Risk Factors Comparison 2024-03-14 to 2023-03-14 Form: 10-K

Legend: **New Text** ~~Removed Text~~ Unchanged Text Moved Text Section

Risks Related to the Development of Our Product Candidates . We may not be successful in..... motivate key employees of any acquired businesses . If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates. Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete, and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, a further review and analysis of this data may change the conclusions drawn from this unaudited data indicating less promising results than we currently anticipate. In some instances, there can be significant variability in safety and / or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, adherence to the dosing regimen and other trial protocols, and the rate of dropout among clinical trial participants. There also may be significant variability in the safety results obtained through the long- term follow-up of patients from ongoing studies. We do not know whether any clinical trial we may conduct or follow- up data we collect will demonstrate consistent or adequate efficacy and / or safety sufficient to obtain regulatory approval to market our product candidates. In addition, the design of a clinical trial may determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. A failure of one or more clinical trials could indicate a higher likelihood that subsequent clinical trials of the same product candidate in the same or other indications or subsequent clinical trials of other related product candidates will be unsuccessful for the same reasons as the unsuccessful clinical trials. We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including: ● regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site; ● we may have delays in reaching or fail to reach agreement on clinical trial contracts or clinical trial protocols with prospective trial sites; ● clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs; ● the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or our participants may drop out of these clinical trials at a higher rate than we anticipate; ~~37~~ ● 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; ● regulators or institutional review boards may require that we or our investigators suspend or terminate clinical trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks; or ● our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials. If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may: ● be delayed in obtaining or not obtain marketing approval for our product candidates; ● obtain approval for indications or patient populations that are not as broad as intended or desired; ● obtain approval with labeling that includes significant use or distribution restrictions including imposition of a Risk Evaluation and Mitigation Strategy (REMS), or safety warnings, including boxed warnings; ● be subject to additional post marketing testing requirements; or ● have the product removed from the market after obtaining marketing approval. The FDA and foreign regulatory authorities may determine that the results from our ongoing and future trials do not support regulatory approval and may require us to conduct an additional clinical trial or trials. If these agencies take such a position, the costs of development of our product candidates could increase materially and their potential market introduction could be delayed. The regulatory agencies could also require that we conduct additional clinical, nonclinical or manufacturing validation studies and submit that data before it will consider an NDA. Our product development costs will also increase if we experience delays in clinical testing or marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured 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 or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. In addition, there are a number of ongoing clinical trials being conducted by other companies for product candidates treating cancer. Patients who would otherwise be eligible for our clinical trials may

instead enroll in clinical trials of our competitors' product candidates, particularly if they view such treatments to be more conventional and established. ~~Patient~~ **38Patient** enrollment is affected by other factors including: ● the size and nature of the patient population; ● severity of the disease under investigation; ● eligibility criteria for the study in question; ● perceived risks and benefits of the product candidate under study in relation to other available treatments including any new treatments that may be approved for the indications we are investigating; ● efforts to facilitate timely enrollment in clinical trials; ● patient referral practices of physicians; ● the ability to monitor patients adequately during and after treatment; ~~38~~ ● proximity and availability of clinical trial sites for prospective patients; and ● constraints on the healthcare system such as **a pandemic** ~~COVID- 19~~ . Furthermore, enrolled patients may drop out of a clinical trial, which could impair the validity or statistical significance of the clinical trial. A number of factors can influence the patient discontinuation rate, including, but not limited to: ● the inclusion of a placebo arm in a trial; ● possible inactivity or low activity of the product candidate being tested at one or more of the dose levels being tested; ● the occurrence of adverse side effects, whether or not related to the product candidate; and ● the availability of numerous alternative treatment options, including clinical trials evaluating competing product candidates, that may induce patients to discontinue their participation in the trial. Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. Preclinical studies and preliminary and interim data from clinical trials of our product candidates are not necessarily predictive of the results or success of ongoing or later clinical trials of our product candidates. If we cannot replicate the results from our preclinical studies and clinical trials of our product candidates, we may be unable to successfully develop, obtain regulatory approval for, and commercialize our product candidates. Preclinical studies and any positive preliminary and interim data from our clinical trials of our product candidates may not necessarily be predictive of the results of ongoing or later clinical trials. Even if we are able to complete our planned clinical trials of our product candidates according to our current development timeline, the positive results from clinical trials of our product candidates may not be replicated in subsequent clinical trial results. Also, our later stage clinical trials could differ in significant ways from earlier stage clinical trials, which could cause the outcome of the later stage trials to differ from our earlier stage clinical trials. For example, these differences may include changes to inclusion and exclusion criteria, efficacy endpoints and statistical design. Many companies in the pharmaceutical and biotechnology industries, including us, have suffered significant setbacks in late stage clinical trials after achieving positive results in an earlier stage of development. If we fail to produce positive results in our planned clinical trials of any of our product candidates, the development timeline and regulatory approval and commercialization prospects for our product candidates, and, correspondingly, our business and financial prospects, would be materially adversely affected. Our approach to the treatment of cancer through cell death, inhibition of tumor growth, and disruption of the tumor microenvironment is relatively unproven, and we do not know whether we will be able to develop any products of significant commercial value. We are developing product candidates to treat cancer by using targeted agents to cause cell death, inhibition of tumor growth, and disruption of the tumor microenvironment, and thereby thwart the growth and proliferation of cancer cells. ~~Research~~ **39Research** on the use of small molecules to cause cell death, inhibition of tumor growth, and disruption of the tumor microenvironment is an emerging field and, consequently, there is still uncertainty about whether defactinib and avutometinib are effective in improving outcomes for patients with cancer. Any products that we develop may not effectively cause cell death, inhibition of tumor growth, and disruption of the tumor microenvironment. While we are currently conducting clinical trials for product candidates that we believe will cause cell death, inhibition of tumor growth, and disruption of the tumor microenvironment, we may not ultimately be successful in demonstrating their efficacy, alone or in combination with other treatments. ~~39The~~ -- **The** approval of our product candidates as single agents or part of a combination therapy for the treatment of certain cancers may be more costly than our prior clinical trials, may take longer to achieve regulatory approval, may be associated with new, more severe or serious and unanticipated adverse events, and may have a smaller market opportunity. Part of our current business model involves conducting clinical trials to study the effects of combining our product candidates with other approved and investigational targeted therapies, chemotherapies, and immunotherapies to treat patients with cancer. Regulatory approval for a combination treatment generally requires clinical trials to evaluate the activity of each component of the combination treatment. As a result, it may be more difficult and costly to obtain regulatory approval of our product candidates for use as part of a combination treatment than obtaining regulatory approval of our product candidates alone. In addition, we also risk losing the supply of any approved or investigational product being combined with our product candidate in these clinical trials. Furthermore, the potential market opportunity for our product candidates is difficult to estimate precisely. For instance, if one of our product candidates receives regulatory approval from a combination study, it may be approved solely for use in combination with the approved or investigational product in a particular indication and the market opportunity our product candidate would be dependent upon the continued use and availability of the approved or investigational product. In addition, because physicians, patients, and third-party payors may be sensitive to the addition of the cost of our product candidates to the cost of treatment with the other products, we may experience downward pressure on the price that we can charge for our product candidates if they receive regulatory approval. Further, we cannot be sure that physicians will view our product candidates, if approved as part of a combination treatment, as sufficiently superior to a treatment regimen consisting of only the approved or investigational product. Additionally, the adverse side effects of our product candidates may be enhanced when combined with other products. If such adverse side effects are experienced, we could be required to conduct additional pre- clinical and clinical studies, and if such adverse side effects are severe, we may not be able to continue the clinical trials of the combination therapy because the risks may outweigh the therapeutic benefit of the combination. We face substantial competition, which may result in others developing or commercializing products before or more successfully than we do. The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates and will face

competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we are developing our product candidates, including Novartis AG, Pfizer, Genentech, Inc., AstraZeneca PLC, Mirati, Amgen, Revolution Medicines, Inc., **SpringWorks Therapeutics, Inc., BeiGene Ltd., Immuneering Corporation, Mapkure, LLC, Erasca, Inc.,** Relay Therapeutics, Inc. **and Kinnate Biopharma** ~~, Boehringer Ingelheim, Moderna~~ , Inc. and others. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization. We are developing our product candidates for the treatment of cancer. There are a variety of available therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Many ~~of~~ **40of** these approved drugs are well established therapies and are widely accepted by physicians, patients and third- party payors. Insurers and other third- party payors may also encourage the use of generic products. We expect that our product candidates, if approved, will be priced at a significant premium over competitive generic products. Many of our competitors have significantly greater financial resources and expertise than we do in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified ~~40scientific~~ **scientific** and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs **. Additionally, new developments, including the development of other drug technologies and methods of preventing the incidence of disease, occur in the pharmaceutical and medical technology industries at a rapid pace. These developments may render our product candidates obsolete or noncompetitive** . In addition, to the extent that products or product candidates of our competitors demonstrate serious adverse side effects or are determined to be ineffective in clinical trials, the commercialization and the development of our product candidates could be negatively impacted. If we fail to obtain regulatory approval in jurisdictions outside the United States, we will not be able to market our products in those jurisdictions. We intend to seek regulatory approval for our product candidates in countries outside of the United States and expect that these countries will be important markets for our products, if approved. Marketing our products in these countries will require separate regulatory approvals in each market and compliance with numerous and varying regulatory requirements. The regulations that apply to the conduct of clinical trials and approval procedures vary from country to country and may require additional testing. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. In addition, in many countries outside the United States, a drug must be approved for reimbursement before it can be approved for sale in that country. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Failure to obtain regulatory approval in one country may have a negative effect on the regulatory approval process in others. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any foreign market. Preclinical testing and clinical trials of our product candidates may not be successful. If we are unable to obtain marketing approval for or successfully commercialize any of our product candidates, or if we experience significant delays in doing so, our business will be materially harmed. We have invested a significant portion of our efforts and financial resources in the research and development of our product candidates. Our ability to generate product revenues will depend heavily on the successful commercialization and development of our product candidates. The success of our product candidates will depend on several factors, including the following: ● initiation and successful enrollment and completion of our clinical trials; ● receipt of marketing approvals from the FDA and other regulatory authorities for our future product candidates, including pricing approvals where required; ● establishing and maintaining commercial manufacturing capabilities or making arrangements with third- party manufacturers; ● obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates; **41** ● establishing and maintaining commercial capabilities, including hiring and training a sales force, and launching commercial sales of the products, if and when approved, whether alone or in collaboration with others; ● acceptance of the products, if and when approved, by patients, the medical community, and third- party payors; ● securing and maintaining coverage and adequate reimbursement for our products from third party payors; ● effectively competing with other therapies; and ● a continued acceptable safety and efficacy profile of the products following approval. Many of these factors are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any collaborator. If we do not achieve one or more of these factors in a timely manner or at all, we could experience ~~41significant~~ **significant** delays or an inability to successfully commercialize our product candidates, which would materially harm our business. If serious adverse or unexpected side effects are identified during the development of our product candidates, we may need to abandon or limit our development of some of our product candidates. Our product candidates are in various stages of clinical development, and their risk of failure is high. It is impossible to predict when or if our other product candidates will prove effective or safe in humans or will receive marketing approval. If our product candidates are associated with undesirable side effects or have characteristics that are unexpected, we may need to abandon their development or limit development to

certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe, or more acceptable from a risk benefit perspective. Patients in our clinical trials have experienced serious adverse events, deemed by us and the clinical investigator to be related to our product candidates. Serious adverse events generally refer to adverse events, that result in death, are life threatening, require hospitalization or prolonging of hospitalization, or cause a significant and permanent disruption of normal life functions, congenital anomalies or birth defects, or require intervention to prevent such outcomes. Avutometinib and defactinib are being administered and studied in our Phase 1 ~~and~~ **,** Phase 2 **, and Phase 3** clinical trials, and the development program continues to progress. For both avutometinib and defactinib, the toxicities reported to date have been predictable and manageable. As a result of adverse events observed to date, or further safety or toxicity issues that we may experience in our clinical trials in the future, we may not receive approval to market any product candidates, which could prevent us from ever generating revenue from the sale of products or achieving profitability. Results of our trials could reveal an unacceptably high severity and prevalence of side effects. In such an event, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our products candidates for any or all targeted indications. Many compounds that initially showed promise in early stage testing for treating cancer have later been found to cause side effects that prevented further development of the compound. In addition, while we and our clinical trial investigators currently determine if serious adverse or unacceptable side effects are drug related, the FDA or other non- U. S. regulatory authorities may disagree with our or our clinical trial investigators' interpretation of data from clinical trials and the conclusion that a serious adverse effect or unacceptable side effect was not drug related. We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success. Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market ~~opportunities~~ **42opportunities** . Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. Any future product candidates that we commercialize may become subject to unfavorable pricing regulations or third- party coverage and reimbursement policies, which would harm our business. In both domestic and foreign markets, any product candidates that may receive marketing approval in the future will depend, in part, on favorable pricing as well as the availability of coverage and amount of reimbursement by third party payors, including governments and private health plans. Substantial uncertainty exists regarding coverage and reimbursement by third party payors of newly approved health care products. Outside the United States, some countries require approval of the sale price of a drug before the product can be marketed. In many such countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing ~~42governmental~~ -- **governmental** control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in product candidates, even if those product candidates obtain marketing approval. Cost containment is a key trend in the United States and elsewhere. Third- party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. 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 coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, the level of reimbursement. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize the product candidates for which we may obtain marketing approval. Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop. We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any other products we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in: ● decreased demand for any product candidates or products that we may develop; ● injury to our reputation and significant negative media attention; ● withdrawal of clinical trial participants; ● significant costs to defend the related litigation; ● substantial monetary awards to trial participants or patients; ● loss of revenue; and ● the inability to commercialize any products that we may develop. We currently hold $ 10. 0 million in product liability insurance coverage in the aggregate, with a per incident limit of $ 10. 0 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we commercialize any future product candidates or if we initiate additional clinical trials in the United States and around the world. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. ~~A~~ **43A** pandemic, epidemic, or outbreak of an infectious disease, such as COVID- 19, has and may in the future adversely affect our business. Broad- based business or economic disruptions could adversely affect our ongoing or planned research and development activities, our financial condition and our results of operations. For example, United States residents and businesses in major urban centers have been hit especially hard by the global spread of COVID- 19, which has resulted in certain disruptions to our business and may in the future result in additional disruptions to our business. Examples of both include: ● Shortages of personnel at clinical trial sites and delay in startup activities. ~~Shortages in personnel in clinics~~ **Clinics** and hospitals ~~have cause some United States sites to institute limits on new clinical trials which could impact our ability to open new sites for our clinical trials. Clinics~~ in Europe

and United States continue to ~~have~~ **cause** delays in startup **and on- going** activities due to the ongoing **staff shortages since** ~~pandemic and the increase in COVID- 19 variant infections. In addition, participant dosing, study monitoring and data analysis may be paused or delayed due to changes in hospital or academic institution policies, federal, state, or local 43regulations, prioritization of hospital resources toward pandemic efforts, or other~~ -- **the onset of** ~~reasons related to~~ the COVID- 19 pandemic ~~. ● Accessibility limitations on our contract research organizations (" CROs "). The ability of principal investigators and site staff to perform their functions, who, as healthcare providers, may have heightened exposure to COVID- 19, could be disrupted and cause elongation or de- prioritization of our clinical trials, increase the costs related to such development, and materially adversely impact our clinical trial operations. ● Capital markets volatility. Equity and debt markets have experienced significant volatility since the spread of COVID- 19 into the United States, which makes it more difficult to raise capital at a reasonable valuation or at all. ● Limitations on third- party manufacturers and distributors. We currently utilize third parties to, among other things, supply raw materials, produce drug substance, drug product, and drug packaging. Some of our third party manufacturers and distributors may in the future be limited and, at times, precluded from delivering us raw materials, drug substance, drug product, and drug packaging on a timely basis, for a variety of reasons, including without limitation to an evolving understanding of how international, federal, and / or state authorities define " essential business ", their inability to remain open due to lost business in other parts of their portfolios, or because of international, federal, and / or state prioritization orders requiring our manufacturers to produce for and our distributors to distribute to governmental entities, competitors and / or other companies before they produce for us. ● Health risks for our employees. The health and wellbeing of our employees, including the employees of our third parties is at risk — if a significant number of our personnel were to be diagnosed with COVID- 19, placed in quarantine due to potential exposure to COVID- 19, or need to care for family members diagnosed with COVID- 19, it may result in significant business disruption~~ . ● Work- from- home limitations. ~~We have adopted~~ **Since 2020,** a ~~hybrid~~ **material portion of our workforce** ~~work~~ **works remotely and we expect this** ~~program allowing our employees the option~~ to **continue** ~~primarily work from home~~ , which could impact our ability to effectively plan, execute, communicate, and maintain our corporate culture. **● Capital markets volatility. Equity** ~~The remote working environment could increase our cyber security risk, create data accessibility concerns,~~ and **debt markets have experienced significant volatility in recent years, which** ~~make~~ **makes** ~~us~~ **it** more ~~susceptible~~ **difficult** to **raise capital at a reasonable valuation** ~~communication disruptions. ● Regulatory disruption. There may be interruptions~~ or **at all** ~~delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines~~ . ● Business interruptions or disruptions. There may be interruptions or disruptions that directly or indirectly adversely affect our or our current or potential collaboration partners' organizations, which may delay or disrupt our business plans or impact a collaboration partner' s ability to fully perform under our agreements with them. Each of these factors could have a material adverse effect on our business and results of operations ~~. The extent to which COVID- 19 impacts our results will depend on many factors and future developments, including new information about COVID- 19 and any new government regulations which may emerge to contain the virus, among others~~ . Risks Related to Our Commercial AgreementsWe depend on Secura for the achievement and payment of the contingent consideration under the asset purchase agreement between us and Secura pursuant to which we sold the COPIKTRA assets to Secura. If Secura is unsuccessful in developing and commercializing COPIKTRA, we may not receive such payments or otherwise capitalize on the market potential of COPIKTRA. On September 30, 2020, we completed the disposition of our rights, title, and interest in and to COPIKTRA to Secura. Under the terms of the asset purchase agreement with Secura, we are entitled to contingent consideration, including milestone payments and royalties, dependent upon the further development and commercial success of COPIKTRA. Accordingly, our ability to receive the contingent consideration will depend on Secura' s ability to successfully develop and commercialize COPIKTRA. ~~44Secura~~ -- **Secura** ' s ability to develop and commercialize COPIKTRA is subject to a number of risks and uncertainties, including the following: ● Secura has significant discretion in determining how to develop further and commercialize COPIKTRA, including through potential collaborators and partners; ● Secura may not commit sufficient resources to development, marketing or distribution of COPIKTRA; ● even if diligently pursued, Secura' s efforts to develop and commercialize COPIKTRA may not be successful; ● Secura may not properly maintain or defend its intellectual property rights or may use its proprietary information in such a way as to invite litigation that could jeopardize or invalidate the intellectual property of COPIKTRA; ● Secura may fail to maintain compliance with ongoing FDA labeling, packaging, storage, advertising, promotion, recordkeeping, safety and other post- market requirements; ● Secura may not be able to obtain regulatory approval in United States for certain oncology indications or obtain approval in jurisdictions outside of the United States and as a result, will not be able to market COPIKTRA for those indications or in those jurisdictions; ~~and~~ **and44** ● disputes may arise between Secura and us that result in the delay of payments or in costly litigation that diverts management attention and resources. Our ability to receive future contingent consideration, including milestone payments and royalties, from the sale of our rights, title, and interest in COPIKTRA to Secura may be adversely affected by lower than expected COPIKTRA sales and Secura' s ability to achieve other developmental and regulatory milestones. On June 30, 2022, the FDA issued a drug safety communication warning that resulted from a clinical trial showing a possible increased risk of death with COPIKTRA compared to another medicine to treat chronic blood cancer called leukemia and lymphoma. The aforementioned clinical trial also found that COPIKTRA was associated with a higher risk of serious side effects, including infections, diarrhea, inflammation of the intestines and lungs, skin reactions, and high liver enzyme levels in the blood. In September 2022, the FDA' s ~~Oncologic Drug Advisory Committee (" ODAC ")~~ voted eight to four against COPIKTRA' s use in patients with relapsed or refractory chronic lymphocytic leukemia / small lymphocytic lymphoma after at least two prior therapies citing an unfavorable risk / benefit profile. The FDA drug safety communication warning, the FDA' s ODAC vote, future actions by the FDA, and any safety concerns associated with COPIKTRA, perceived or real, may materially and adversely affect Secura' s development and commercialization success of COPIKTRA and, consequently, our ability to receive future contingent consideration from our sale of our right, title, and interest in COPIKTRA to Secura. If we do not realize the anticipated benefits of our license agreements

