Risk Factors Comparison 2025-03-20 to 2024-03-14 Form: 10-K

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

Risks Related to the Development of Our Product Candidates **.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 ~~,including avutometinib and defactinib,for which the FDA has accepted for review our NDA under the accelerated approval pathway for the treatment of adult patients with recurrent LGSOC,who received at least one prior systemic therapy and have a KRAS mutation~~ .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 ~~current and~~ 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 significant delays or an **inability to successfully commercialize our product candidates,which would materially harm our business** . 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~~ **39A** 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; ● 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 **; or ● significant changes to the policies or regulations of the FDA or foreign regulatory authorities regarding the development, approval, and marketing of pharmaceutical products, including but not limited to as a result of the 2024 United States presidential**

election . 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 **or abandoned** . 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~~ **40If** 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~~ **foreign** 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. ~~38Patient~~ -- **Patient** 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; ● proximity and availability of clinical trial sites for prospective patients; and ● constraints on the healthcare system such as a pandemic. 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 **, initial " top- line "** and interim data from clinical trials of our product candidates **, or statistical analyses and projections based thereon,** 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 **, initial " top- line, "** 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~~ **41produce** 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. ~~39Research~~ -- **Research** 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. The **market opportunities for our product candidates, if approved, may be smaller than we estimate,**

and the FDA and other comparable foreign regulatory authorities may approve our product candidates for a more limited patient population than we anticipate. The potential market opportunity for our product candidates is difficult to estimate precisely. For example, the number of patients suffering from each of recurrent KRAS mutant LGSOC and recurrent KRAS wild- type LGSOC populations we are targeting near term (for KRAS mutant LGSOC) and longer term (for KRAS wild type LGSOC) is small and has not been established with precision. Due to the rarity of our target indications, there is no comprehensive patient registry or other method of establishing with precision the actual number of patients with KRAS mutant LGSOC and KRAS wild- type LGSOC. As a result, we have had to rely on other available sources to derive clinical prevalence estimates for our target indications. We make estimates regarding the incidence and prevalence of target patient populations, the rate of recurrence and the median survival for particular diseases, including with respect to LGSOC, based on various third- party sources and internally generated analysis and use such estimates in making decisions regarding our drug development strategy determining indications on which to focus in preclinical or clinical trials. Our estimates of the patient population, pricing and revenue opportunities for our product candidates, including for KRAS mutant patients with recurrent LGSOC, are based on a number of internal and third- party estimates, including, without limitation, internal forecasts of potential market penetration, the median duration of treatment from initial interim clinical data and the assumed prices at which we can commercialize our product candidates. These estimates may be inaccurate or based on imprecise data. If approved by the FDA, the market opportunity of our product candidates will depend on, among other things, acceptance by the medical community, patient access, drug pricing and reimbursement. The number of patients in the addressable market may turn out to be lower than we estimate, patients may not be otherwise amenable to treatment with our drugs, or new patients may become increasingly difficult to identify or gain access to, all of which may significantly harm our business, financial condition, results of operations, and prospects. In addition, even if we obtain approval for any of our product candidates, such approvals may be for more limited patient populations than we had anticipated, the potential market for our product candidates will be smaller than our current estimates. Obtaining approval for only a smaller patient population of our target indications for which we anticipate seeking approval would have a materially adverse effect on our ability to achieve commercialization and generate revenues. 42The 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~~ **BMS** , Amgen, Revolution Medicines, Inc., ~~SpringWorks Therapeutics, Inc.,~~ BeiGene Ltd., ~~Immuneering~~ **Quanta Therapeutics, Inc., Erasca, Inc., Roche Holding AG, Incyte** Corporation ~~, Mapkure, LLC, Erasca, Inc., Relay Therapeutics, Inc.~~ and **Eli Lilly and Company** ~~Kinnate Biopharma, 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 ~~40of~~ **of** 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~~ **43with** large and established companies. These third parties compete with us in recruiting and retaining qualified 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. **Further, we and our collaboration partners are currently conducting clinical trials, and may in the future conduct additional clinical trials, outside the United States, including the Phase 1 / 2 clinical trial evaluating VS- 7375 by GenFleet in China. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to conditions imposed by the FDA. For example, the FDA will generally not approve the application unless the data are applicable to the United States population and United States medical practice and the FDA is able to validate the data through an on- site inspection or other appropriate means. The FDA or any comparable foreign regulatory authority may not accept data from trials conducted outside of the United States or the applicable jurisdiction, which may result in the need for additional trials that could be costly and time consuming and could result in the product candidate not receiving approval for commercialization in the applicable jurisdiction.** 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....., 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, 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 **appear to be** manageable. ~~As~~ **44As** 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 ~~42opportunities~~ -- **opportunities** . 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 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~~ **45If** 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. Clinics and hospitals in Europe and United States continue to cause delays in startup and on- going activities due to the ongoing staff shortages since the onset of the COVID- 19 pandemic. ● Work- from- home limitations. Since 2020, a material portion of our workforce works remotely and we expect this to continue, which could impact our ability to effectively plan, execute, communicate, and maintain our corporate culture. ● Capital markets volatility. Equity and debt markets have experienced significant volatility in recent years, which makes it more difficult to raise capital at a reasonable valuation or at all. ● 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. 