life- threatening condition and the product demonstrates the potential to address unmet medical needs for this condition, the product sponsor may apply for Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe one of our product candidates 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. A breakthrough therapy is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious or life- threatening disease or condition, and preliminary clinical evidence indicates that the product 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 products 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. 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 may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if a product candidate qualifies as a breakthrough therapy, the FDA may later decide that the product no longer meets the conditions for qualification and rescind the Breakthrough Therapy Designation. The results of clinical trials conducted at clinical trial sites outside the United States might not be accepted by the FDA, and data developed outside of a foreign jurisdiction similarly might not be accepted by such foreign regulatory authority. Some of the prior clinical trials for our product candidates were conducted outside the United States, and we intend to conduct additional clinical trials outside the United States. Although the FDA, EMA or comparable foreign regulatory authorities may accept data from clinical trials conducted outside the relevant jurisdiction, acceptance of these data is subject to certain conditions. For example, the FDA requires that the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with ethical principles such as IRB or ethics committee approval and informed consent, the trial population must adequately represent the U. S. population, and the data must be applicable to the U. S. population and U. S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to the applicable local laws, acceptance of the data by the FDA will be dependent upon its determination that the trials were conducted consistent with all applicable U. S. laws and regulations. There can be no assurance that the FDA will accept data from trials conducted outside of the United States as adequate support of a marketing application. Similarly, we must also ensure that any data submitted to foreign regulatory authorities adheres to their standards and requirements for clinical trials and there can be no assurance a comparable foreign regulatory authority would accept data from trials conducted outside of its jurisdiction. Our relationships with healthcare providers and physicians 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, contractual damages, reputational harm and diminished profits and future earnings. Healthcare providers, physicians and third- party payors in the United States and elsewhere play a primary role in the recommendation and prescription of pharmaceutical products. Arrangements with third- party payors and customers can expose pharmaceutical manufacturers to broadly applicable fraud and abuse and other healthcare laws and regulations, including, without limitation, the federal Anti- Kickback Statute, or AKS, and the federal False Claims Act, or FCA, which may constrain the business or financial arrangements and relationships through which such companies sell, market and distribute pharmaceutical products. In particular, the research of our product candidates, as well as the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self- dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission (s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. For more information, see the section titled “ Business – Other healthcare laws ” in this Form 10- K. The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record- keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products. Pharmaceutical companies may also be subject to federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies continue to closely scrutinize interactions between healthcare companies and healthcare

providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time and resource-consuming and can divert a company's attention from the business. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in federal and state funded healthcare programs, contractual damages and the curtailment or restricting 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, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Any action for violation of these laws, even if successfully defended, could cause a biopharmaceutical manufacturer to incur significant legal expenses and divert management's attention from the operation of the business. Prohibitions or restrictions on sales or withdrawal of future marketed products could materially affect business in an adverse way. Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions. Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even though the FDA granted marketing approval of ~~to~~ OGSIVEO for the treatment of adults with progressing desmoid tumors requiring systemic therapy **and marketing approval of GOMEKLI for the treatment of adult and pediatric patients two years of age and older with NF1 who have symptomatic PN not amenable to complete resection**, the EMA or comparable foreign regulatory authorities must also approve the manufacturing, marketing and promotion of the product candidate in those countries, and we may be unable to obtain such additional approvals. 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 preclinical studies or clinical trials, as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets and / or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed. Even if we receive regulatory approval of any product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates. Our approved ~~product~~ **products** and any product candidates which receive approval in the future are and will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety, efficacy and other post-marketing information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with cGMP and GCP requirements for any clinical trials that we conduct post-approval. Manufacturers and manufacturers' facilities are required to comply with extensive FDA, EMA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations and applicable product tracking and tracing requirements. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA, BLA, or other marketing application and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. Any regulatory approvals that we receive for our product candidates may 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 testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product candidate. Additionally, under FDORA, sponsors of approved drugs and biologics must provide 6 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. The FDA may also require a risk evaluation and mitigation strategies, or REMS, program as a condition of approval of our product candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA, EMA or a comparable foreign regulatory authority approves our product candidates, we will have to comply with requirements including submissions of safety and other post-marketing information and reports and registration. The FDA may impose consent decrees or withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, imposition of post-marketing studies or clinical trials to assess

new safety risks or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things: • restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls; • fines, warning letters or holds on clinical trials; • refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals; • product seizure or detention or refusal to permit the import or export of our product candidates; and • injunctions or the imposition of civil or criminal penalties. The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. Certain endpoint data we hope to include in any approved product labeling also may not make it into such labeling, including exploratory or secondary endpoint data such as patient-reported outcome measures, which could impact our ability to promote products for which we obtain approval. The policies of the FDA, EMA and comparable foreign regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability. Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, if approved, which could make it difficult for us to sell any product candidates profitably. The success of our approved **product products** and product candidates, if approved, depends on the availability of coverage and adequate reimbursement from third- party payors. We cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates or assure that coverage and reimbursement will be available for any product that we may develop. For more information, see the section titled “ Business – Coverage, pricing and reimbursement ” in this Form 10- K. Patients who are provided medical treatment for their conditions generally rely on third- party payors to reimburse all or part of the costs associated with their treatment. Coverage and adequate reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Government authorities and other third- party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. In the United States, no uniform policy of coverage and reimbursement for products exists among third- party payors. As a result, obtaining coverage and reimbursement approval of a product from a government or other third- party payor is a time- consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost- effectiveness data for the use of our products on a payor- by- payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co- payments that patients find unacceptably high. Additionally, third- party payors may not cover, or provide adequate reimbursement for, long- term follow- up evaluations required following the use of product candidates, once approved. Patients are unlikely to use our product candidates, once approved, unless coverage is provided and reimbursement is adequate to cover a significant portion of their cost. There is significant uncertainty related to insurance coverage and reimbursement of newly approved products. It is difficult to predict at this time what third- party payors will decide with respect to the coverage and reimbursement for our product candidates. 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 manufacturer price, average sales price and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs. Payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. Moreover, increasing efforts by governmental and other 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. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Ongoing healthcare legislative and regulatory reform measures may have a material adverse effect on our business and results of operations. 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. For more information, see the section titled “ Business – Current and future legislation ” in this Form 10- K. We cannot predict the initiatives that may be adopted in the future. 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 product candidates, if we obtain regulatory approval; • our ability to set a price that we believe is fair for our approved products; • 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. Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions

on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. See “ — Coverage and reimbursement may be limited or unavailable in certain market segments for our approved **product products** and product candidates, if approved, which could make it difficult for us to sell any product candidates profitably. ” These laws, and future state and federal healthcare reform measures may be adopted in the future, any of which may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. **Existing regulatory policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. In June 2024, the U. S. Supreme Court overruled the Chevron doctrine, which gives deference to regulatory agencies’ statutory interpretations in litigation against federal government agencies, such as the FDA, where the law is ambiguous. This decision may result in more lawsuits against the FDA to challenge longstanding decisions and policies of the FDA, which could undermine the FDA’s authority, lead to uncertainties in the industry, and disrupt the FDA’s normal operations, any of which could delay the FDA’s review of our regulatory submissions. We cannot predict the full impact of this decision, future judicial challenges brought against the FDA, or the nature or extent of government regulation that may arise from future legislation or administrative action. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, our business, financial condition and results of operations could be negatively affected.** If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects. We participate in the Medicaid Drug Rebate program, the 340B drug pricing program, and the VA’s FSS pricing program. Under the Medicaid Drug Rebate program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for our drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data reported by us on a monthly and quarterly basis to CMS, the federal agency that administers the Medicaid Drug Rebate program. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the **United States U.S.** in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions. Our failure to comply with these price reporting and rebate payment obligations could negatively impact our financial results. The ACA made significant changes to the Medicaid Drug Rebate program. CMS issued a final regulation, which became effective on April 1, 2016, to implement the changes to the Medicaid Drug Rebate program under the ACA. The issuance of the final regulation has increased and will continue to increase our costs and the complexity of compliance, has been and will continue to be time- consuming to implement, and could have a material adverse effect on our results of operations, particularly if CMS challenges the approach we take in our implementation of the final regulation. Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the Public Health Service’s 340B drug pricing program in order for federal funds to be available for the manufacturer’s drugs under Medicaid and Medicare Part B. The 340B program requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B “ ceiling price ” for the manufacturer’s covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low- income patients. The 340B ceiling price is calculated using a statutory formula based on the average manufacturer price and Medicaid rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate program, and in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. Any additional future changes to the definition of average manufacturer price and the Medicaid rebate amount under the ACA, other legislation, or in regulation could affect our 340B ceiling price calculations and negatively impact our results of operations. The Health Resources and Services Administration, or HRSA, which administers the 340B program, issued a final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities, which became effective on January 1, 2019. We also are required to report our 340B ceiling prices to HRSA on a quarterly basis. Implementation of the civil monetary penalties regulation and the issuance of any other final regulations and guidance could affect our obligations under the 340B program in ways we cannot anticipate. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in the inpatient setting. Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies and the courts. In the case of our Medicaid pricing data, if we become aware that our reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, we are obligated to resubmit the corrected data for up to three years after those data originally were due. Such restatements and recalculations increase our costs for complying with the laws and regulations governing the Medicaid Drug Rebate program and could result in an overage or underage in our rebate liability for past quarters. Price recalculations also may affect the ceiling price at which we are required to offer our products under the 340B program or could require us to issue refunds to 340B covered entities. Significant civil monetary penalties can be applied if we are found to have knowingly submitted any false pricing information to CMS, or if we fail to submit the required price data on a timely basis. Such conduct also could be grounds for CMS to terminate our Medicaid drug rebate agreement, in which case federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs. Significant civil monetary penalties also can be applied if we are found to have knowingly and intentionally charged 340B covered entities more than the statutorily mandated ceiling price. We