with Pfizer for the FAK program and Chugai for the dual RAF / MEK candidate program, **or from the GenFleet Agreement,** our business could be adversely affected. Our license agreements with Pfizer for defactinib ~~and~~ **,** Chugai for avutometinib **, and the GenFleet Agreement for up to three oncology programs,** may fail to further our business strategy as anticipated or to achieve anticipated benefits and success. We may make or have made assumptions relating to the impact of the acquisition of defactinib and avutometinib **or entering into the GenFleet Agreement** on our financial results relating to numerous matters, including: ● the cost of development and commercialization of defactinib and avutometinib; **● the cost of development and commercialization of any of the three oncology programs if we elect to exercise any of our GenFleet Options;** and ● other financial and strategic risks related to the ~~license~~ agreements with Pfizer ~~and~~ **,** Chugai **and GenFleet** . Further, we may incur higher than expected operating and transaction costs, and we may encounter general economic and business conditions that adversely affect us relating to our ~~license~~ agreements with Pfizer ~~and~~ **,** Chugai **or GenFleet** . If one or more of these assumptions are incorrect, it could have an adverse effect on our business and operating results, and the benefits from our license agreements with Pfizer for defactinib and Chugai for avutometinib **and the GenFleet Agreement** may not be realized or be of the magnitude expected **. We depend on GenFleet to fully perform under the GenFleet AgreementOn August 24, 2023, we entered into the GenFleet Agreement pursuant to which we obtained three GenFleet Options that may be exercised on a program- by- program basis. Pursuant to the GenFleet Agreement, we are reliant on GenFleet to fulfil their responsibilities including the execution of the Phase 1 clinical trials for all three oncology programs. Accordingly, our ability to realize the anticipated benefits and success of the GenFleet Agreement is dependent upon GenFleet fulfilling their obligations. If GenFleet does not successfully carry out their responsibilities, the benefits of the GenFleet Agreement may not be realized** . 45Risks Related to Our Financial Position and Need for Additional CapitalWe have incurred significant losses since our inception. We may incur losses for the foreseeable future and may never achieve or maintain profitability. Since inception, we have incurred significant operating losses. As of December 31, ~~2022~~ **2023** , we had an accumulated deficit of $ ~~737~~ **824** . ~~5~~ **9** million. To date, we have generated minimal product revenues and have financed our operations primarily through public and private offerings of our common stock ~~and~~ **,** preferred stock **, and pre- funded warrants, offerings of convertible notes** , sales of our common stock pursuant to our at- the- market equity offering programs, our loan and security agreement (the " Loan Agreement ") with Oxford Finance LLC (" Oxford "), our loan and security agreement, as amended, with Hercules Capital Inc. (" Hercules "), ~~the issuance of our 5. 00 % Convertible Senior Notes due 2048 (" 2018 Notes "),~~ upfront payments under our license and collaboration agreements with Yakult, CSPC, and Sanofi, and the upfront payment under the Secura APA. We have devoted substantially all of our efforts to research and development. We expect to continue to incur significant expenses and may incur operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we: ● continue our ongoing clinical trials with our product candidates, including with defactinib and avutometinib; ● initiate additional clinical trials for our product candidates; ● maintain, expand, and protect our intellectual property portfolio; ● acquire or in- license other products and technologies; ● hire additional clinical, development, and scientific personnel; and ● establish and maintain a sales, marketing and distribution infrastructure to commercialize any products for which we obtain marketing approval. To become and remain profitable, we must develop and eventually commercialize a product or products with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, obtaining marketing approval for these product candidates, and manufacturing, marketing, and selling those products for which we may obtain marketing approval. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of the company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment. We ~~may~~ **will** need additional funding. If we are unable to raise capital if needed, we would be forced to delay, reduce, or eliminate our product development programs or commercialization efforts, including for avutometinib. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the clinical development of our product candidates. We expect our ~~existing~~ cash ~~resources~~ **, cash equivalents and investments** at December 31, ~~2022~~ **2023** will **not** be sufficient to fund our current operating plan and capital expenditure requirements **for the** ~~through at least~~ next ~~twelve~~ **12** months from the issuance ~~date~~ of these financial statements. **We** ~~This estimate does not reflect the possibility that we may not be able to access a portion of our existing cash, cash equivalents and investments due to market conditions. For example, on March 10, 2023, the Federal Deposit Insurance Corporation (the " FDIC "), took control and was appointed receiver of Silicon Valley Bank (" SVB "). On March 12, 2023, the Department of the Treasury, the Federal Reserve, and the FDIC announced that all depositors of SVB will be fully protected and have access to all their money starting March 13, 2023. As of March 13, 2023, we had approximately $ 2 million on deposit at SVB. If other banks and financial institutions enter receivership or become insolvent in the future in response to financial conditions affecting the banking system and financial markets, our ability to access our existing cash, cash equivalents and investments may be threatened and could have a material adverse effect on our business and financial condition. 46We~~ may need to obtain additional funding in connection with our continuing operations, including for our clinical development programs. Our future capital requirements will depend on many factors, including: ● the scope, progress, and results of our ongoing and potential future clinical trials; ● the extent to which we acquire or in- license other product candidates and technologies; ● the costs, timing, and outcome of regulatory review of our product candidates (including our efforts to seek approval and fund the preparation and filing of regulatory submissions); ● revenue received from commercial sales of our product candidates, should any of our product candidates receive marketing approval; ● the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights, and defending intellectual property related claims; and **46** ● our ability to establish

collaborations or partnerships on favorable terms, if at all. Conducting clinical trials is a time consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval of any of our product candidates. Our commercial revenues will be derived from sales of products. Even if our product candidates gain approval, it may take several years to achieve a significant level of sales, and as a result we may need to continue to rely on additional financing to further our clinical development objectives. Adequate additional financing may not be available to us on acceptable terms, or at all **. We will require additional financing to execute our operating plan and continue to operate as a going concern. As required under Accounting Standards Update 2014- 15, Presentation of Financial Statements- Going Concern (ASC 205- 40), we have the responsibility to evaluate whether conditions and / or events raise substantial doubt about our ability to meet our future financial obligations as they become due within one year after the date the consolidated financial statements are issued. The Company believes that it may have sufficient funds to meet its obligations within the next 12 months from the issuance of these financial statements. However, this belief relies on the achievement of certain mitigation efforts. The analysis under ASC 205- 40, initially cannot take into consideration the potential mitigating effects of plans that have not been fully implemented as of the date the financial statements are issued. Accordingly, these uncertainties and risk factors meet the ASC 205- 40 standard for raising substantial doubt about our ability to continue as a going concern within one year of the issuance date of our consolidated financial statements. Lack of necessary funds may require us, among other things, to delay, scale back, or eliminate some or all of our planned clinical trials. Because we continue to experience net operating losses, our ability to continue as a going concern is subject to our ability to obtain necessary capital from outside sources, including obtaining additional capital from the sale of our securities or assets, achieving milestones for additional drawdowns under our Loan Agreement or obtain loans from financial institutions, or entering into additional partnership arrangements. There can be no assurances that we will be able to obtain such capital on favorable terms or at all. If we are unable to raise capital when needed, we may be forced to delay, reduce or eliminate our research and development activities for our product candidates, or ultimately not be able to continue as a going concern** . Unfavorable economic conditions could have a material adverse effect on our business, financial condition, results of operations, or cash flows. Unfavorable macroeconomic conditions and other adverse macroeconomic factors have resulted, among other matters, in tightening in the debt and equity markets, and high levels of inflation. For example, tightening of the equity markets, makes it more difficult to raise capital at a reasonable valuation or at all. In addition, the U. S. Bureau of Labor Statistics has reported for the period from **December** ~~June 2021 to June~~ 2022 **to December 2023** , the Consumer Price Index for All Urban Consumers rose ~~9~~ **3** . **4 %** ~~1 percent,~~ which ~~is~~ **remains above** the **U. S. Federal Reserve' s inflation** ~~largest~~ **target of 2 %. If inflationary pressures** increase ~~since the 12 month period ended November 1981. The U. S. Bureau of Labor Statistics reported for~~ **or** ~~the period from December 2021 to December 2022, the Consumer Price Index for All Urban Consumers increased 6. 5 percent. If the inflationary pressure continues~~ **continue** for a prolonged period, it may continue to result in increased costs of labor, cost of clinical trials, and costs of manufacturing which could adversely affect our results of operations. **In addition, unrest in the banking sector has in the past and may in the future have an effect on our ability to access funds when needed.** Our ability to use our net operating loss carryforwards may be limited. As of December 31, ~~2022~~ **2023** , we had U. S. federal and state net operating loss (" NOL ") carryforwards of approximately $ ~~436~~ **473** . 6 million and $ ~~203~~ **189** . ~~3~~ **0** million, respectively. As of December 31, ~~2022~~ **2023** , we also had federal and state tax credits of $ **9.** 5 ~~. 6~~ million and $ ~~1~~ **2** . ~~9~~ **2** million, respectively, which may be used to offset future tax liabilities. The NOL and tax credit carryforwards will expire at various dates through ~~2042~~ **2043** , except for $ ~~240~~ **277** . 9 million of federal NOL carryforwards which may be carried forward indefinitely. Sections 382 and 383 of the Internal Revenue Code and similar provisions under state law limits the annual use of NOL carry- forwards and tax credit carryforwards, respectively, following an ownership change pursuant to section 382 of the Internal Revenue Code and similar state provisions. In general, an ownership change occurs for purposes of Section 382 if there are certain cumulative changes in the ownership interest of significant stockholders over a three- year period in excess of 50 %. ~~Based~~ **47Based** on our analysis under Section 382, we believe that our federal NOL carryforwards, state NOL carryforwards, research and development credits, and orphan drug credits are limited by Section 382 and similar provisions under state law as of December 31, ~~2022~~ **2023** . The portion of federal NOL carryforwards, state NOL carryforwards, research and development credits, and orphan drug credits that were determined to be limited by Section 382 and similar provisions under state law have been written off as of December 31, ~~2022~~ **2023** . Future changes in our stock ownership, some of which are outside of our control, could result in ownership changes in the future. We may not be able to use some or all of our NOL and tax credit carryforwards, even if we attain profitability. ~~47Risks~~ -- **Risks** Related to Our IndebtednessOur level of indebtedness and debt service obligations could adversely affect our financial condition and may make it more difficult for us to fund our operations. In March 2022, we entered into a Loan Agreement with Oxford, as collateral agent and a lender, and Oxford Finance Credit Fund III LP, as a lender (" OFCF III " and together with Oxford, the " Lenders "), pursuant to which the Lenders have agreed to lend us up to an aggregate principal amount of $ 150. 0 million in a series of term loans (the " Term Loans "). As of December 31, ~~2022~~ **2023** , there was $ ~~25~~ **40** . 0 million outstanding under the Loan Agreement. In connection with the Loan Agreement, we granted Oxford a security interest in all of our personal property now owned or hereafter acquired, excluding intellectual property (but including the right to payments and proceeds of intellectual property), and a negative pledge on intellectual property. This indebtedness may create additional financing risk for us, particularly if our business or prevailing financial market conditions are not conducive to paying off or refinancing our outstanding debt obligations at maturity. This indebtedness could also have other important negative consequences, including we will need to repay our indebtedness by making payments of interest and principal, which will reduce the amount of money available to finance our operations, our research and development efforts and other general corporate activities. To the extent additional debt is added to our current debt levels, the risks described above could increase. We may not have cash available in an amount sufficient to enable us to make interest or principal payments on our indebtedness