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. ~~Secura~~ **46Secura** ' 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; ~~and44 --~~ **and** ● 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 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, 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 agreements with Pfizer, 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 agreements with Pfizer, 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~~ **47We** depend on GenFleet to fully perform under the GenFleet ~~AgreementOn --~~ **Agreement inclusive of our supply agreement with GenFleet. On** 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. **In December 2023, we announced the selection of a potential best- in class oral and selective KRAS G12D (ON / OFF) inhibitor VS- 7375 as the lead program. GenFleet is currently conducting a Phase 1 / 2 trial in China evaluating VS- 7375 in patients with KRAS G12D- mutated advanced solid tumors. In January 2025, we exercised early the GenFleet Option for the lead compound VS- 7375 and expect to initiate a Phase 1 / 2a study in middle of 2025 in the United States.** Pursuant to the GenFleet Agreement, we are reliant on GenFleet to fulfil their responsibilities including **ongoing discovery and lead optimization for** the **second and third programs and** execution of the Phase 1 clinical trials for ~~all three --~~ **the** ~~oncology~~ **second and third** programs. Accordingly, our ability to realize the anticipated benefits and success of the GenFleet Agreement is dependent upon GenFleet fulfilling their obligations. **Furthermore, we have entered into a supply agreement with GenFleet pursuant to which we expect to obtain VS- 7375 finished product from GenFleet for use in our planned clinical trial in the United States. If GenFleet does not perform under the supply agreement, our ability to obtain VS- 7375 and consequently our planned clinical trial in the United States investigating VS- 7375 will be materially adversely impacted.** If GenFleet does not successfully carry out their responsibilities, the benefits of the GenFleet Agreement **and our collaboration with GenFleet** may not be realized. ~~45Risks~~ **48Risks** 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, ~~2023~~ **2024** , we had an accumulated deficit of $ ~~824~~ **955** . ~~9~~ **5** million. To date, we have generated minimal product revenues and have financed our operations primarily through public and private offerings of our common stock, preferred stock, **warrants** and pre- funded warrants, offerings of convertible notes, sales of our common stock pursuant to our at- the- market equity offering programs, our **Note Purchase Agreement (the " Note Purchase Agreement ") with RGCM SA LLC, as purchaser agent, Oberland Capital Management LLC (" Oberland ") and certain funds managed by Oberland, as purchasers, (together with the other purchasers party thereto referred to as the " Note Purchase Agreement Purchasers ") our former** loan and security agreement (the " Loan Agreement ") with Oxford Finance LLC (" Oxford "), our loan and security agreement, as amended, with Hercules Capital Inc. (" Hercules "), upfront payments under our license and collaboration agreements with Yakult, CSPC, and Sanofi, and the upfront payment **and milestone payments** 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: **● prepare for the anticipated commercialization of avutometinib and defactinib;** ● 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~~ **49We** 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 **and defactinib** . We expect our expenses to increase in connection with our ongoing activities, particularly ~~as we~~ **in connection with our planned commercialization of avutometinib and defactinib and the** ~~continue~~ **continued** ~~the~~ clinical development of our product candidates. We expect our cash, cash equivalents and investments at December 31, ~~2023~~ **2024** will not be sufficient to fund our current operating plan and capital expenditure requirements for the next 12 months from the issuance of these financial statements. We 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 **costs and timing of activities in anticipation of potential commercialization for avutometinib and defactinib and product candidates for which we expect to receive marketing approval; ● 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 **, if any,** received from commercial sales of our product candidates **, including avutometinib and defactinib** , 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 **. ● receipt of milestone payments and royalties pursuant to the Secura APA including timing of such receipt** . 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~~ **Although the FDA has accepted for review our NDA under the accelerated approval pathway for avutometinib in combination with defactinib for the treatment of adult patients with recurrent LGSOC who received at least one prior systemic therapy and have a KRAS mutation, the NDA may not be approved by the FDA and, even if approved, avutometinib and defactinib may not achieve commercial success. We expect that 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 **(" NOL ")** , 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~~ **50favorable** 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. **Similarly, changes in U. S. federal policy that affect the geopolitical landscape could give rise to circumstances outside our control that could have negative impacts on our business operations.** For example, **on March 4, 2025, the U. S. imposed a 25 % tariff on imports from Canada and Mexico that do not satisfy the U. S.- Mexico- Canada Agreement rules of origin with certain exemptions and a 20 % additional tariff on imports from China. Historically, tariffs have led to increased trade and political tensions. In response to tariffs, other countries have implemented retaliatory tariffs on U. S. goods. Political tensions resulting from trade policies could reduce trade volume, investment, technological exchange and other economic activities between major international economies, resulting in a material adverse effect on global economic conditions and the stability of global financial markets.** ~~tightening~~ **Tightening** of the equity markets ~~,~~ makes it more difficult to raise capital at a reasonable valuation or at all **. Any changes in political, trade, regulatory, and economic conditions, including U. S. trade policies, could have a material adverse effect on our financial condition or results of operations** . In addition, the U. S. Bureau of Labor Statistics has reported for the period from December ~~2022~~ **2023** to December ~~2023~~ **2024** , the Consumer Price Index for All Urban Consumers rose ~~3~~ **2** . ~~4~~ **9** % which remains above the U. S. Federal Reserve' s inflation target of 2 %. If inflationary pressures increase or 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, ~~2023~~ **2024** , we had U. S. federal and state ~~net operating loss (“~~ NOL ~~”)~~ carryforwards of approximately $ ~~473~~ **370** . 6 million and $ ~~189~~ **56** . ~~0~~ **7** million, respectively. As of December 31, ~~2023~~ **2024** , we also had federal and state tax credits of $ ~~9~~ **2** . ~~5~~ **6** million and $ ~~2~~ **0** . 2 million, respectively, which may be used to offset future tax liabilities. The NOL and tax credit carryforwards will expire at various dates through ~~2043~~ **2044** , except for $ ~~277~~ **333** . ~~9~~ **4** million of federal NOL carryforwards which may be carried forward indefinitely. Sections 382 and 383 of the Internal Revenue Code **(“ IRC ”)** 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 **IRC** ~~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 %. ~~47Based on our analysis~~ **During 2024, we believe we triggered ownership changes** under Section 382 **of the IRC and similar provisions under state law. As a result** , 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, ~~2023~~ **2024** . ~~The~~ **A** portion of federal NOL carryforwards ~~,~~ **and** state NOL carryforwards **that we expect we will not be able to utilize were written off. Similarly** , **we wrote off all federal and state** research and development credits, and **federal** orphan drug credits **we** ~~that were~~ determined ~~to~~ **we will not** be ~~limited by Section 382~~ **able to utilize due to limitation** and **expiration periods. We** ~~similar provisions under state law~~ have **approximately $ 346. 