cannot assure you that our submissions will not be found by CMS or HRSA to be incomplete or incorrect. In order to be eligible to have our products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies and grantees, as noted above, we participate in the VA's FSS pricing program. As part of this program, we are obligated to make our products available for procurement on an FSS contract under which we must comply with standard government terms and conditions and charge a price that is no higher than the statutory Federal Ceiling Price, or FCP, to four federal agencies (the VA, U. S. Department of Defense, or DOD, Public Health Service, and the U. S. Coast Guard). The FCP is based on the Non-Federal Average Manufacturer Price, or Non-FAMP, which we calculate and report to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to significant penalties for each item of false information. These obligations also contain extensive disclosure and certification requirements. We also participate in the Tricare Retail Pharmacy program, under which we pay quarterly rebates on utilization of innovator products that are dispensed through the Tricare Retail Pharmacy network to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP. We are required to list our covered products on a Tricare Agreement in order for these products to be eligible for DOD formulary inclusion. If we overcharge the government in connection with our FSS contract or Tricare Agreement, whether due to a misstated FCP or otherwise, we are required to refund the difference to the government. Failure to make necessary disclosures and / or to identify contract overcharges can result in allegations against us under the FCA and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects. Off-label use or misuse of our products may harm our reputation in the marketplace or result in injuries that lead to costly product liability suits. We have received regulatory approval to market OGSIVEO for the treatment of adults with progressing desmoid tumors in adults requiring systemic therapy and ~~we are developing mirdametinib~~ **regulatory approval to market GOMEKLI for the treatment of adult and pediatric patients two years of age and older with NF1 –who have symptomatic PN not amenable to complete resection.** We may only promote or market OSGIVEO, GOMEKLI, and our other product candidates, if approved by the FDA, for their specifically approved indications and in a manner consistent with the approved labeling. We will train our marketing and sales force against promoting our product candidates for uses outside of the approved indications for use, known as "off-label uses." We cannot, however, prevent a physician from using our products off-label, when in the physician's independent professional medical judgment, he or she deems it appropriate. Furthermore, the use of our products for indications other than those approved by the FDA may not effectively treat such conditions. Any such off-label use of our product candidates could harm our reputation in the marketplace among physicians and patients. There may also be increased risk of injury to patients if physicians attempt to use our products for any off-label uses, which could lead to product liability suits that that might require significant financial and management resources and that could harm our reputation. Additionally, the FDA imposes stringent restrictions on manufacturers' communications regarding off-label uses and if we, or our collaborators, do not promote our products, if approved, in a manner consistent with the approved labeling, we, or they, may be subject to warnings or enforcement action for off-label marketing. Violation of the Federal Food, Drug, and Cosmetic Act and other statutes, including the FCA, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state healthcare fraud and abuse laws and state consumer protection laws. Disruptions at the FDA, the SEC and other government agencies caused by funding shortages ~~or~~, global health concerns **or significant leadership, personnel and policy changes,** could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business. **Currently, federal agencies in the United States are operating under a continuing resolution that is set to expire on March 14, 2025. Without appropriation of additional funding to federal agencies, our business operations related to our product development activities for the U. S. market could be impacted.** The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes, and other events that may otherwise affect the FDA's ability to perform routine functions. 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, in recent years, including in 2018 and 2019, the U. S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities. 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. ~~If~~ **Currently, federal agencies in the U. S. are operating under a continuing resolution that is set to expire on March 14, 2025. A** prolonged government shutdown ~~occurs,~~ **significant leadership, personnel, and / or if policy changes, or other substantial modification in agency activities (including due to global health concerns prevent the FDA or geopolitical factors)** ~~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 or delays could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations. EU drug marketing and reimbursement regulations may materially affect our ability to market and receive coverage for our products in the European member states. We intend to seek approval to market our product candidates in both the United States and in selected foreign jurisdictions. If we

obtain approval in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in the EU, the pricing of drugs is subject to governmental control and other market regulations which could put pressure on the pricing and usage of our product candidates. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a product candidate. In addition, market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third- party payors for our product candidates and may be affected by existing and future healthcare reform measures. Much like the AKS prohibition in the United States, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to physicians is governed by the national anti- bribery and other laws of EU Member States, and operations in the United Kingdom would be subject to relevant United Kingdom laws, including the United Kingdom Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician' s employer, his or her competent professional organization and / or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment. In addition, in most foreign countries, including the European Economic Area, or EEA, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low- priced and high- priced member states, can further reduce prices. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. In some countries, we may be required to conduct a clinical study or other studies that compare the cost- effectiveness of any of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for biopharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the United States and generally prices tend to be significantly lower. Publication of discounts by third- party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales and the potential profitability of any of our product candidates in those countries would be negatively affected. Moreover, if the current conflict between Russia and Ukraine expands into the region, there is the potential for us to face higher costs or reduced availability of materials or manufacturing slots for product candidates in the EU and other jurisdictions. We may incur substantial costs in our efforts to comply with evolving global data protection laws and regulations, and any failure or perceived failure by us to comply with such laws and regulations may harm our business and operations. We collect, store, process and transmit sensitive data, including legally protected health information, or PHI, personally identifiable information, intellectual property and proprietary business information. As we seek to expand our business, we are, and will increasingly become, subject to numerous state, federal and foreign laws, regulations and standards, as well as contractual obligations, relating to the collection, use, retention, security, disclosure, transfer and other processing of sensitive and personal information in the jurisdictions in which we operate. In many cases, these laws, regulations and standards apply not only to third- party transactions, but also to transfers of information between or among us, our subsidiaries and other parties with which we have commercial relationships. These laws, regulations and standards may be interpreted and applied differently over time and from jurisdiction to jurisdiction, and it is possible that they will be interpreted and applied in ways that will materially and adversely affect our business, financial condition and results of operations. The regulatory framework for data privacy, data security and data transfers worldwide is rapidly evolving, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business, and as a result, interpretation and implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future. **Any failure or perceived failure by us** to comply with any of these laws and regulations could result in enforcement actions against us, including fines, imprisonment of company officials and public censure, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, **financial condition, results of operations and prospects**. In addition, many states in which we operate have laws that protect the privacy and security of sensitive and personal information. Certain state laws may be more stringent or broader in scope, or offer greater individual rights, with respect to sensitive and personal information than federal, international or other state laws, and such laws may differ from each other, which may complicate compliance efforts. Where state laws are more protective than HIPAA, we must comply with the state laws we are subject to, in addition to HIPAA. In certain cases, it may be necessary **for us** to modify our planned operations and procedures to comply with these more stringent state laws. Further, in some cases where we process sensitive and personal information of individuals from numerous states, we may find it necessary to comply with the most stringent state laws applicable to any of the information. **The California recently enacted the California Consumer Privacy Act, or CCPA, which creates created new** individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA **will require requires** covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt- out of certain sales or transfers of personal information. **The CCPA went into effect on January 1, 2020, and the California State Attorney**