when due. Failure to satisfy our current and future debt obligations under the Loan Agreement or breaching any covenants under the Loan Agreement, subject to specified cure periods with respect to certain breaches, could result in an event of default and, as a result, could accelerate all of the amounts due. In the event of an acceleration of amounts due under the Loan Agreement, we may not have enough available cash or be able to raise additional funds through equity or debt financings to repay such indebtedness at the time of such acceleration. In that case, we may be required to delay, limit, reduce or terminate our product candidate development or grant to others the rights to develop and market our product candidates that we would otherwise prefer to develop and market internally. Oxford could also exercise its rights as collateral agent to take possession and dispose of the collateral securing the term loans for its benefit, which collateral includes substantially all of our property other than our intellectual property. Our business, financial condition and results of operations could be materially adversely affected as a result of any of these events. Risks Related to Our Dependence on Third PartiesWe rely in part on third parties to conduct our clinical trials and preclinical testing, and if they do not properly and successfully perform their obligations to us, we may not be able to obtain regulatory approvals for and commercialize any of our other product candidates. We rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators, to conduct, provide monitors for, and manage data from all of our clinical trials. We compete with many other companies for the resources of these third parties. ~~Any~~ **48Any** of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities and ultimately the commercialization of our product candidates. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA and other regulatory agencies require us to comply with standards, commonly referred to as Good Clinical Practices ~~(" GCP ")~~ for conducting, recording, and reporting the results of clinical trials to assure ~~48that~~ -- **that** data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators, and trial sites. If we or any of our CROs fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or other regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements. We also are required to register ongoing clinical trials and post the results of completed clinical trials on government- sponsored databases, such as ClinicalTrials. gov, within certain timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for some of our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. We rely on third parties to conduct investigator- sponsored clinical trials of our product candidates. Any failure by a third party to meet its obligations with respect to the clinical development of our product candidates may delay or impair our ability to obtain regulatory approval for our product candidates. We rely on academic and private non-academic institutions to conduct and sponsor clinical trials relating to our product candidates. We will not control the design or conduct of the investigator sponsored trials, and it is possible that the FDA or non- U. S. regulatory authorities will not view these investigator- sponsored trials as providing adequate support for future clinical trials, whether controlled by us or third parties, for any one or more reasons, including elements of the design or execution of the trials or safety concerns or other trial results. Such arrangements will provide us certain information rights with respect to the investigator sponsored trials, including access to and the ability to use and reference the data, including for our own regulatory filings, resulting from the investigator-sponsored trials. However, we do not have control over the timing and reporting of the data from investigator- sponsored trials, nor do we own the data from the investigator- sponsored trials. If we are unable to confirm or replicate the results from the investigator sponsored trials or if negative results are obtained, we would likely be further delayed or prevented from advancing further clinical development of our product candidates. Further, if investigators or institutions breach their obligations with respect to the clinical development of our product candidates, or if the data proves to be inadequate compared to the firsthand knowledge we might have gained had the investigator- sponsored trials been sponsored and conducted by us, then our ability to design and conduct any future clinical trials ourselves may be adversely affected. Additionally, the FDA or non- U. S. regulatory authorities may disagree with the sufficiency of our right of reference to the preclinical, manufacturing, or clinical data generated by these investigator- sponsored trials, or our interpretation of preclinical, manufacturing, or clinical data from these investigator- sponsored trials. If so, the FDA or other non- U. S. regulatory authorities may require us to obtain and submit additional preclinical, manufacturing, or clinical data before we may initiate our planned trials and / or may not accept such additional data as adequate to initiate our planned trials. ~~We~~ **49We** contract with third parties for the manufacture of our product candidates and for compound formulation research, and these third parties may not perform satisfactorily. We do not have any manufacturing facilities or personnel. We currently obtain all of our supply of our product candidates for clinical development from third- party manufacturers or third- party collaborators, and we expect to continue to rely on third parties for the manufacture of clinical quantities of our product candidates. In addition, we currently rely on third parties for the development of various formulations of our product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost or quality, which could delay, prevent, or impair our development or commercialization efforts. ~~49We~~ **We** do not currently have arrangements in place for redundant supply or a second source for bulk drug substance or drug product. Even though we have supply agreements in place with our third- party manufacturers, reliance on third- party manufacturers entails additional risks, including: ● reliance on the third party for regulatory compliance and quality assurance; ● the possible breach of the manufacturing agreement by the third

party, including the misappropriation of our proprietary information, trade secrets, and know- how; ● the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and ● disruptions to the operations of our manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier or a catastrophic event affecting our manufacturers or suppliers. Third- party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third- party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products and harm our business and results of operations. Any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any interruption of the development or operation of the manufacturing facilities due to, among other reasons, events such as order delays for equipment or materials, equipment malfunction, quality control, and quality assurance issues, regulatory delays and possible negative effects of such delays on supply chains and expected timelines for product availability, production yield issues, shortages of qualified personnel, discontinuation of a facility or business, failure, or damage to a facility by natural disasters or public health crises, such as the COVID- 19 pandemic, could result in the cancellation of shipments, loss of product in the manufacturing process, or a shortfall in available product candidates or materials. If our current contract manufacturers cannot perform as agreed or these parties cease to provide quality manufacturing and related services to us, we may be required to replace that manufacturer. If we are not able to engage appropriate replacements in a timely manner, our ability to manufacture our product candidates in sufficient quality and quantity required for planned pre- clinical testing, clinical trials and potential commercial use of our product candidates would be adversely affected. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement, as well as producing the drug product and obtaining regulatory approvals for the new manufacturer. In addition, we have to enter into technical transfer agreements and share our know- how with the third- party manufacturers, which can be time consuming and may result in delays. In light of the lead time needed to manufacture our product candidates, and the availability of underlying materials, we may not be able to, in a timely manner or at all, establish or maintain sufficient commercial manufacturing arrangements on commercially reasonable terms necessary to provide adequate supply of our product candidates to meet demands that exceed our clinical assumptions. Furthermore, we may not be able to obtain the significant financial capital that may be required in connection with such arrangements. Even after successfully engaging third parties to execute the manufacturing ~~process~~ **50process** for our product candidates, such parties may not comply with the terms and timelines they have agreed to for various reasons, some of which may be out of their or our control, which could impact our ability to execute our business plans on expected or required timelines in connection with the commercialization of and the continued development of our product candidates. We may also be required to enter into long- term manufacturing agreements that contain exclusivity provisions and / or substantial termination penalties, which could have a material adverse effect on our business prior to and after commercialization. Our current and anticipated future dependence upon others for the manufacture of our other 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. ~~50If~~ **If** we are not able to establish collaborations, we may have to alter our development and commercialization plans. Our drug development programs and the potential commercialization of our product candidates will require additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator' s resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator ~~'~~**'** s evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, and the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. Collaborations are complex and time consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of certain product candidates, reduce or delay our development programs, delay potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue. We may depend on collaborations with third parties for the development and commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of our product candidates. We may seek third- party collaborators for the development and commercialization of our product candidates. Our likely collaborators for any collaboration arrangements include large and mid- size pharmaceutical companies, regional and national pharmaceutical companies, and biotechnology companies. If we do enter

into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators ~~'~~ **'** abilities to successfully perform the functions assigned to them in these arrangements. ~~Collaborations~~ **51Collaborations** involving our product candidates would pose the following risks to us: ● collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations; ● collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator' s strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates 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 or product ~~51candidates~~ -- **candidates** if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours; ● a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products; ● collaborators may not properly 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 proprietary information or expose us to potential litigation; ● disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and ● collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates. Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. Our operations in foreign jurisdictions, and those of third parties for which we rely on, may be impacted by economic, political and social conditions in such jurisdictions. ~~Tensions~~ **Our business could be adversely affected by conditions the adverse geopolitical and macroeconomic developments, including the military conflict** between ~~the~~ Ukraine and Russia ~~have~~ **, the ongoing military conflict in the Middle East, and any** ~~escalated~~ --- **related sanctions** ~~in recent months, culminating in Russia' s recent invasion of the Ukraine~~ . While we do not currently have clinical trials in Ukraine ~~or~~ **,** Russia **, or Middle East** , we have clinical trial sites in Europe. We also source clinical supply for our product candidates from third party contract manufacturing organizations in Europe. **Additionally, GenFleet intends to file an IND for the lead oncology program in first half of 2024 in China and expects the Phase 1 clinical trial to be conducted in China. For such activities conducted in China, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the policies of the U. S. or Chinese governments, political unrest or unstable economic conditions including sanctions on China or any of our China- based counterparties.** Furthermore, **the conflicts between Ukraine** ~~Seeura' s sublicensee, Sanofi, has exclusive rights to develop~~ and ~~commercialize products containing duvelisib in~~ Russia, the **ongoing military conflict in** ~~Commonwealth of Independent States (" CIS ") including Ukraine, Turkey,~~ the Middle East **,** and ~~Africa (collectively~~ the **associated** ~~" Sanofi Territory ") for which we are entitled to receive future milestones and royalties pursuant to the Seeura APA. The invasion of Ukraine and the retaliatory~~ measures taken or that may be taken by the United States, North Atlantic Treaty Organization (" NATO ") and others create global security concerns, including the possibility of expanded regional or global conflict, and are likely to have short- term and likely longer- term negative impacts on regional and global economies, any or all of which could disrupt our supply chain, **and** adversely affect our ability to conduct ongoing and future clinical trials of our product candidates ~~, and the recognition of future milestones and royalties pursuant to the Seeura APA in the Sanofi Territory~~ . Risks Related to Our Intellectual PropertyIf we fail to comply with our obligations under our intellectual property licenses with third parties, we could lose license rights that are important to our business. We are a party to a number of intellectual property license agreements with third parties, including Pfizer and Chugai, and expect to enter into additional license agreements in the future. Our existing license agreements ~~impose~~ **52impose** , and we expect that future license agreements will impose, various diligence, milestone payment, royalty, insurance, and other obligations on us. For example, under our license agreements with Pfizer and Chugai, we are required to use diligent or commercially reasonable efforts to develop and commercialize licensed products under the agreement and to satisfy other specified obligations. If we fail to comply with our obligations under these licenses, our licensors may have the right to terminate these license agreements, in which event we might not be able to market any product that is covered by these agreements, or to convert the exclusive licenses to non-exclusive licenses, which could materially adversely affect the value of the product candidate being developed under these license agreements. Termination of these license agreements or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms, which may not be possible. If Pfizer were to terminate its license agreement with us for any reason, we would lose our rights to defactinib. If Chugai were to terminate its license agreement with us for any reason, we could lose our rights to avutometinib. **In addition, we rely on certain of our licensors to prosecute patent applications and maintain patents and otherwise protect the intellectual property we license from them and may continue to do so in the future. We have limited control over these 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 any licensors' infringement proceeding, or defense activities may be less vigorous than had we conducted them ourselves.** If we are unable to obtain and maintain patent protection for our products, or if our licensors are unable to obtain and maintain patent protection for the products that we