4 million of federal NOLs generated prior to such ownership changes inclusive of $ 309. 3 million of federal NOLs which may be carried forward indefinitely. Since the $ 309. 3 million of federal NOLs may be carried forward indefinitely these have not** been written off as of December 31, ~~2023~~ **2024 , but due to the limitations under Section 382, generally we can only use $ 1. 6 million per year against taxable income in the future** . Future changes in our stock ownership, some of which are outside of our control, could result in **further** ownership changes ~~in~~ **under section 382 of** the ~~future~~ **IRC** . We may not be able to use some or all of our NOL and tax credit carryforwards, even if we attain profitability. ~~Risks~~ **51Risks** 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~~ **On January 13,** ~~2022~~ **2025 (the “ Note Purchase Agreement Closing Date ”)** , we entered into ~~a Loan~~ **the Note Purchase** Agreement ~~with Oxford~~ **pursuant to which we may sell to the Note Purchase Agreement Purchasers** , ~~as collateral agent~~ and **the Note Purchase Agreement Purchasers may buy from us notes** ~~a lender, and Oxford Finance Credit Fund III LP, as a lender~~ (**the** “ **Notes** ~~OFCF III ” and together with Oxford, the “ Lenders~~ ”) **in** ~~, pursuant to which the Lenders have agreed to lend us up to~~ an aggregate principal amount ~~of~~ **not to exceed** $ 150. 0 million **, consisting** ~~in a series~~ of ~~term loans~~ **the following: ● an initial sale of $ 75. 0 million principal amount of Notes; ● at our option, a second sale** (the “ ~~Term Loans~~ **Second Sale** ”) ~~. As~~ of **$ 25. 0 million principal amount of Notes, at any time prior to** December 31, ~~2023~~ **2025** , **upon the FDA approval sufficient for the promotion and sale of avutometinib and defactinib for the treatment of LGSOC and subject to certain** ~~there~~ - **other** ~~was~~ **customary conditions precedent; and ● at our option, a third sale (the “ Third Sale ”) of up to** $ ~~40~~ **50** . 0 million **principal amount of Notes, at any time prior to December 31, 2026, provided that trailing six- month worldwide net sales of avutometinib and defactinib are at least $ 55. 0 million and subject to certain other customary conditions precedent. The** outstanding **principal amount of the Notes bear interest at a rate per annum equal to the sum of (i) the greater of the Term SOFR (as defined in the Note Purchase Agreement) and 4. 29 %, and (ii) 3. 71 %, subject to adjustment in certain circumstances set forth in the Note Purchase Agreement and an overall cap of 9. 75 %, payable quarterly in arrears until the seventh anniversary of the Note Purchase Agreement Closing Date or the date on which all amounts owing to the Note Purchase Agreement Purchasers** under the ~~Loan~~ **Note Purchase** Agreement **have been paid in full (the “ Note Purchase Agreement Maturity Date ”)** . ~~In connection~~ **For the first eight (8) quarters following the Note Purchase Agreement Closing Date, at our option, up to 50 % of the interest due may be paid- in- kind and added to the then- outstanding principal balance of the Notes. Upon the occurrence and during the continuance of an Event of Default (as defined in the Note Purchase Agreement) under the Note Purchase Agreement, the then- applicable interest rate on all outstanding obligations may be increased by an additional 5. 00 %. The Note Purchase Agreement Purchasers will receive 1. 00 % (the “ Revenue Participation Percentage ”) of the first $ 100. 0 million of net sales of each Included Product (as defined in the Note Purchase Agreement) by us or our licensees in each calendar year, payable quarterly. “ Included Products ” is defined in the Note Purchase Agreement to include (a) avutometinib and defactinib, including any product that contains either one of the foregoing in combination** with **any** ~~the~~ **other** ~~Loan~~ **active ingredient (s), and (b) all other compounds, chemical entities or pharmaceutical products being designed, developed, licensed, manufactured or commercialized by us or our subsidiaries from time to time. The Revenue Participation Percentage will increase pro rata immediately upon the occurrence of the Second Sale and the Third Sale, such that the Revenue Participation Percentage shall increase to a maximum of 2. 00 % in the event that $ 150. 0 million in aggregate principal amount of Notes has been purchased pursuant to the Note Purchase** Agreement **following the Third Sale. The outstanding principal amount of the Notes** , ~~we granted Oxford~~ **interest accrued thereon and any other amounts owing to the Note Purchase Agreement Purchasers under the Note Purchase Agreement will be due in two equal installments on (a) the sixth anniversary of the Note Purchase Agreement Closing Date, and (b) the Note Purchase Agreement Maturity Date. The Note Purchase Agreement contains no financial covenants. Our obligations under the Note Purchase Agreement are subject to customary covenants, including limitations on our ability to dispose of assets, undergo a change of control, merge with or acquire other entities, incur debt, incur liens, pay dividends or other distributions to holders of our capital stock, repurchase stock and make investments, in each case subject to certain exceptions. Our obligations under the Note Purchase Agreement are secured**

by a security interest ~~in~~ **on substantially** all of our **and** ~~personal property now owned or~~ **our** ~~hereafter acquired~~ **subsidiaries' assets** , ~~excluding~~ **including our** intellectual property **related** ~~(but including the right~~ to ~~payments~~ **avutometinib** and **defactinib** ~~proceeds of intellectual property)~~ , and a negative pledge on **intellectual property related to the Company' s collaboration and option agreement with GenFleet, subject to certain exceptions relating to our development of our** 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~~ **52maturity** . 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. **Further, our agreement to pay Oberland the Revenue Participation Percentage with respect to potential future sales of certain of our product candidates may limit future revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval, as well as our ability to generate revenues that are significant or large enough to achieve profitability. In addition, we may be delayed in satisfying the criteria required under the Note Purchase Agreement to exercise the Second Sale and Third Sale, or may never satisfy such criteria, which may require us to find other sources of funding to finance our operations.** 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~~ **Note Purchase** Agreement or breaching any covenants under the ~~Loan~~ **Note Purchase** 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~~ **Note Purchase** 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~~ **The Note Purchase Agreement Purchasers** could also exercise ~~its~~ **their** rights as collateral agent to take possession and dispose of the collateral securing the **Notes** ~~term loans~~ for ~~its~~ **their** 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 **contract research organizations (" 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. ~~48Any~~ -- **Any** 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 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~~ **53If** 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 **and commercial requirements** from third- party manufacturers or third- party collaborators, and we expect to continue to rely on third parties for the manufacture of clinical **and commercial** 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. We do not currently have arrangements in place for redundant supply or a second source **throughout** ~~for bulk drug substance or~~ **our** ~~drug product~~ **supply chain** . 