General submitted final regulations for review on June 2, 2020, which were finalized and are now effective. The California State Attorney General has commenced enforcement actions against violators as of July 1, 2020. Further, a new California privacy law, the California Privacy Rights Act, or CPRA **amended the**, was passed by California voters on November 3, 2020. The CPRA **CCPA and**, which became effective on January 1, 2023, **creates created** additional obligations with respect to processing and storing personal information. **Similar laws have been passed and proposed in numerous other states and certain states have also passed laws specifically regulating health information (such as Washington's My Health My Data Act) or other specific categories of personal information, such as biometric information.** We will continue to monitor developments related to the CPRA and anticipate additional costs and expenses associated with ~~CPRA~~ compliance. ~~Four other states have passed comprehensive privacy laws and other U. S. states also are considering omnibus privacy legislation. While the CCPA and CPRA contain an exception for certain activities involving PHI under HIPAA, we cannot yet determine the impact the CCPA, CPRA or other such future laws, regulations and standards may have on our business.~~ In addition to our operations in the United States, which may be subject to healthcare and other laws relating to the privacy and security of health information and other personal information, we may seek to conduct clinical trials in EEA / UK and may become subject to additional European data privacy laws, regulations and guidelines. Where we conduct clinical trials and enroll subjects in our ongoing or future clinical trials in the European Economic Area, or EEA or in the United Kingdom, or UK, we may be subject to European data protection regulations which include additional privacy restrictions. The collection, use, storage, disclosure, transfer, or other processing of personal data regarding individuals in the EEA and UK, including personal health data, is subject to the EU General Data Protection Regulation, or EU GDPR, with respect to the EEA and the UK General Data Protection Regulation and UK Data Protection Act 2018 with respect to the UK, or UK GDPR, and collectively with the EU GDPR referred to as the "GDPR" in this document unless specified otherwise. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing **of special categories of personal data (such as health and other sensitive data)**, **relying on a legal basis or condition for processing personal data, where required** obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, conducting privacy impact assessments for "high risk" processing, implementing safeguards to protect the security and confidentiality of personal data, implementing limitations on the retention of personal data, providing mandatory notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA and UK to non-adequate territories, including the United States in certain circumstances unless derogation exists or a valid GDPR transfer mechanism (for example, the **EC European Commission** approved Standard Contractual Clauses, or SCCs, and the UK International Data Transfer Agreement / Addendum, or UK IDTA) have been put in place. Where relying on the SCCs / 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. Failure to comply with the GDPR, and any supplemental EEA Member State or UK national data protection laws which may apply by virtue of the location of the individuals whose personal data we collect, may result in substantial penalties, including potential fines of up to € 20 million (£ 17.5 million for the UK GDPR) or 4 % of annual global revenues for the preceding financial year, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. The GDPR increases our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and requires us to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities. Although the EU GDPR and the UK GDPR currently impose substantially similar obligations, it is possible that over time the UK GDPR could become less aligned with the EU GDPR. **The UK Government has introduced a**, particularly with the introduction of the new **Data Reform Protection and Digital Information Bill into to reform the UK data protection legal framework which failed in** the UK legislative process. **A new Data (Use and Access) Bill ("UK Bill") has been introduced into parliament. 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 EC. Further, this may lead to additional compliance costs and could increase our overall risk.** In addition, EEA Member States have adopted national laws which may partially deviate from the EU GDPR, and the competent authorities in the EEA Member States may interpret EU GDPR obligations slightly differently from country to country, such that we do not expect to operate in a uniform legal landscape in the EEA. Also, as it relates to processing and transfer of genetic data, the GDPR specifically allows national laws to impose additional and more specific requirements or restrictions, and European laws have historically differed quite substantially in this field, leading to additional uncertainty. The **possible divergence** potential of the respective provisions and enforcement of the EU GDPR and UK GDPR **further diverging** in the future creates additional regulatory challenges and uncertainties for us. The lack of clarity on future UK laws and regulations and their interaction with EU laws and regulations could add legal risk, uncertainty, complexity and compliance cost to the handling of European personal data and our privacy and data security compliance, **and could require us to amend our processes and procedures to implement different compliance measures for the UK and the EEA.** We expect that we will continue to face uncertainty as to whether our efforts to comply with any obligations under European privacy laws will be sufficient. If we are investigated by a European data protection authority, we may face fines and other penalties. Any such investigation or charges by European data protection authorities could have a negative effect on our existing business and on our ability to attract and retain new clients or biopharmaceutical partners. We may also experience hesitancy, reluctance or refusal by European or multi-national clients or biopharmaceutical partners to continue to use our products and solutions due to the

potential risk exposure as a result of the current (and, in particular, future) data protection obligations imposed on them by certain data protection authorities in interpretation of current law, including the GDPR. Such clients or biopharmaceutical partners may also view any alternative approaches to compliance as being too costly, too burdensome, too legally uncertain or otherwise objectionable and therefore decide not to do business with us. Any of the foregoing could materially harm our business, prospects, financial condition and results of operations.

All of these evolving compliance and operational requirements impose significant costs, such as costs related to organizational changes, implementing additional protection technologies, training employees and engaging consultants and legal advisors, which are likely to increase over time. In addition, such requirements may require us to modify our data processing practices and policies, utilize management's time and / or divert resources from other initiatives and projects. The use of new and evolving technologies, such as artificial intelligence, in our business may result in spending material resources and presents risks and challenges that can impact our business including by posing security and other risks to our confidential and / or proprietary information, including personal information, and as a result we may be exposed to reputational harm and liability. We may use and integrate artificial intelligence into our business processes, and this innovation presents risks and challenges that could affect its adoption, and therefore our business. If we enable or offer solutions that draw controversy due to perceived or actual negative societal impact, we may experience brand or reputational harm, competitive harm or legal liability. The use of certain artificial intelligence technology can give rise to intellectual property risks, including compromises to proprietary intellectual property and intellectual property infringement. Additionally, we expect to see increasing government and supranational regulation related to artificial intelligence use and ethics, which may also significantly increase the burden and cost of research, development and compliance in this area. For example, the EU's Artificial Intelligence Act ("AI Act") — the world's first comprehensive AI law — which has entered into force on August 1, 2024 and most provisions of which will become effective on August 2, 2026. This legislation imposes significant obligations on providers and deployers of high-risk artificial intelligence systems, and encourages providers and deployers of artificial intelligence systems to account for EU ethical principles in their development and use of these systems. If we develop or use AI systems that are governed by the AI Act, it may necessitate ensuring higher standards of data quality, transparency, and human oversight, as well as adhering to specific and potentially burdensome and costly ethical, accountability, and administrative requirements. The rapid evolution of artificial intelligence will require the application of significant resources to design, develop, test and maintain our products and services to help ensure that artificial intelligence is implemented in accordance with applicable law and regulation and in a socially responsible manner and to minimize any real or perceived unintended harmful impacts. Our vendors may in turn incorporate artificial intelligence tools into their offerings, and the providers of these artificial intelligence tools may not meet existing or rapidly evolving regulatory or industry standards, including with respect to privacy and data security. Further, bad actors around the world use increasingly sophisticated methods, including the use of artificial intelligence, to engage in illegal activities involving the theft and misuse of personal information, confidential information and intellectual property. Any of these effects could damage our reputation, result in the loss of valuable property and information, cause us to breach applicable laws and regulations, and adversely impact our business.