license from them, or if the scope of the patent ~~52protection~~ -- **protection** obtained is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our products may be adversely affected. Our success depends in large part on our and our licensors **'** ~~'~~ ability to obtain and maintain patent protection in the United States and other countries with respect to our products **, their respective components, formulations, combination therapies, methods used to manufacture them and methods of treatment and development that are important to our business. If we or our licensors do not adequately protect our or our licensors' intellectual property rights, competitors may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability** . We and our licensors seek to protect our proprietary position by filing patent applications in the United States and abroad related to our products that are important to our business. We **may in the future also license or purchase patent applications filed by others. If we or our licensors are unable to secure or maintain patent protection with respect to our products and any proprietary products and technology we develop, our business, financial condition, results of operations, and prospects could be materially harmed. We also** cannot be certain that any patents will issue with claims that cover our ~~product~~ **products** ~~candidates~~ **. If the scope of the patent protection we or our licensors obtain is not sufficiently broad, we may not be able to prevent others from developing and commercializing products and technology similar or identical to ours. The degree of patent protection we require to successfully compete in the marketplace may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our or our licensors' patents have, or that any of our or our licensors' pending patent applications that mature into issued patents will include, claims with a scope sufficient to protect our products or otherwise provide any competitive advantage. In addition, to the extent that we license intellectual property, we cannot make assurances that those licenses will remain in force. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed (21 years if first filed as a provisional application). Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Even if they are unchallenged, our or our licensors' patents and pending patent applications, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our or our licensors' patent claims to circumvent our patents by developing similar or alternative technologies or therapeutics in a non- infringing manner. For example, a third party may develop a competitive therapy that provides benefits similar to 53our products but that uses a formulation and / or a method that falls outside the scope of our patent protection. If the patent protection provided by the patents and patent applications we hold, license, or pursue with respect to our products is not sufficiently broad to impede such competition, our ability to successfully commercialize our products could be negatively affected, which would harm our business. Similar risks would apply to any patents or patent applications that we may own or license** . The patent prosecution process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner **. 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 do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering products that we license from third parties and are reliant on our licensors. Therefore, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. If such licensors fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated. The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability, and commercial value of our and our licensors **'** ~~'~~ patent rights are highly uncertain. Our and our licensors **'** ~~'~~ pending and future patent applications may not result in patents being issued which protect our products or which effectively prevent others from commercializing competitive products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the ~~value of~~ our ~~patents~~ **ability to protect our inventions, maintain and enforce our intellectual property rights,** or narrow the scope of our patent protection **, or affect the value of our intellectual property** . The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases, at all. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions. Assuming the other requirements for patentability are met, in the United States, for patents that have an effective filing date prior to March 15, 2013, the first to make the claimed invention is entitled to the patent, while outside the United States, the first to file a patent application is entitled to the patent. In March 2013, the United States transitioned to a first inventor to file system in which, assuming the other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent. We may be subject to a third- party pre- issuance submission of prior art to the U. S. Patent and Trademark Office, or become involved in opposition, derivation, reexamination, inter parties review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding, or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third- party patent rights. Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us, or otherwise provide us with any competitive advantage. **The scope of the invention claimed in a patent application**

can be significantly reduced before the patent is issued, and this scope can be reinterpreted after issuance. Even where patent applications we currently own, license, or that we may license in the future issue as patents, they may not issue in a form that will provide us with adequate protection to prevent competitors or other third parties from competing with us, or otherwise provide us with a competitive advantage. Any patents that eventually issue may be challenged, narrowed or invalidated by third parties. Consequently, we do not know whether any of our products will be protectable or remain protected by valid and enforceable patent rights. Our competitors **or other third parties** may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non- infringing manner. ~~The~~ **54The** issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. **There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. We may in the future, become subject to a third- party pre- issuance submission of prior art or opposition, derivation, revocation, re- examination, post- grant and inter partes review, or interference proceeding and other similar proceedings challenging our patent rights or the patent rights of others in the USPTO or other foreign patent office.** Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical products, or limit the duration of the patent protection of our products. **In addition,** ~~Given~~ **given** the amount of time required for the development, testing, and regulatory review of new ~~product~~ **products** ~~candidates~~, patents protecting such ~~candidates~~ **products** might ~~53expire~~ -- **expire** before or shortly after such ~~candidates~~ **products** are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. ~~the institution' s~~ **.We may not be successful in obtaining necessary** rights **to compounds and product candidates for our development pipeline through acquisitions and** in ~~technology resulting~~ **- licenses.We may seek to acquire new compounds and product candidates** from ~~the~~ **other** ~~collaboration.Regardless of~~ **pharmaceutical and biotechnology companies,academic scientists and other researchers,** such ~~option~~ **as our exclusive in- license from Pfizer** , **and Chugai** ~~we may be unable~~ to **research,develop,commercialize,and manufacture products in oncology indications containing defactinib and avutometinib,respectively.The success of this strategy depends partly upon our ability to identify,select,discover and acquire promising pharmaceutical product candidates and products.The process of proposing,** ~~negotiate~~ **negotiating and implementing** a license **or acquisition of a product candidate or approved product is lengthy and complex.Other companies,including some** ~~within~~ -- **with** ~~the specified timeframe~~ **substantially greater financial,marketing,and sales resources,may compete with us** ~~or~~ **for** ~~under terms~~ **the license or acquisition of product candidates and approved products.In addition,companies** that **perceive** ~~are acceptable to~~ us ~~.If we are unable~~ to **be a competitor** ~~do so,the institution~~ may ~~offer the intellectual property~~ **be unwilling to assign or license** rights to ~~others,potentially blocking~~ **us.We have limited resources to identify and execute the acquisition** ~~our~~ - **or in- licensing of** ~~ability to pursue our program.If we are unable to successfully obtain rights to required~~ third- ~~56party 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~~ products ~~.More established companies may have a competitive advantage over us due to their size~~ , **businesses** ~~cash resources~~ and **technologies** ~~greater clinical development~~ and ~~commercialization capabilities~~ **integrate them into our current infrastructure** .Moreover,we may devote resources to potential acquisitions or in- licensing opportunities that are never completed,or we may fail to realize the anticipated benefits of such efforts.We also may be unable to license or acquire the relevant compound or product candidate on terms that would allow us to make an appropriate return on our investment.Any product candidate that we acquire may require additional development efforts prior to commercial sale,including manufacturing,pre- clinical testing,extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities.All product candidates are prone to risks of failure typical of pharmaceutical product development.In addition,future product or business acquisitions may entail numerous operational and financial risks,including:● exposure to unknown liabilities;● disruption of our business and diversion of our management ~~'~~ **'** s time and attention to develop acquired products,product candidates,or technologies;● higher than expected acquisition and integration costs;● increased amortization expenses;and ● incurrence of substantial debt,dilutive issuances of securities or depletion of cash to pay for acquisitions. Future business acquisitions may also entail certain additional risks,such as:● difficulty in combining the operations and personnel of any acquired businesses with our operations and personnel;● impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership;and ● inability to motivate key employees of any acquired businesses ~~. Obtaining and maintaining our patent protection depends on compliance with various procedural,document submission,fee~~ We may become involved in lawsuits to protect or enforce our patents, 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 a patent of ours is invalid or 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 proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly **and could put our patent applications at risk of not issuing. Defense against these assertions, non- infringement, invalidity or unenforceability regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may**

have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. Post- grant proceedings provoked by third parties or brought by the USPTO may be brought to determine the validity or priority of inventions with respect to our patents or 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 post- grant proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, 59misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as those within 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 this type of litigation. In addition, our licensors may have rights to file and prosecute such claims, and we are reliant on them. Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. Our commercial success depends upon our ability and the ability of our collaborators to commercialize, develop, manufacture, market, and sell our ~~product~~ **products** ~~candidates~~ without infringing the proprietary rights of third parties. We have yet to conduct comprehensive freedom to operate searches to determine whether our use of certain of the patent rights owned by or licensed to us would infringe patents issued to third parties. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products, including interference proceedings before the U. S. Patent and Trademark Office. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third party ' **'** s intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non- exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing product. In addition, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our ~~product~~ **products** ~~candidates~~ or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business **. If a third party alleges that we infringe its intellectual property rights, we may face a number of issues, including, but not limited to: ● infringement and other intellectual property misappropriation 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 or misappropriation, which we may have to pay if a court decides that the product or technology at issue infringes on or violates the third- party' s rights, and, if the court finds we have willfully infringed intellectual property rights, we could be ordered to pay treble damages and the patent owner' s attorneys' fees; ● an injunction prohibiting us from manufacturing, marketing or selling our products, or from using our proprietary technologies, unless the third party agrees to license its patent rights to us; ● even 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 protecting our products; and ● we may be forced to try to redesign our products or processes so they do not infringe third- party intellectual property rights, an undertaking which may not be possible or which 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. Patents issued in the United States by law enjoy a presumption of validity that can be rebutted only with evidence that is 60 " clear and convincing, " a heightened standard of proof. There may be issued third- party patents of which we are currently unaware with claims to compositions, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our products. Patent applications can take many years to issue. There may be currently pending patent applications which may later result in issued patents that may be infringed by our products. Moreover, we may fail to identify relevant patents or incorrectly conclude that a patent is invalid, not enforceable, exhausted, or not infringed by our activities. If any third- party patents, held now or obtained in the future by a third party, were found by a court of competent jurisdiction to cover the manufacturing process of our products, constructs or molecules used in or formed during the manufacturing process, or any final product or methods use of the product, the holders of any such patents may be able to block our ability to commercialize the product 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 any aspect of our formulations, any combination therapies or patient selection methods, the holders of any such patent may be able to block our ability to develop and commercialize the product 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 products 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 patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize our products. 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 products. Defense of these claims, regardless of their merit, could involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need or may choose to obtain licenses from third parties to advance our research or allow commercialization of our products. 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 products, which could harm our business significantly. We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property. We generally enter into confidentiality and intellectual property assignment agreements with our employees, consultants, and contractors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, those agreements may not be honored and may not effectively assign intellectual property rights to us. Moreover, there may be some circumstances, where we are unable to negotiate for such ownership rights. Disputes regarding ownership or inventorship of intellectual property can also arise in other contexts, such as collaborations and sponsored research. If we are subject to a dispute challenging our rights in or to patents or other intellectual property, such a dispute could be expensive and time- consuming. If we were unsuccessful, we could lose valuable rights in intellectual property that we regard as our own . We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers. Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees 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 these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee ~~'~~ **'** s former employer. 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~~ **61property** rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management. Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities. Even if resolved in our favor, 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 ~~54negative~~ -- **negative** , it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. In addition to seeking patents for some of our products, we also rely on trade secrets, including unpatented know- how, technology, and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non- disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. **These parties may also be subject to cyberattacks that result in such information becoming available to competitors, including in jurisdictions where we or such parties may not be able to enforce our rights.** Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time consuming, and the outcome is unpredictable **. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results and financial condition. 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** . In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets **. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad** . If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed. **If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our marks of interest and our business may be adversely affected. Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be**