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 **54** ● 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 ~~50process --~~ **process** 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. If we are not able to establish **additional** 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~~ **55We** face significant competition in seeking appropriate collaborators. Whether we reach ~~a~~ definitive ~~agreement~~ **agreements** 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~~ **foreign** 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~~ **not realize the benefits of our current or future** collaborations **or licensing arrangements** with third parties for the development and commercialization of our product candidates **and may be** ~~. If those collaborations are not successful~~ **unsuccessful in consummating future partnerships or** ~~, we may not be able to capitalize~~ **capitalizing** on the market potential of our product candidates. ~~We~~ **Our current or future collaborations or licensing arrangements** may ~~seek~~ **not be successful. Additionally, we have partnered, and intend to further partner, with** third ~~- party collaborators for~~ **parties with respect to** the **clinical** development and commercialization **, if approved,** of **certain of** our ~~product candidates~~ **programs, and we may not be successful in identifying, negotiating and executing partnerships** . Our likely **future** collaborators for any collaboration arrangements include large and mid- size pharmaceutical companies, regional and national pharmaceutical companies, and biotechnology companies. **Any** ~~If we do enter into any~~ such arrangements with any third parties ~~, we will likely have~~ **may result in us having** 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. ~~-~~**For example, we have engaged in a strategic collaboration with IQVIA, pursuant to which we intend to leverage IQVIA' s expertise and resources for the commercialization and launch of the investigational combination of avutometinib plus defactinib for the treatment of recurrent KRAS mutant LGSOC. Accordingly, we will depend on IQVIA and their performance under the strategic collaboration arrangements for the successful commercialization and launch of avutometinib and defactinib for the treatment of recurrent KRAS mutant LGSOC. If IQVIA does not successfully carry out their responsibilities under the collaboration agreements or does not perform to the standard or level we anticipate, the benefits of the strategic collaboration with IQVIA may not be realized and our commercialization efforts will be harmed.** ~~51Collaborations~~ -- **Collaborations** involving our product candidates ~~would pose the following~~ **are subject to numerous** risks ~~to us~~ **, which may include that** : ● 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~~ **56develop** with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours; ● **agreements with collaborators may not provide exclusive rights to use their intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and product candidates in the future; ● collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates; ●** a collaborator with marketing ~~and~~ **, manufacturing or** distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products **or otherwise not perform satisfactorily in carrying out these activities** ; ● 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. Our business could be adversely affected by conditions the adverse geopolitical and macroeconomic developments, including the military conflict between Ukraine and Russia, the ongoing military conflict in the Middle East, and any related sanctions. While we do not currently have clinical trials in Ukraine, Russia, or **the** 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 **is conducting a** ~~intends to file an IND for the lead oncology program in first half of 2024 in China and expects the~~ Phase 1 **/ 2** clinical trial ~~to be conducted~~ **evaluating GFH375 / VS- 7375** 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 and Russia, the ongoing military conflict in the Middle East, and the associated 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. 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 ~~52impose --~~ **impose** , 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~~ **57licenses** , 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 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 products. 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 --~~ **our** 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~~ **58The** 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 our 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. ~~54The~~ -- **The** issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. 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~~ **59examination** , 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 the amount of time required for the development, testing, and regulatory review of new products, patents protecting such products might expire before or shortly after such 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. Moreover, some of our owned and in- licensed patents and patent applications are, and may in the future be, co- owned with third parties. If we are unable to obtain an exclusive license to any such third- party co- owners' interest in such patents or patent applications, such co- owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we or our licensors may need the cooperation of any such co- owners of our owned and in- licensed patents in order to enforce such patents against third parties, and such cooperation may not be provided to us or our licensors. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects. If our efforts to protect the proprietary nature of the intellectual property related to our products are not adequate, we may not be able to compete effectively in our market. We rely upon a combination of patents, confidentiality agreements, trade secret protection and license agreements to protect the intellectual property related to our products. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. We, or any partners, collaborators, or licensors, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to strengthen our patent position. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope, or requests for patent term adjustments. If we or our partners, collaborators, or licensors fail to establish, maintain or

protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our partners, collaborators, or licensors are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our patents or patent applications, such patents may be invalid and / or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business. We anticipate additional patent applications will be filed both in the United States and in other countries, as appropriate. However, we cannot predict: ● if additional patent applications covering new technologies related to our products will be filed; ● if and when patents will issue; ● the degree and range of protection any issued patents will afford us against competitors, including whether third parties will find ways to invalidate or otherwise circumvent our patents; ~~55~~ ● whether any of our intellectual property will provide any competitive advantage; ● whether any of our patents that may be issued may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage; ● whether or not others will obtain patents claiming aspects similar to those covered by our patents and patent applications; or **60** ● whether we will need to initiate or defend litigation or administrative proceedings which may be costly regardless of whether we win or lose. Additionally, we cannot be certain that the claims in our pending patent applications covering our products and their methods of use will be considered patentable by the USPTO, or by patent offices in foreign countries, or that the claims in any of our issued patents will be considered valid or patentable by courts in the United States or foreign countries. Method of use patents protect the use of a product for the specified method. These types of patents do not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products " off- label. " Although off- label prescriptions may, but not necessarily, contribute to a finding of infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute. We may not be successful in obtaining or maintaining necessary rights to product components and processes for our development pipeline through acquisitions and in- licenses. Presently we have rights to certain patents and applications through licenses from third parties and own patents and patent applications related to our products. Additional product candidates or therapies, including combination therapies, with avutometinib and / or defactinib, may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in- license or use these proprietary rights. We may be unable to acquire or in- license compositions, methods of use, processes or other intellectual property rights from third parties that we identify as necessary or important to our business operations. If we fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, it would harm our business. We may need to cease use of the additional product candidates or methods covered by such third- party intellectual property rights, and / or may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if it is possible and we were able to develop such alternatives. Even if we are able to obtain a license, it may be non- exclusive, thereby giving our competitors access to the same technologies that we have licensed. In that event, we may be required to expend significant time and resources to develop or license replacement technologies. Moreover, the specific product candidates or methods that may be used with our products may be covered by the intellectual property rights of others. Additionally, we may seek to acquire new compounds and product candidates from other pharmaceutical and biotechnology companies, academic scientists and other researchers, such as our exclusive in- license from Pfizer, and Chugai 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, negotiating and implementing a license or acquisition of a product candidate or approved product is lengthy and complex. Furthermore, we have and may continue to collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions provide us with an option to negotiate a license to any of the institution' s rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program. If we are unable to successfully obtain rights to required third- ~~56party~~ -- **party** intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer. The licensing and acquisition of third- party intellectual property rights is a competitive area, and companies, which may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third- party intellectual property rights that we may consider necessary or attractive in order to commercialize our products. More established companies may have a competitive advantage over us due to their ~~size~~ **61size** , cash resources and greater clinical development and commercialization capabilities. 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 payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. Some of our pending patent applications may not be allowed in the future. We cannot be certain that an allowed patent application will become an issued patent. There may be events that cause withdrawal of the allowance of a patent application. For example, after a patent application has been allowed, but prior to being issued, material that could be relevant to patentability may be identified. In such circumstances, the applicant may pull the application from allowance in order for the USPTO to review the application in view of the new material. We cannot be certain that the USPTO will issue the application in view of the new material. Further, periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign countries may require the payment of maintenance fees or patent annuities during the lifetime of a patent application and / or any subsequent patent that issues from the application. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and following the issuance of a patent. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application. Such noncompliance can result in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result ~~57in~~ **in** abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non- payment of fees and failure to properly legalize and submit formal documents. Such an event could have a material adverse effect on our business. Issued patents covering our products could be found invalid or unenforceable if challenged in court or the USPTO. If we or one of our licensing partners initiate legal proceedings against a third party to enforce a patent covering our products, the defendant could counterclaim that the patent covering our products, as applicable, is ~~invalid~~ **62invalid** and / or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and / or unenforceability are commonplace, and there are various grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re- examination, inter partes review, post grant review and equivalent proceedings in foreign jurisdictions (such as opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our products. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and / or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our products. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and products. Changes to patent law in the United States and in foreign jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products. As is the case with other drug and biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the drug and biopharmaceutical industry involves both technological and legal complexity, and is therefore costly, time- consuming and inherently uncertain. In addition, the United States has passed wide- ranging patent reform legislation under the ~~AIA~~ **America Invents Act** . Moreover, recent U. S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U. S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. We cannot predict how future decisions by the courts, Congress or the USPTO may impact the value of our patents. Similarly, any adverse changes in the patent laws of other jurisdictions could have a material adverse effect on our business and financial condition. Changes in the laws and regulations governing patents in other jurisdictions could similarly have an adverse effect on our ability to obtain and effectively enforce our patent rights. We have limited foreign intellectual property rights and may not be able to protect our intellectual property rights throughout the world. We may not be able to pursue patent coverage of our products in certain countries outside of the United States. Filing, prosecuting and defending patents on products in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States may be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. The breadth and strength of our patents issued in foreign jurisdictions or regions may not be the same as the corresponding patents issued in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to certain territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. ~~58Many~~ -- **Many** companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protections, particularly those relating to drug and biopharmaceutical