Additional laws and regulations governing international operations could negatively impact or restrict our operations. As we further expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The U. S. Foreign Corrupt Practices Act, or FCPA, prohibits any U. S. individual or business from paying, offering, authorizing payment or offering anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of any 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 us to maintain books and records that accurately and fairly reflect all transactions of the company, 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 of any such laws and regulations. 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. Risks related to managing business and operations Public health outbreaks, epidemics and pandemics, such as the COVID- 19 pandemic, could adversely impact our business, including our preclinical studies and clinical trials. Public health outbreaks, epidemics and pandemics could adversely impact our business. For example, the novel strain of coronavirus, severe acute respiratory syndrome coronavirus 2, or SARS- CoV- 2, identified in Wuhan, China in December 2019, and the resulting disease from SARS- CoV- 2, or COVID- 19, became a global pandemic. While we did not experience any material disruptions to the execution of the research and development activities that we currently have underway as a result of the pandemic, however with respect to any future epidemics, all of which remain uncertain and difficult to predict, we may continue to experience disruptions that could severely impact research and development, and commercialization timelines and outcomes, including, but not limited to: • delays or difficulties in enrolling patients in our clinical trials; • delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff; • diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials; • interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal, state or foreign governments, employers and others or interruption of clinical trial subject visits and study procedures (such as procedures that are deemed non- essential under law, regulation or institutional policies), which may impact the integrity of subject data and clinical study endpoints and the inability of patients to travel to trial sites or complete scheduled study visits; • interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines; • interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems; • interruptions in preclinical studies due to restricted or limited operations at our contracted research facilities; • deterioration of worldwide credit and financial markets that could limit our ability to obtain external financing to fund our operations and capital expenditures; • investment- related risks, including difficulties in liquidating investments due to current market conditions and adverse investment performance; • limitations on employee resources that would otherwise be focused on the conduct of our research and development activities, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people; and • interruptions or limitations of the types described affecting our service providers and collaboration partners, including contract research organizations running clinical trials and collaboration partners sponsoring clinical trials in which we are supplying our product candidates or otherwise participating. If we lose key management personnel, or if we fail to recruit additional highly skilled personnel, our ability to pursue our business strategy will be impaired, could result in loss of markets or market share and could make us less competitive. Our ability to compete in the highly competitive biopharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, scientific and medical personnel, including Saqib Islam, our Chief Executive Officer, Frank Perier, our Chief Financial Officer, Bhavesh Ashar, our Chief Commercial Officer, Badreddin Edris, our Chief Operating Officer, James Cassidy, our Chief Medical Officer, Kristin Patterson, our Chief **People Officer, Daniel Pichl, our General Counsel and Secretary, Herschel Weinstein, our Chief** Technical Officer, **and** Tai- An Lin, our Chief Scientific **Officer, and Joe Zimmerman, our Chief Compliance and Privacy** Officer. The loss of the services of any of our executive officers, other key employees, and other scientific and medical advisors, and our inability to find suitable replacements for these individuals, could harm our business. Competition for skilled personnel in our industry is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms, in a timely manner or at all. To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided equity incentive awards that vest over time, and from time to time we will consider additional forms of incentives given then- prevailing company circumstances and market conditions. The value to employees of restricted stock units and awards and stock options that vest over time may be significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific and development teams are at- will employees and may terminate their employment with us on short notice. We do not maintain “ key man ” insurance policies on the lives of these individuals or the lives of any of our other employees. Given the stage of our programs and our plans to expand operations, our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid- level and senior personnel across our organization. Our business could be negatively affected by cyber security threats. A cyberattack or similar incident could occur and result in information theft, data corruption, operational disruption, damage to our reputation, or financial loss. We are increasingly dependent on information technology systems and infrastructure, including mobile technologies, to operate our business. Our technologies, systems, networks, or other proprietary information, and those of our vendors, suppliers and other business partners, may become the target of cyberattacks or information security breaches that could result in the unauthorized release, gathering, monitoring, misuse, loss, or destruction of proprietary and other information, or could otherwise lead to the disruption of our business operations. Cyberattacks are becoming more sophisticated and certain cyber incidents, such as surveillance, may remain undetected for an extended period and could lead to disruptions in critical systems or the unauthorized release of confidential or otherwise protected information. These events could lead to financial loss due to remedial actions, loss of business, disruption of operations, damage to our reputation, or potential liability. Our systems and insurance coverage for protecting against cybersecurity risks may not be sufficient. Furthermore, as cyberattacks continue to evolve, we may be required to expend significant additional resources to continue to modify or enhance our protective measures or to investigate