infringing on other marks. We rely on both registration and common law protection for our trademarks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During the trademark registration process, we may receive Office Actions from the USPTO objecting to the registration of our trademark. Although we would be given an opportunity to respond to those objections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and / or to seek the cancellation of registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our 62trademarks may not survive such proceedings. 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. European patents and patent applications could be challenged in the recently created Unified Patent Court for the European Union. Our owned or our licensors' European patents and patent applications could be challenged in the recently created Unified Patent Court (" UPC ") for the European Union. We may decide to opt out our European patents and patent applications from the UPC. However, if certain formalities and requirements are not met, our European patents and patent applications could be challenged for non- compliance and brought under the jurisdiction of the UPC. We cannot be certain that our or our licensors' European patents and patent applications will avoid falling under the jurisdiction of the UPC, if we decide to opt out of the UPC. Under the UPC, a granted European patent would be valid and enforceable in numerous European countries. A successful invalidity challenge to a European patent under the UPC would result in loss of patent protection in those European countries. Accordingly, a single proceeding under the UPC could result in the partial or complete loss of patent protection in numerous European countries, rather than in each validated European country separately as such patents always have been adjudicated. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize our technology and products and, resultantly, on our business, financial condition, prospects and results of operations. Risks Related to Achieving Regulatory Approval of Our Product Candidates and Other Legal Compliance MattersIf we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our product candidates, we will not be able to commercialize such candidates, and our ability to generate revenue will be materially impaired. Obtaining approval of an NDA can be a lengthy, expensive, and uncertain process. The activities associated with a product candidate ~~'~~**'** s development and commercialization, including its design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, and distribution are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain marketing approval for product candidates will prevent us from commercializing such product candidates. We have not received approval to market any of our current product candidates from regulatory authorities in any jurisdiction in the United States. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third- party contract research organizations to assist us in this process. Securing FDA approval requires the submission of extensive preclinical and clinical data and supporting information to the FDA for each therapeutic indication to establish the product candidate ~~'~~**'** s safety and efficacy. Securing FDA approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the FDA. A product candidate may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity, and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA has substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical, or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing ~~55could --~~ **could** delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be subject to more limited indications than those we propose or subject to restrictions or post approval commitments that render the approved product not commercially viable. ~~If~~ **63If** we experience delays in obtaining approval or if we fail to obtain approval of a product candidate, its commercial prospects may be harmed and our ability to generate revenues will be materially impaired. We have received orphan drug designation for certain of our product candidates, but there can be no assurance that we will be able to prevent third parties from developing and commercializing products that are competitive to these product candidates. We received orphan drug designation in the United States ~~and~~ **, the** European Union **, and Australia** for the use of defactinib in ovarian cancer, and in the United States, the European Union, and Australia for the use of defactinib in mesothelioma. Orphan drug exclusivity grants seven years of marketing exclusivity under the ~~Federal Food, Drug and Cosmetic Act (" FDCA ")~~, up to ten years of marketing exclusivity in Europe, and five years of marketing exclusivity in Australia. Other companies have received orphan drug designations for compounds other than defactinib for the same indications for which we may have received orphan drug designation in corresponding territories. While orphan drug exclusivity for defactinib provides market exclusivity against the same active ingredient for the same indication, we would not be able to exclude other companies from manufacturing and / or selling drugs using the same active ingredient for the same indication beyond that timeframe on the basis of orphan drug exclusivity. Furthermore, the marketing exclusivity in Europe can be reduced from ten years to six years if the orphan designation criteria are no longer met or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Even if we are the first to obtain marketing authorization for an orphan drug indication, there are circumstances under which the FDA may approve a competing product for the same indication during the seven- year

period of marketing exclusivity, such as if the later product is the same compound as our product but is shown to be clinically superior to our product, or if the later product is a different drug than our product candidate. Further, the seven- year marketing exclusivity would not prevent competitors from obtaining approval of the same compound for other indications or of another compound for the same use as the orphan drug. A decision in 2021 by the U. S. Court of Appeals for the Eleventh Circuit in Catalyst Pharmaceuticals, Inc. vs. Becerra regarding interpretation of the Orphan Drug Act' s exclusivity provisions as applied to drugs and biologics approved for orphan indications narrower than the product' s orphan designation has the potential to significantly broaden the scope of orphan exclusivity for such products. FDA announced on January 24, 2023 that despite the Catalyst decision, it will continue to apply its longstanding regulations, which tie the scope of orphan exclusivity to the uses or indications for which the drug is approved, rather than to the designation. FDA' s application of its orphan drug regulations post- Catalyst could be the subject of future legislation or to further challenges in court, which could impact our ability to obtain or seek to work around orphan exclusivity, and might affect our ability to retain orphan exclusivity that the FDA previously has recognized for our products. We **have sought and obtained fast track designation from the FDA for one of our product candidates, and** may seek **such** fast track designation for one ~~or~~ more **additional** ~~of our~~ product candidates, but we might not receive such **additional** designation, and ~~even if we do,~~ such designation may not actually lead to a faster development or regulatory review or approval process ~~, and~~ **nor does** it ~~does not~~ ensure that we will receive marketing approval. Any sponsor may seek fast track designation for a drug if it is intended for the treatment of a serious condition and nonclinical or clinical data demonstrate the potential to address unmet medical need for this condition, a drug sponsor may apply for FDA fast track designation. ~~If we~~ **In January 2024, the FDA granted fast track designation for combination of avutometinib and LUMAKRAS for the treatment of patients with KRAS G12C- mutant metastatic NSCLC who have received at least one prior systematic therapy and have not been previously treated with a KRAS G12C inhibitor. We may also** seek fast track designation for ~~a~~ **additional** product ~~candidate~~ **candidates** , **which** we may not receive ~~it~~ from the FDA. However ~~, even if we receive fast track designation~~ , fast track designation does not ensure that we will receive marketing approval or that approval will be granted within any particular timeframe. We may not experience a faster development or regulatory review or approval process with fast track designation compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA ~~'~~ **'** s priority review procedures. ~~Any~~ **64Any** product candidate for which we obtain marketing approval could be subject to restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved. ~~56Any~~ -- **Any** product candidate for which we obtain marketing approval, along with the manufacturing processes, post approval clinical data, labeling, advertising, and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control, quality assurance, and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post marketing testing and surveillance to monitor the safety or efficacy of the product, including the imposition of a REMS. The FDA closely regulates the post approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers ~~'~~ **'** communications regarding off label use, and if we do not market our products for their approved indications, we may be subject to enforcement action for off label marketing. In addition, later discovery of previously unknown problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including: ● restrictions on such products, manufacturers, or manufacturing processes; ● restrictions on the labeling or marketing of a product; ● restrictions on product distribution or use; ● requirements to conduct post marketing clinical trials; ● warning or untitled letters; ● withdrawal of the products from the market; ● refusal to approve pending applications or supplements to approved applications that we submit; ● recall of products; ● fines, restitution, or disgorgement of profits or revenue; ● suspension or withdrawal of marketing approvals; ● refusal to permit the import or export of our products; ● product seizure; or ● injunctions or the imposition of civil or criminal penalties. The FDA ~~'~~ **'** s and other regulatory authorities ~~'~~ **'** policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. 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 fail to obtain any marketing approvals, lose any marketing approval that we may have obtained and we may not achieve or sustain profitability. Our business operations, including our relationships with healthcare providers, third- party payors, and patients, 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, including physicians, and third- party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our ~~future~~ arrangements with healthcare providers, third- party payors, patients and other parties within the healthcare industry may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell, and distribute any products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare and regulatory ~~laws~~ **65laws** and regulations within the United States include the following **, some of which will apply only if and when we have a marketed product** : ● the federal healthcare anti- kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in ~~57kind~~ -- **kind** , to induce or reward either the referral of