products. This difficulty with enforcing patents could make it difficult for us to stop the infringement of our patents or marketing of competing products otherwise generally in violation of our proprietary rights. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being ~~invalidated~~ **63invalidated** or interpreted narrowly, put our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. If we do not obtain patent term extension and data exclusivity for any of our current products, our business may be materially harmed. Depending upon the timing, duration and specifics of any FDA marketing approval of our current products, one or more of our U. S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch- Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply for a patent extension within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we believe we are entitled to, our competitors may obtain approval of competing products sooner than we would expect, and our business, financial condition, results of operations, and prospects could be materially harmed. 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~~ -- **misappropriation** 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~~ **64Third** 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 products 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 products 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~~ **65the** 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 ~~61property~~ -- **property** 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~~ **66normal** responsibilities. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. 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~~ **trademarks** 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~~ **67patent** 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. **Although the FDA has accepted for review our NDA under the accelerated approval pathway for avutometinib in combination with defactinib for the treatment of adult patients with recurrent LGSOC who received at least one prior systemic therapy and have a KRAS mutation, the NDA may not be approved.** Obtaining approval of an NDA can be a lengthy, expensive, and uncertain process **, and the FDA has substantial discretion in the review and approval process and may decide that our data is insufficient for approval and require additional preclinical, clinical, or other studies. While we have engaged in discussions with the FDA with respect to the scope and nature of our NDA submission for avutometinib in combination with defactinib, the FDA may, for example, require additional data under the RAMP 301 study before approving the NDA for the scope we request, or at all. There can be no assurance regarding the timing and outcome of the FDA review and approval of our NDA submission** . 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 **have relied on 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 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. ~~63If~~ **If** 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~~ **68We** 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~~ **In March 2024, the FDA granted orphan drug designation to avutometinib, alone or in combination with defactinib for the treatment of patients with recurrent LGSOC. In July 2024, the FDA granted orphan drug designation to avutometinib, in combination with defactinib, for the treatment of pancreatic cancer. Defactinib has** received orphan drug designation in the United States, the European Union, and Australia for the ~~use~~ **treatment** of ~~defactinib in~~ **patients with** 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 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 more additional product candidates, but we might not receive such additional designation, and such designation may not actually lead to a faster development or regulatory review or approval process nor does it 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. 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. **In April 2024, the FDA granted fast track designation for avutometinib, in combination with defactinib plus LUMAKRAS for the treatment of patients with KRAS G12C- mutated metastatic NSCLC who received at least one prior systematic therapy.** We may also seek fast track designation for additional product candidates, which we may not receive from the FDA. However, 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. ~~69~~**We have completed an NDA submission under the FDA' s accelerated approval pathway for one of our product candidates, and we may seek accelerated approval for one more additional product candidates. The FDA has substantial discretion regarding approvals under the accelerated**

approval pathway, and we may not be able to obtain accelerated approval for any of our product candidates. The FDA has accepted for review our NDA under the accelerated approval pathway for avutometinib in combination with defactinib for the treatment of adult patients with recurrent LGSOC, who received at least one prior systemic therapy, and have a KRAS mutation. We may explore regulatory strategies for our other product candidates that involve use of the FDA' s accelerated approval pathway. Under the accelerated approval program, the FDA may grant accelerated approval to a drug designed to treat a serious or life- threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the drug has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. As a condition of approval, the FDA requires that a sponsor of a drug receiving accelerated approval perform a post- marketing confirmatory clinical trial or trials. FDA has broad discretion with regard to approval under the accelerated approval program, and FDA' s interpretation of the criteria for accelerated approval, such as what it considers to be available therapies, is subject to change. No assurance can be given that other therapeutics will not receive full approval prior to our potential receipt of accelerated approval. If that were to occur, no assurance can be given that we would be successful in proving meaningful benefit over those later approved products. If we were unable to prove meaningful benefit over any available therapies, we would be effectively blocked from receiving accelerated approval. Even if we receive approval for any of our product candidates through the accelerated approval program, we will be subject to rigorous post- marketing requirements, including the completion of one or more post- market confirmatory studies, to verify the clinical benefit of our product candidate, and submission to the FDA of all promotional materials prior to their dissemination. The FDA could seek to withdraw the approval, if received, for multiple reasons, including if we fail to conduct any required post- market confirmatory trial with due diligence, our post- market confirmatory trial does not confirm the predicted clinical benefit, other evidence shows that our product candidate is not safe or effective under the conditions for use, or we disseminate promotional materials that are found by FDA to be false or misleading. ~~64Any~~ -- **Any delay in obtaining, or inability to obtain, approval through the accelerated approval pathway, or any issues in maintaining any such approvals that we receive, would delay or prevent commercialization of our product candidates, and would materially adversely affect our business, financial condition, results of operations, and cash flows. Any** 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. 