and remediate any vulnerability to cyberattacks. We are increasingly dependent on critical, complex, and interdependent information technology (IT) systems and data to operate our business. Any failure, inadequacy, interruption, or security lapse of that technology, including security attacks, incidents, and / or breaches, could harm our ability to operate our business effectively. We have outsourced significant parts of our IT and business infrastructure to third- party providers, and we currently use these providers to perform critical IT and business services for us. We are therefore vulnerable to cybersecurity attacks and incidents on the associated networks and systems, whether they are managed by us directly or by the third parties with whom we contract, and we have experienced and may in the future experience such cybersecurity threats and attacks. The way we work continues to have and will likely continue to contain a significant remote component in most aspects of the business and we will continue to factor this into our cybersecurity risk management strategy. In addition, due to our reliance on third- party providers, we have experienced and may in the future experience interruptions, delays, or outages related to IT service availability due to a variety of factors outside of our control, including technical failures, natural disasters, fraud, or security attacks experienced by or caused by these third- party providers. Interruptions in the service provided by these third- party providers could affect our ability to perform critical tasks. As a global pharmaceutical company, our systems are subject to frequent cyber- attacks. Due to the nature of some of these attacks, there is a risk that they may remain undetected for a period of time. While we have invested in the protection of data and information technology, our efforts may not prevent service interruptions or security breaches (e. g., ransomware attacks). Any such interruption or breach of our systems could adversely affect our business operations and / or result in the loss of critical or sensitive confidential information or intellectual property, and could result in financial, legal, business, and reputational harm to us. We maintain cyber liability insurance; however, this insurance may not be sufficient to cover the financial, legal, business, or reputational losses that may result from an interruption or breach of our systems. Despite the implementation of security technical and organizational measures, our internal computer systems, and those of third parties with which we contract, are vulnerable to damage from security incidents, breaches, and / or attacks (e. g., ransomware, computer viruses, worms, and other destructive or disruptive software), unauthorized access, natural disasters, terrorism, war, and telecommunication and electrical failures. System failures, accidents, or security attacks and / or breaches of our systems could result in operational interruptions and / or a material disruption of our clinical and commercialization activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. The loss or compromised integrity of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any systems disruptions, security incidents, or security breaches were to result in a loss of, damage to, or compromised integrity of our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and our product research, development, and commercialization efforts could be disrupted or delayed. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events. We could be subject to risks caused by misappropriation, misuse, leakage, falsification, or intentional or accidental disclosure or loss of information maintained in the information systems and networks of our company, including personal information of our personnel. In addition, outside parties may attempt to penetrate our systems or those of our vendors or fraudulently induce our personnel or personnel of our vendors to disclose sensitive information to gain access to our data. Like other companies, we have on occasion, and will continue to experience, threats to our data and systems, including malicious codes and viruses, and other security incidents, breaches, and attacks. The number and complexity of these threats continue to increase over time. Although we have experienced some of the events described above, to date, they have not had a material impact on our operations. Still, the occurrence of any of the events described above in the future could disrupt our business operations and result in enforcement actions or liability, including potential fines and penalties, claims for damages, and shareholder litigation. Security incidents could also include supply chain attacks which, if successful, could cause a delay in the manufacturing of our product or drug candidates. Our key business partners face similar risks, and any security breach of their systems could adversely affect our security posture. In addition, our increased use of cloud technologies could heighten these and other operational risks, and any failure by cloud technology service providers to adequately safeguard their systems and prevent cyber- attacks, could disrupt our operations and result in misappropriation, corruption, or loss of confidential or proprietary information. Finally, as we increase our commercial activities and our brand becomes more widely known and recognized, we may become a more attractive target for malicious third parties. If a material breach of our security or that of our third- party providers occurs, the market perception of the effectiveness of our security measures could be harmed, we could lose business and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information assets and / or information systems. We could also be required to change third- party providers and / or products at significant cost. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes are costly and require ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely. Any breach of our security measures by third- party actions, employee negligence and / or error, malfeasance, defects, or compromise of the confidentiality, integrity or availability of our data could result in: • severe harm to our reputation or brand, or a material and adverse effect on the overall market perception of our technical and organizational measures to protect the confidentiality, integrity, and availability of our information; • individual and / or class action lawsuits, which could result in financial judgments against us potentially causing us to incur legal fees and costs; • legal or regulatory enforcement action, which could result in fines and / or penalties and which would cause us to incur legal fees and costs; and / or • additional costs associated with responding to business interruption or security incidents and / or breaches, such as investigative and remediation costs, the costs of providing individuals and / or data owners with notice of the breach, legal fees, the costs of any additional fraud or cyber detection activities, or the costs of prolonged system disruptions or shutdowns. Any of these events could materially adversely impact our business and results of

operations. Our employees, independent contractors, consultants, academic collaborators, partners and vendors may engage in misconduct or other improper activities, including ~~non-compliance~~ **compliance** with regulatory standards and requirements. We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, academic collaborators, partners and vendors. Misconduct by these parties could include intentional, reckless and / or negligent conduct that fails to comply with the laws of the FDA, EMA and comparable foreign regulatory authorities, provide true, complete and accurate information to the FDA, EMA and comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws, or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. These laws may impact, among other things, our current activities with principal investigators and research patients, as well as proposed and future sales, marketing and education programs. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter misconduct by our employees, independent contractors, consultants, academic collaborators, partners and vendors, and the precautions we take to detect and prevent such activities may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could result in the imposition of civil, criminal and administrative penalties, damages, monetary fines, imprisonment, disgorgement, possible exclusion from participation in government healthcare programs, 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, contractual damages, reputational harm, diminished profits and future earnings and the curtailment of our operations. If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business. We are subject to numerous environmental, health and safety laws and regulations, including those governing the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our development activities involve the use of biological and hazardous materials and can produce hazardous waste products. We cannot eliminate the risk of contamination or injury from these materials, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and / or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological waste or hazardous waste insurance coverage, workers compensation or property and casualty and general liability insurance policies that include coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Changes in tax law 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 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 such changes have been made and changes are likely to continue to occur in the future. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. Shareholders should consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock. Our ability to use our net operating loss carryforwards and certain tax credit carryforwards may be subject to limitation. As of December 31, ~~2023~~ **2024**, we had federal, state and city net operating loss carryforwards of \$ ~~472-581~~ **1-2** million, \$ ~~365-425~~ **5-7** million and \$ ~~3.7-8~~ million, respectively, which are available to reduce future taxable income. Federal net operating loss carryforwards generated 2018 through ~~2023~~ **2024** of \$ ~~467-576~~ **8-9** million will be limited to offset 80 % of taxable income for an indefinite period of time, until fully utilized. Federal net operating loss carryforwards of \$ 4.3 million reported in 2017, and the state and city net operating loss carryforwards expire at various dates ~~through~~ **beginning 2037-2032**. We also have federal tax credits of \$ ~~33-36~~ **5-0** million, which may be used to offset future tax liabilities. These tax credit carryforwards will expire at various dates beginning in 2038. Under Sections 382 and 383 of the Internal Revenue Code of 1986, or the Code, as amended, changes in our ownership may limit the amount of our net operating loss carryforwards and tax credit carryforwards that could be utilized annually to offset our future taxable income, if any. This limitation would generally apply in the event of a cumulative change in ownership of our company of more than 50 % within a three-year period. Any such limitation may significantly reduce our ability to utilize our net operating loss carryforwards and tax credit carryforwards before they expire. Private placements and other transactions that have occurred since our inception, as well as our initial public offering, may trigger such an ownership change pursuant to Sections 382 and 383 of the Code. Any such limitation, whether as the result of the initial public offering, prior private placements, sales of our common stock by our existing stockholders or