an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the anti- kickback statute or specific intent to violate it in order to have committed a violation; ● the federal False Claims Act (" FCA "), which imposes criminal and civil penalties on individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government and actions under the FCA may be brought by private whistleblowers as well as the government. In addition, the government may assert that a claim including items and services resulting from a violation of the federal anti- kickback statute constitutes a false or fraudulent claim for purposes of the FCA; ● the federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer of remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary ~~'~~**'** s selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state healthcare program; ● the federal Health Insurance Portability and Accountability Act of 1996 (" HIPAA "), as amended, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also establishes requirements related to the privacy, security, and transmission of individually identifiable health information which apply to many healthcare providers, physicians, and third- party payors with whom we interact; ● the federal false statements statute prohibits knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; ● the federal anti- kickback prohibition known as Eliminating Kickbacks in Recovery Act, or EKRA, which prohibits certain payments related to referrals of patients to certain providers (recovery homes, clinical treatment facilities, and laboratories) and applies to services reimbursed by private health plans as well as government health care programs; ● the FDCA, which, among other things, strictly regulates drug product and medical device marketing, prohibits manufacturers from marketing such products for off- label use and regulates the distribution of samples; ● federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under governmental healthcare programs; ● federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; ● **state medical privacy and comprehensive privacy statutes, which regulate the privacy and security of personal information; ●** the so- called federal ~~"~~**"** ~~"~~**"** sunshine law ~~"~~**"** ~~"~~**"** or Open Payments which requires manufacturers of drugs, devices, biologics, and medical supplies to report to the Centers for Medicare & Medicaid Services information related to payments and other transfers of value to teaching hospitals, physicians, and other healthcare practitioners, as well as ownership and investment interests held by physicians and their immediate family members; and ● analogous state laws and regulations, such as state anti- kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third- party payors, including private insurers, and state laws which regulate interactions between pharmaceutical companies and healthcare providers, require pharmaceutical companies to comply with the pharmaceutical industry ~~'~~**'** s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, require pharmaceutical companies to report information on transfers of value to other healthcare providers, marketing ~~expenditures~~ **66expenditures** or pricing information and / or require licensing of sales representatives. State laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. ~~58Similar~~ -- **Similar** healthcare and data privacy laws and regulations exist in the European Union and other foreign jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers and laws governing the privacy and security of certain protected information. For example ~~, in May 2018, a new privacy regime~~ , the General Data Protection Regulation (" GDPR "), **impose** ~~took effect enhancing our~~ obligations with respect to operations in the European Economic Area (" EEA "), and increasing the scrutiny applied to transfers of personal data from the EEA (including health data from our clinical sites in the EEA) to countries that are considered by the European Commission to lack an adequate level of data protection, such as the United States. The compliance obligations imposed by the GDPR have required us to revise our operations and increased our cost of doing business. In addition, the GDPR ~~imposes~~ **provides for** substantial fines for breaches of data protection requirements, and it confers a private right of action on data subjects for breaches of data protection requirements. In connection with the separation from the European Union, the United Kingdom adopted similar legislation **, and many other countries and more than twelve U. S. states have adopted comprehensive data privacy laws that may increase the costs of compliance, inhibit the sharing of personal data across national boundaries, and impact operations** . The number and complexity of both federal and state laws continues to increase; the laws contain ambiguous requirements or require administrative guidance for implementation; government interpretations of the laws continue to evolve; and additional governmental resources are being used to enforce these laws and to prosecute companies and individuals who are believed to be violating them. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Governmental authorities may potentially conclude that our business practices, including arrangements we may have with physicians and other healthcare providers, or patient assistance programs, may not comply with ~~current or future statutes, regulations or case law involving~~ applicable ~~fraud and abuse or other healthcare~~ laws ~~and regulations~~ . If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, 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, and the curtailment or restructuring of our operations. If any of the physicians or other 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 criminal, civil, or administrative sanctions, including exclusions from

government funded healthcare programs. Further, defending against any such actions can be costly, time- consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Our employees, independent contractors, principal investigators, CROs, consultants, and vendors may engage in misconduct or other improper activities, including non- compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation. We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in fraud or other misconduct, including intentional failures to: comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards, or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions. ~~Rccently~~ **67Recently** enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain. In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, ~~59among~~ -- **among** other things, prevent or delay marketing approval of our product candidates, restrict or regulate post approval activities, and affect our ability to profitably sell any of our product candidates for which we obtain marketing approval. The U. S. healthcare industry generally and U. S. government healthcare programs in particular are highly regulated and subject to frequent and substantial changes. The U. S. government and individual states have been aggressively pursuing healthcare reform. For example, the **ACA** ~~Healthcare Reform Act~~ , enacted in March 2010, was intended to broaden access to health insurance through a Medicaid expansion and the implementation of the individual mandate for health insurance coverage, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry, and impose additional health policy reforms. The law, for example, increased drug rebates under state Medicaid programs for brand name prescription drugs and extended those rebates to Medicaid managed care and assessed a fee on manufacturers and importers of brand name prescription drugs reimbursed under certain government programs, including Medicare and Medicaid. **Beyond the ACA,** ~~There~~ **there are ongoing and widespread health care reform efforts, a number of which have focused on regulation of prices or payment for drug products. Drug pricing and payment reform has been a focus of the Biden Administration. For example, federal legislation enacted in 2021 eliminates a statutory cap on Medicaid drug rebate program rebates effective January 1, 2024. For example, federal legislation enacted in 2021 eliminates a statutory cap on Medicaid drug rebate program rebates effective January 1, 2024. As another example, the Inflation Reduction Act (" IRA ") of 2022 includes a number of changes intended to address rising prescription drug prices in Medicare Parts B and D, with varying implementation dates. These changes include caps on Medicare Part D out- of- pocket costs, Medicare Part B and Part D drug price inflation rebates, a new Medicare Part D manufacturer discount drug program (replacing the ACA Medicare Part D coverage gap discount program) and a drug price negotiation program for certain high spend Medicare Part B and D drugs (with the first list of drugs announced in 2023). Subsequent to the enactment of the IRA, in 2022, the Biden administration released an executive order directing the Department of Health and Human Services (" HHS ") to report on how the CMMI could be leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. The report was issued in 2023 and proposed various models that CMMI is currently developing which seek to lower the cost of drugs, promote accessibility, and improve quality of care, models are currently still in development. Healthcare reform efforts** have been ~~ongoing efforts~~ **and may continue** to **be subject to scrutiny and legal challenge.** ~~modify or repeal certain provisions of the Healthcare Reform Act~~ For example **, with respect to the ACA** , tax reform legislation was enacted ~~at the end of 2017~~ that eliminated the tax penalty **established** for individuals who do not maintain mandated health insurance coverage beginning in 2019 **and, in** ~~. The Healthcare Reform Act has also been subject to judicial challenge. In~~ 2021, the U. S. Supreme Court dismissed the **latest** ~~most recent~~ judicial challenge to the **ACA** ~~Healthcare Reform Act~~ brought by several states without specifically ruling on the constitutionality of the **ACA** ~~Healthcare Reform Act~~ . **As another example** ~~Beyond the Healthcare Reform Act~~ , **revisions to regulations under** ~~there~~ -- **the federal anti- kickback statute would remove protection** ~~have been ongoing health care reform efforts, some of which affect pricing or payment~~ for **traditional** ~~drug products. For example, legislation enacted in 2018 increased the discount that manufacturers of~~ Medicare Part D **discounts offered by pharmaceutical manufacturers to pharmacy benefit managers** ~~brand~~ -- **and health plans** ~~name drugs must provide to Medicare Part D beneficiaries during the coverage gap from 50 % to 70 % starting in 2019~~ . ~~The Biden Administration has focused~~ **Pursuant to court order, the removal was delayed and recent legislation imposed a moratorium** on **implementation** ~~increasing access to health care coverage as well as drug pricing and payment reform. As an example, legislation enacted in 2021 eliminates the statutory Medicaid drug rebate cap, currently set at 100 %~~ of **the rule until** ~~a drug' s average manufacturer price, for single source and innovator multiple source drugs, beginning~~ January ~~1, 2024~~ **2032** . As another example, ~~in 2022,~~ the ~~Inflation Reduction Act (~~ IRA ~~) of 2022 contains numerous drug pricing and payment reforms. Among other provisions, the IRA imposes a yearly cap ($ 2, 000 in 2025) on out- of- pocket prescription drug costs in Medicare Part D, implements a new Medicare Part~~

~~D manufacturer discount drug program in 2025; requires manufacturers to pay a rebate to the federal government if prices for single- source drugs and biologicals covered under Medicare Part B and nearly all covered drugs under Part D increase faster than the rate of inflation and, starting in 2026, creates a~~ drug price negotiation program **has been challenged in litigation filed** ~~under which the prices for certain high Medicare spend drugs and biologicals without generic or biosimilar competition will be limited~~ by ~~a cap that is~~ **various pharmaceutical manufacturers and industry groups. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations** ~~defined~~ **designed to control pharmaceutical product pricing, including price constraints, restrictions on copayment assistance** by ~~reference to~~ **pharmaceutical manufacturers** , ~~among~~ **marketing cost disclosure and transparency measures, and, in some cases, measures designed to encourage importation from** other **countries** ~~things, a specified non- federal average manufacturer price. We continue to evaluate federal~~ and **bulk purchasing** ~~state health care reform efforts and the effect that such efforts may have on our business. Healthcare reform measures that may be adopted in the future could have a material adverse effect on our industry generally and on our ability to successfully commercialize our products and product candidates~~ . In addition, other broader legislative changes have been adopted that could have an adverse effect upon, and could prevent, our products' commercial success. For example, the Budget Control Act of 2011, as amended, resulted in the imposition of reductions in Medicare (but not Medicaid) payments to providers in 2013 and remains ~~in~~ **68in** effect through ~~2031~~ **2032** ~~(except May 1, 2020 to March 31, 2022)~~ unless additional Congressional action is taken. Any significant spending reductions affecting Medicare, Medicaid or other publicly funded or subsidized health programs that may be implemented and / or any significant taxes or fees that may be imposed on us could have an adverse impact on our results of operations. **We** ~~Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price constraints, restrictions on copayment assistance by pharmaceutical manufacturers, marketing cost disclosure and transparency measures, and, in some cases, measures designed to encourage importation from other countries and bulk purchasing. 60We~~ cannot be sure whether additional legislative changes will be enacted, or whether the regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates may be. In addition, increased scrutiny by the U. S. Congress of the FDA' s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post marketing testing and other requirements. **We continue to evaluate federal and state health care reform efforts and the effect that such efforts may have on our business. Healthcare reform measures that may be adopted in the future could have a material adverse effect on our industry generally and on our ability to successfully commercialize any product candidates if and when approved. Disruptions at the FDA and other government agencies caused by funding shortages could prevent our product candidates from being developed, approved, or commercialized in a timely manner, or at all, which could negatively impact our business. The ability of the FDA and foreign regulatory authorities to review or approve new product candidates can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA' s or foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA' s or foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. For example, over the last several years, the U. S. federal government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. If a prolonged government shutdown occurs, preventing the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Separately, in response to the COVID- 19 pandemic, the FDA announced its intention to postpone most inspections of foreign and domestic manufacturing facilities and products at various points. Even though the FDA has since resumed standard inspection operations of domestic facilities where feasible, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID- 19 pandemic, and any resurgence of the virus, including as a result of the emergence of new variants may lead to further inspectional delays. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID- 19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting business as usual or conducting 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 effect on our business.** Risks Related to Employee Matters and Managing GrowthOur future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain and motivate qualified personnel. We are highly dependent on ~~Brian Stuglik~~ **the efforts and abilities of the principal members of our senior management and other key personnel** , **including Daniel Paterson, our President and** Chief Executive Officer and Daniel ~~Paterson~~ **Calkins** , our ~~President and~~ Chief ~~Operating~~ **Financial** Officer. Although we have formal employment agreements with ~~Brian Stuglik and~~ Daniel Paterson **and Daniel Calkins** , these agreements do not prevent them from terminating their employment with us at any time. We do not maintain " key person " insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives. ~~Recruiting~~ **69Recruiting** and retaining qualified scientific, clinical, manufacturing, and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies,