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~~ **70In** 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, **are or** will be subject to **a broad range of** ~~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 **if our activities are challenged as non- compliant** . ~~Healthcare providers~~ **Pharmaceutical manufacturers and their products are subject to extensive federal and state regulation** , including ~~physicians,~~ **laws intended to prevent fraud** and **abuse** ~~third- party payors play a primary role~~ in the ~~recommendation and prescription of any product candidates~~ **healthcare industry. These laws may constrain the business** ~~for~~ **or financial arrangements and relationships through** which **we conduct business, including how we conduct research regarding, market, sell, and distribute our products. In the United States, these laws include, but are not limited to the following, some of which are likely to apply only if or when** we obtain marketing approval ~~. Our 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 65laws and regulations within the United States include the following, some of which will apply only if and when we have~~ a ~~marketed~~ product **candidate** : ● 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 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; **71** ● 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 **calculate,** report **and certify** certain ~~calculated~~ **complex** 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 **, which data may be used in the calculation of reimbursement and / or discounts on approved products** ; ● federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; ● **federal and** state medical privacy and comprehensive privacy statutes, which regulate the privacy and security of personal information **, and may vary significantly, complicating compliance efforts** ; ● 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 ~~66expenditures~~ -- **expenditures** 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~~ . 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, the General Data Protection Regulation (" GDPR "), impose 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 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~~ **72arrangements** 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 applicable laws. 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, **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 actions resulting non- compliance with regulatory standards and requirements such as those described above. 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.** ~~defending~~ **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. **The FDA** ~~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 **could require clearance or approval of an in vitro diagnostic or companion diagnostic device as a condition of approval for any product candidates that require or would commercially benefit from such tests , including the combination of avutometinib and defactinib. If we are unable to successfully validate, develop and obtain regulatory approval for companion diagnostic tests for our product candidates that require or would commercially benefit from such tests, or experience significant delays in doing so, we may not realize the full commercial potential of these product candidates and our drug development strategy and operational results may be harmed. If safe and effective use of any of our product candidates depends on an in vitro diagnostic, then the FDA generally will require approval or clearance of that test, known as a companion diagnostic, at the same time that the FDA approves our product candidates. Companion diagnostics, which** provide ~~accurate~~ information **that is essential for the safe and effective use of a corresponding therapeutic product, are subject** to **regulation by** the FDA ~~or~~ **and other** comparable ~~foreign~~ regulatory authorities ~~, comply~~ **as medical devices and require separate regulatory authorization from therapeutic approval prior to commercialization. The development programs for some of our product candidates contemplate working** with ~~manufacturing standards we~~ **developers or obtaining access to marketed companion diagnostic tests, which are assays or tests to identify an appropriate patient population. For example, in connection with our NDA for the treatment of adult patients with recurrent LGSOC, who received at least one prior systemic therapy and** have ~~established~~ **a KRAS mutation** , ~~comply~~ **we may be required to obtain FDA approval or clearance of a companion diagnostic. If safe and effective use of any of our product candidates we may develop depends on a companion diagnostic, we may not receive marketing approval, or marketing approval may be delayed, if we are unable to or are delayed in developing, identifying, or obtaining regulatory approval or clearance for the companion diagnostic product for use** with ~~federal~~ **our product candidate. In addition, the process of obtaining or creating such companion diagnostics is time consuming** and **costly** ~~state healthcare fraud~~ and ~~abuse laws~~ **we,** and ~~regulations~~ **/ or future collaborators, may encounter difficulties in developing** and **obtaining** ~~similar laws and regulations established and enforced by comparable foreign~~ regulatory **clearance** ~~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~~ **or approval** ~~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~~ **for** ~~unmanaged risks or losses or in protecting us from governmental investigations or other~~ -- **the companion diagnostics** ~~actions or lawsuits stemming from a failure to be in compliance with such laws, standards, or regulations~~ . **Current** ~~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. 67Recently enacted~~ and future ~~legislation~~ **health care reforms** 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, 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~~ **73The** 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, 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 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~~ **an ongoing** focus ~~of the Biden Administration~~ . For example, federal legislation ~~enacted in 2021 eliminates~~ **eliminated** 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 IRA is anticipated to have a significant impact on** the ~~first list~~ **pharmaceutical industry. Subsequent to the enactment** of ~~drugs~~ **the IRA, in 2024, the Biden Administration** announced **its commitment** ~~in 2023).~~ ~~Subsequent~~ to **expanding certain** ~~the enactment of the~~ IRA ~~, in 2022,~~ **reforms. There have been significant and wide-ranging reforms to federal policy and** the ~~Biden~~ **federal government under the new Trump** ~~administration~~ **Administration** ~~released~~ **. The focus on drug pricing** ~~an~~ **and payment reform is likely to continue under the new Trump Administration. Other potential healthcare reform efforts under the Trump Administration could affect access to healthcare coverage or the funding of health care benefits. There is significant uncertainty regarding the nature or impact of any such reform implemented by the Trump Administration through** executive **action** ~~order directing the Department of Health and Human Services (" HHS ") to report on how the CMMI could be leveraged to test new models for~~ - **or by Congress** ~~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 and may continue to be subject to scrutiny and legal challenge. For example, with respect to the ACA, tax reform legislation was enacted that eliminated the tax penalty established for individuals who do not maintain mandated health insurance coverage beginning in 2019 and, in 2021, the U. S. Supreme Court dismissed the latest judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. As another example, revisions to regulations under the federal anti- kickback statute would remove protection for traditional Medicare Part D discounts offered by pharmaceutical manufacturers to pharmacy benefit managers and health plans. Pursuant to court order, the removal was delayed and recent legislation imposed a moratorium on implementation of the rule until January **1** 2032. As ~~another~~ **a further** example, the IRA drug price negotiation program has been challenged in litigation filed by various pharmaceutical manufacturers and industry groups. **Recently, there has been considerable public and government scrutiny of pharmaceutical pricing and proposals to address the perceived high cost of pharmaceuticals. There have also been efforts at the federal level to implement measures to regulate drug pricing or payment for pharmaceutical products, including legislation on drug importation.