additional sales of our common stock by us, could have a material adverse effect on our results of operations in future years. Generally, under current law, federal net operating losses generated after December 31, 2017 are not subject to expiration and may not be carried back to prior taxable years. However, the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, suspended the 80 % taxable income limitation for net operating losses generated in 2018, 2019, and 2020 to the extent these losses are exhausted during the special five- year carryback period or during the 2018, 2019 or 2020 tax years. Additionally, as noted above, for taxable years beginning after December 31, 2020, the CARES Act provisions no longer apply and the deductibility of such federal net operating losses is limited to 80 % of our taxable income in any future taxable year. Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations. Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. Portions of our future clinical trials may be conducted outside of the United States and unfavorable economic conditions resulting in the weakening of the U. S. dollar would make those clinical trials more costly to operate. In addition, regarding the current ~~Russia-~~ **conflicts in the** Ukraine and ~~the Middle East~~ **Israel-Hamas conflicts**, while we do not have any clinical trial sites or operations in the currently affected regions, if the current conflict expands further into the region or continues, resulting heightened economic sanctions from the United States and the international community, in addition to environmental regulations, could limit our ability to procure or use certain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials. Furthermore, the most recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets, and we have observed increased economic uncertainty in the United States and abroad.

Significant political, trade, or regulatory developments in the jurisdictions in which we sell our products, such as those stemming from the change in U. S. federal administration, are difficult to predict and may have a material adverse effect on us. Similarly, changes in U. S. federal policy that affect the geopolitical landscape could give rise to circumstances outside our control that could have negative impacts on our business operations. For example, on February 1, 2025, the U. S. imposed a 25 % tariff on imports from Canada and Mexico, which were subsequently suspended for a period of one month, and a 10 % additional tariff on imports from China. Historically, tariffs have led to increased trade and political tensions. In response to tariffs, other countries have implemented retaliatory tariffs on U. S. goods. Political tensions as a result of trade policies could reduce trade volume, investment, technological exchange and other economic activities between major international economies, resulting in a material adverse effect on global economic conditions and the stability of global financial markets. Any changes in political, trade, regulatory, and economic conditions, including U. S. trade policies, could have a material adverse effect on our financial condition or results of operations. A severe or prolonged economic downturn (including inflation or uncertainty caused by political violence and chaos) could result in a variety of risks to our business, including a reduced ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy or international trade disputes could also strain our suppliers, some of which are located outside of the United States, possibly resulting in supply disruption, including lack of renewals. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business. ~~Increasing scrutiny~~ **Environmental, social and governance matters may impact our business and reputation. In addition to the changing rules and regulations related to environmental, social and governance, or ESG, matters imposed by governmental and self- regulatory organizations, a variety of third- party organizations, institutional investors and customers evaluate the performance of companies on ESG topics, and the results of these assessments are widely publicized. These changing rules, regulations and stakeholder expectations from governments have resulted in, and are likely to continue to result in, increased general and administrative expenses and increased management time and attention spent complying with or meeting such regulations and expectations. Reduced access to or increased cost of capital may occur as financial institutions and investors increase expectations related to ESG matters. Developing and acting on initiatives within the scope of ESG, and collecting, measuring and reporting ESG- related information and metrics can be costly, difficult and time consuming and is subject to evolving reporting standards. We may also communicate certain initiatives and goals, regarding environmental matters, diversity, social investments and other ESG- related matters, in our SEC filings or in other public disclosures. These initiatives and goals within the scope of ESG could be difficult and expensive to implement, the technologies needed to implement them may not be cost effective and may not advance at a sufficient pace, and we could be criticized for the accuracy, adequacy or completeness of the disclosure. Furthermore, statements about our ESG- related initiatives and goals, and progress against those goals, may be based on standards for measuring progress that are still developing, internal controls and processes that continue to evolve and assumptions that are subject to change in the future. In addition, we could be criticized for the scope or nature of such initiatives or goals, or for any revisions to these goals. If our ESG- related data, processes and reporting are incomplete or inaccurate, or if we fail to achieve progress with respect to Environmental, Social and Governance, or our goals, including our previously announced commitments to reduce greenhouse gas emissions, within the scope of ESG on a timely basis, or at all, our reputation, business, financial performance and growth could be adversely affected. In addition, in recent years “ anti- ESG ” sentiment has gained momentum across the U. S., with several states and Congress having proposed or enacted “ anti- ESG ” policies, legislation, or initiatives or issued related legal opinions, and the President having recently issued ~~and- an~~ **practices may cause us to incur additional costs- executive order opposing diversity equity and inclusion, or expose us to additional risks- DEI, initiatives in the private sector**. There has been increasing public focus **Such anti- ESG and anti- DEI- related policies, legislation, initiatives, litigation, legal opinions,** and scrutiny from investors and governmental and nongovernmental organizations on corporate ESG practices. Our ESG practices may not meet the standards of all of our stockholders and advocacy groups may campaign for further changes. A failure, or perceived failure, to respond to related expectations could cause harm to our business and reputation and have a negative impact on the market price of our securities. New governmental regulations could result in new**