universities, and research institutions for similar personnel. Although we have implemented a retention plan for certain key employees, our retention plan may not be successful in incentivizing these employees to continue their employment with us. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors, including our scientific co- founders, may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. We may expand our development, regulatory and future sales and marketing capabilities over time, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations. We may experience significant growth over time in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs, and sales and marketing. To manage our anticipated future growth, we may continue to implement and improve our managerial, operational, and financial systems, expand our facilities, and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel when we expand. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations. Our business and operations may be materially adversely affected in the event of computer system breaches or failures. **There are growing risks related to the security, confidentiality, and integrity of personal and corporate information stored and transmitted electronically due to increasingly diverse and sophisticated threats to networks, systems, and data security.** Despite our ~~effort~~ **efforts** to implement security measures, our ~~internal computer~~ **information technology** systems, and those of our contract research organizations and other third parties **who process information** ~~, including software providers,~~ on ~~which we rely~~ **our behalf or have access to our systems** , are vulnerable to damage from computer viruses, ransomware, unauthorized access, natural disasters, fire, terrorism, war, and telecommunication and electrical failures **. Similarly, our information system providers and their software and hardware supply chains are vulnerable to attacks. These attacks may not be identified or addressed quickly enough to avoid harm, particularly when threat actors use stealthy and persistent tactics** . Cybersecurity breaches may be the result of negligent or unauthorized activity by our employees and contractors, as well as by third parties who use cyberattack techniques involving malware, ransomware, hacking and phishing, among others. **Cyberattacks have increased in frequency and potential harm over time, and the methods used to gain unauthorized access constantly evolve, making it increasingly difficult to anticipate, prevent, and / or detect incidents successfully in every instance. We are required to expend significant resources in an effort to protect against security incidents and may be required or choose to spend additional resources or modify our business activities, particularly where required by applicable data privacy and security laws or regulations or industry standards. The SEC and other regulatory bodies are increasingly focusing on cybersecurity enforcement, and the costs of complying with these regulatory initiatives may be significant.** If ~~such an event~~ **a security incident or data breach** were to occur and cause interruptions in our operations, it could result in a material disruption of our key business processes and clinical development programs. For example, the loss of clinical trial data from ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could be exposed to **substantial remediation costs, claims or litigation, regulatory enforcement,** liability **including under laws that protect the privacy of personal information** , **and additional reporting requirements, any of** which could have a material adverse effect on our operating results and financial condition, affect our reputation, undermine market and ~~61commercial~~ -- **commercial** confidence, erode goodwill, and possibly delay the further development and commercialization of our product candidates. ~~Risks~~ **70Risks** Related to Our Capital StockProvisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management. Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition, or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions: ● establish a classified board of directors such that not all members of the board are elected at one time; ● allow the authorized number of our directors to be changed only by resolution of our board of directors; ● limit the manner in which stockholders can remove directors from the board; ● establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors; ● require that stockholder actions must be affected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent; ● limit who may call stockholder meetings; ● authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a" poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and ● require the approval of the holders of at least 75 % of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws. Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15 % of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15 % of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. The market price of our common stock has been, and may continue to be,

highly volatile. Our stock price has been volatile. Since January 27, 2012, when we became a public company, the price for one share of our common stock has reached a high of $ ~~18~~ **194** . ~~82~~ **53** and a low of $ ~~0~~ **3** . ~~30~~ **54** through December 31, ~~2022~~ **2023 , on a post reverse stock split basis** . We cannot predict whether the price of our common stock will rise or fall. The market price for our common stock may be influenced by many factors, including: ● the success of competitive products or technologies; ● results of clinical trials of our product candidates or those of our competitors; ● regulatory or legal developments in the United States and other countries; ● developments or disputes concerning patent applications, issued patents or other proprietary rights; ● the recruitment or departure of key personnel; ● the level of expenses related to any of our product candidates or clinical development programs; ~~62~~ ● the results of our efforts to discover, develop, acquire, or in- license additional product candidates or products; **71** ● actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts; ● variations in our financial results or those of companies that are perceived to be similar to us; ● changes in the structure of healthcare payment systems; ● market conditions in the pharmaceutical and biotechnology sectors; ● general economic, industry and market conditions; and ● the other factors described in this" Risk Factors" section. In addition, the stock market in general and the market for small pharmaceutical companies and biotechnology companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of particular companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, following periods of volatility in the market, securities class action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management' s attention and resources, which could materially and adversely affect our business and financial condition. ~~Our common stock may be at risk for delisting from the Nasdaq Global Market in the future. Delisting could adversely affect the liquidity of our common stock, the market price of our common stock could decrease, and other unfavorable impacts. Our common stock is currently listed on the Nasdaq Global Market. The Nasdaq Stock Market LLC (" Nasdaq ") has minimum requirements that a company must meet in order to remain listed on the Nasdaq Global Market, including a requirement that we maintain a minimum closing bid price of $ 1. 00 per share. On November 4, 2022 we received a letter from the listing qualifications department (the " Staff ") of Nasdaq notifying us that for the last 30 consecutive business days the bid price of our common stock had closed below $ 1. 00 per share minimum bid price requirement for continued inclusion on the Nasdaq Global Market pursuant to Nasdaq Listing Rule 5450 (a) (1) (the " Bid Price Requirement "). In accordance with Nasdaq Listing Rule 5810 (c) (3) (A) (the " Compliance Period Rule "), we have been provided a period of 180 calendar days, or until May 3, 2023 (the " Compliance Date "), to regain compliance with the Bid Price Requirement. If, at any time before the Compliance Date, the bid price for the common stock closes at $ 1. 00 or more for a minimum of 10 consecutive business days, as required under the Compliance Period Rule, the Staff will provide written notification to us that it has regained compliance with the Bid Price Requirement. If we do not regain compliance with the Bid Price Requirement by the Compliance Date, we may be eligible for an additional 180 calendar day compliance period. To qualify, we will be required to meet the continued listing requirement for market value of its publicly held shares and all other initial listing standards for The Nasdaq Global Market, with the exception of the Bid Price Requirement, and will need to provide written notice of our intention to cure the deficiency during the second 180 calendar day compliance period, by effecting a reverse stock split, if necessary. If we do not regain compliance with the Bid Price Requirement by the Compliance Date and are not eligible for an additional compliance period at that time, or the Staff concludes that we will not be able to cure the deficiency during the additional compliance period, the Staff will provide written notification to us that our common stock will be subject to delisting. At that time, we may appeal the Staff' s delisting determination to a Nasdaq hearings panel. However, there can be no assurance that, if we receive a delisting notice and appeals the delisting determination by the listing qualifications department of Nasdaq to the Nasdaq hearings panel, such appeal would be successful. We intend to monitor the closing bid price of our common stock and may, if appropriate, consider available options to regain compliance with the Bid Price Requirement, which could include seeking to effect a reverse stock split. However, there can be no assurance that we will be able to regain compliance with the Bid Price Requirement. 63The delisting of our common stock would significantly affect the ability of investors to trade our common stock and negatively impact the liquidity and price of our common stock. In addition, the delisting of our common stock could materially adversely impact our ability to raise capital on acceptable terms or at all. Delisting from Nasdaq could also have other negative results, including the potential loss of confidence by our current or prospective third- party providers and collaboration partners, the loss of institutional investor interest, the triggering of a default under the Loan Agreement with Oxford, which in turn could cause our borrowings to become immediately due, and fewer licensing and partnering opportunities.** Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be the source of gain for our stockholders. We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings to finance the growth and development of our business. In addition, the terms of any current or future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future. We can issue and have issued shares of preferred stock, which may adversely affect the rights of holders of our common stock. We have in the past issued, and we may at any time in the future issue, shares of preferred stock, and as of ~~February 28~~ **December 31** , 2023 we have 1, 000, 000 shares of our Series A convertible preferred stock, par value $ 0. 0001 per share (the " Series A **Convertible** Preferred Stock ") and 1, 200, 000 shares of our Series B convertible preferred stock, par value $ 0. 0001 per share (the " Series B **Convertible** Preferred Stock " and together with the Series A **Convertible** Preferred Stock, the " Preferred Stock ") outstanding. Our amended and restated certificate of incorporation authorizes us to issue up to 5, 000, 000 shares of preferred stock with designations, rights and preferences determined from time- to- time by our board of directors. Accordingly, our board of directors is empowered, without stockholder approval, to issue preferred stock with dividend, liquidation, conversion, voting or other rights superior to those of holders of our common stock. For example, our

Series B **Convertible** Preferred Stock ranks senior to our common stock, and the holders of our Series B **Convertible** Preferred Stock are entitled to a liquidation preference of $ 1. 00 per share of Series B **Convertible** Preferred Stock in the event of our liquidation, dissolution or winding up, which could limit or eliminate any payments that the holders of our common stock could expect to receive upon our liquidation. Additionally, holders of our Preferred Stock are entitled to receive, on an as converted basis, dividends and consideration in the event of certain transactions equivalent to the dividends and consideration received by the holders of our common stock, which would make paying dividends and engaging in certain transactions more expensive. We also may not make any changes to our amended and restated certificate of incorporation that would limit the rights of the holders of our either series of our preferred stock without the affirmative vote of a majority of such series of preferred stock, which may make it more difficult to take certain corporate actions in the future. Our stockholders will experience substantial dilution if shares of our Series B **Convertible** Preferred Stock are converted into common stock **or our pre- funded warrants are exercised for common stock** . As of ~~February 28~~ **December 31** , 2023, there were 1, 200, 000 shares of our Series B **Convertible** Preferred Stock outstanding, which are convertible without payment of additional consideration into **4, 236,** ~~50~~ **570** ~~, 838, 840~~ shares of our common stock, subject to certain ownership limitations **and pre- funded warrants to purchase 1, 538, 591 shares of our common stock for an exercise price equal to $ 0. 001 per share of common stock** . The conversion of the outstanding shares of our Series B **Convertible** Preferred Stock into common stock **or exercise of our pre- funded warrants** would ~~be~~ **72be** substantially dilutive to existing stockholders. Any ~~dilatation~~ **dilution** or potential dilution may cause our stockholders to sell their shares, which may contribute to a downward movement in the stock price of our common stock. Raising additional capital or entering into certain licensing arrangements may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our product candidates. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, grants and government funding, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or **securities** convertible ~~debt~~ **into our common stock** , the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing stockholders. To the ~~64extent~~ -- **extent** that we enter into certain licensing arrangements, the ownership interest of our existing stockholders may be diluted if we elect to make certain payments in shares of our common stock. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish future revenue streams or valuable rights to product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. ~~65~~ **73**