** 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 **. We expect continued scrutiny on drug pricing and government price reporting from Congress, agencies, and other bodies** . 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 ~~68in~~ **in** effect through 2032 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~~ **74We** 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. **The U. S. Supreme Court' s June 2024 decision in Loper Bright Enterprises v. Raimondo overturned the longstanding Chevron doctrine, under which courts were required to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The Loper decision could result in additional legal challenges to regulations and guidance issued by federal agencies, including the FDA, on which we rely. Any such legal challenges, if successful, could have a material impact on our business. Additionally, the Loper decision may result in increased regulatory uncertainty, inconsistent judicial interpretations, and other impacts to the agency rulemaking process, any of which could adversely impact our business and operations. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action or as a result of legal challenges, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, our business could be materially harmed.** 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. **Due** ~~Separately, in response~~ to the ~~COVID- 19 pandemic~~ **recent change in presidential administration , we face uncertainty regarding potential regulatory developments that may adversely affect our business. We face uncertainty regarding the potential for changes in the regulatory environment following the change in presidential administration in January 2025. While many of the Trump administration' s proposed policies appear to be focused on deregulation, the new administration and federal government could adopt legislation, regulation, or policy that adversely affects our business or creates a more challenging and costly environment to pursue the development and commercialization of our current or future product candidates. For example, the federal government, including** the FDA ~~announced its intention~~ **, may implement legislative, regulatory, or policy changes regarding the standards for approving drugs that we may be unable** to ~~postpone most inspections~~ **satisfy or regarding the marketing** of ~~foreign~~ **approved drugs that may limit or prohibit the advertising** and ~~domestic manufacturing facilities and~~ **promotion of our current or future** ~~products~~ **product** ~~at various points~~ **candidates, if approved** . ~~Even though~~ **Additionally, because one objective of the current Trump administration appears to be to decrease spending in the federal government,** 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 **face staff reductions** ~~significantly impact the ability of the FDA to timely review and process our regulatory submissions~~ , which could ~~have a material effect~~ **impact the FDA' s ability to engage in routine regulatory and oversight activities and result in delays or limitations** on our **ability to proceed with clinical development programs and obtain regulatory approvals. It is difficult to predict how executive actions that may be 75taken under the current Trump administration may affect the FDA' s ability to exercise its regulatory authority. If such executive actions impose constraints on the FDA' s ability to engage in routine oversight and product review activities in the normal course, our** business **may be negatively impacted** . 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 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 Calkins, our Chief Financial **Officer, and Matthew Ros, our Chief Operating** Officer. Although we have formal employment agreements with Daniel Paterson ~~and ,~~ Daniel Calkins **, Matthew Ros and other members of our senior management and key personnel** , 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. ~~69Recruiting --~~ **Recruiting** 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 efforts to implement security measures, our information technology systems, and those of our contract research organizations and other third parties who process information on 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~~ **76We** 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 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 commercial confidence, erode goodwill, and possibly delay the further development and commercialization of our product candidates. ~~70Risks~~ -- **Risks** 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~~ **77The** 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 **closing** price for one share of our common stock has reached a high of $ 194. 53 and a low of $ ~~3~~ **2** . ~~54~~ **20** through December 31, ~~2023~~ **2024** , 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; ● 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 **; ● developments regarding the commercialization of our product candidates, including avutometinib and defactinib** ; ● 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. 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 December 31, ~~2023~~ **2024** 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 **0** ~~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 ") **issued and** 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~~ **78other** 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~~ **outstanding warrants** ~~our~~ **or** ~~Series B Convertible Preferred Stock are converted into common stock or our~~ pre- funded warrants are exercised for **shares** common stock. As of December 31, ~~2023~~ **2024** , 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, 570 shares of our common stock, subject to certain ownership limitations and~~ pre- funded warrants to purchase ~~1~~ **up to 5** , ~~538~~ **000** , ~~591~~ **000** shares of our common stock ~~for~~ **and warrants to purchase up to 18, 083, 334 shares of our common stock outstanding. The pre- funded warrants have** an exercise price equal to $ 0. 001 per **underlying** share of common stock **and do not expire. Each warrant has an exercise price equal to $ 3. 50 and is exercisable for one shares of our common stock (or, in certain limited circumstances in lieu of a share of common stock, a pre- funded warrant for one share of our common stock at the warrant exercise price less the exercise price of the pre- funded warrant purchased). The warrants expire on January 25, 2026** . The conversion of the outstanding ~~shares of our Series B Convertible Preferred Stock into common stock or exercise of our~~ pre- funded warrants **and warrants into shares of common stock** would ~~72be~~ **be** substantially dilutive to existing stockholders. Any dilution or potential dilution may cause our stockholders to sell their shares, which may contribute to a downward movement in the stock price of our common stock. 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 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 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. **Additional** ~~Debt~~ **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.