regulations and new or more stringent forms of **investigations ESG oversight and enforcement actions, disclosures which may lead to increased expenditures for or sustainability initiatives sustaining reputational harm.** Risks related to a company's financial position and need for additional capital The amount of our future losses is uncertain and our quarterly and annual 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 timing and level of investment in commercialization efforts to support product candidates, both before and after regulatory approval is obtained; • 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; 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 financial 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. Risks related to common stock An active trading market for our common stock may not be sustained. Our shares of common stock began trading on The Nasdaq Global Select Market on September 13, 2019. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares will not be sustained, which could put downward pressure on the market price of our common stock and thereby affect the ability of our stockholders to sell their shares. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or products by using our shares of common stock as consideration. The price of our stock is and may continue to be volatile, and stockholders could lose all or part of their investment. The trading price of our common stock has been and is likely to continue to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control and often unrelated or disproportionate to our financial performance, including limited trading volume. In addition to the factors discussed in this "Risk factors" section and elsewhere in this report, these factors include: • **the results of our potentially registrational clinical trial - ability to commercialize OGSIVEO and GOMEKLI, including our ability to successfully establish and maintain commercial manufacturing and supply chains for mirdametinib - OGSIVEO and GOMEKLI, and our expectations regarding the size and growth potential of the commercial markets for OGSIVEO and GOMEKLI**; • any delay in our regulatory filings for our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information; • adverse results from or delays in future clinical trials; • our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial; • adverse regulatory decisions, including failure to receive regulatory approval of our product candidates or any future product candidate; • changes in laws or regulations applicable to our product candidates or any future product candidate, including but not limited to clinical trial requirements for approvals; • changes in the structure of healthcare payment systems; • adverse developments concerning our manufacturers; • our inability to obtain adequate product supply for any approved product or inability to do so at acceptable prices; • our inability to establish collaborations or partnerships, if needed; • our failure to commercialize our product candidates, if approved; • additions or departures of key medical, scientific or management personnel; • unanticipated serious safety concerns related to the use of our product candidates; • introduction of new products or services offered by us or our competitors; • clinical trial results for other product candidates that could compete with our product candidates; • announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors; • our ability to effectively manage our growth; • actual or anticipated variations in quarterly operating results; • our cash position; • our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public; • publication of research reports about us or our industry, or product candidates in particular, or positive or negative recommendations or withdrawal of research coverage by securities analysts; • changes in the market valuations of similar companies; • overall performance of the equity markets; • sales of our common stock by us or our stockholders in the future; • trading volume of our common stock; • changes in accounting practices; • ineffectiveness of our internal controls; • disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies; • significant lawsuits, including patent or stockholder litigation; • general political and economic conditions; and • other events or factors, many of which are beyond our control. In addition, the stock market in general, and the market for biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations resulting from the COVID- 19 pandemic and other macroeconomic factors (including global conflicts and political instability) and have often been unrelated or disproportionate to the operating performance of these companies. Broad market

and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. If the market price of our common stock does not exceed a stockholder's purchase price, such stockholder may not realize any return on their investment in us and may lose some or all of their investment. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources, which would harm our business, operating results or financial condition. We incur significant costs as a result of operating as a public company, and our management is required to devote substantial time to new and existing compliance initiatives. As a public company, we incur significant legal, accounting and other expenses. We are subject to the reporting requirements of the Exchange Act which require, among other things, that we file, with the SEC, annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes- Oxley Act, as well as rules subsequently adopted by the SEC and Nasdaq to implement provisions of the Sarbanes- Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, in July 2010, the Dodd- Frank Wall Street Reform and Consumer Protection Act, or the Dodd- Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd- Frank Act that require the SEC to adopt additional rules and regulations in these areas such as "say on pay" and proxy access. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Sales of a substantial number of shares of our common stock by our existing stockholders in the public market could cause our stock price to fall. If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. As of December 31, 2023-2024, we had 73-74, 486-403, 699-278 shares of common stock outstanding, of which 106-11, 834-101 shares are restricted shares subject to future vesting. As of December 31, 2023-2024, approximately 36-38.8-0% of our shares of common stock are beneficially held by directors, executive officers and holders of more than 5% of our common stock and will be subject to certain limitations of Rule 144 under the Securities Act. In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our existing equity compensation plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline. Additionally, the number of shares of our common stock reserved for issuance under the 2019 Stock Option and Equity Incentive Plan will automatically increase on January 1 of each year, with January 1, 2020 having been the first of such increases and continuing through and including January 1, 2030, by 5% of the total number of shares of our capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares as determined by our board of directors. Unless our board of directors elects not to increase the number of shares available for future grant each year, our stockholders may experience additional dilution. If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline. The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline. If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock. Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes- Oxley Act, or Section 404, and the related rules and regulations of the SEC and the Public Company Accounting Oversight Board (United States) or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock. We will be required to disclose changes made in our internal controls and procedures on a quarterly basis and our management will be required to assess the effectiveness of these controls annually. Our independent registered public accounting firm is required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. An independent assessment of the effectiveness of our internal controls over financial reporting could detect problems that our management's assessment did not, and could lead to additional findings, potentially including material weaknesses. Material weaknesses in our internal controls over financial reporting could lead to restatements of our financial statements and require us to incur the expense of remediation. Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud. We are subject to certain reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, 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 or insufficient disclosures due to error or fraud may occur and not be detected.