Risk Factors Comparison 2024-02-15 to 2023-02-16 Form: 10-K

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The following risk factors and other information included in this Annual Report on Form 10- K should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. We believe the risks described below include risks that are material to us as well as other risks that may adversely affect our business, financial condition, results of operations and growth prospects. Please see review the discussion regarding some of the forward- looking statements that are qualified by these risk factors contained elsewhere in this Annual Report on Form 10- K. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. Risks Related to Commercialization We are in the process of growing as a commercial company and the marketing and sale of AYVAKIT / AYVAKYT ~~, GAVRETO~~ or any future approved drugs may be unsuccessful or less successful than anticipated. We have two approved precision therapies, AYVAKIT / AYVAKYT and GAVRETO. While we have been commercializing AYVAKIT in the U. S. and AYVAKYT in Europe and **were** co- commercializing GAVRETO with Roche in the U. S., we only have several years **'** experience as a commercial company, and we have a limited track record demonstrating our ability to successfully overcome the many of the risks and uncertainties encountered by companies commercializing drugs in the biopharmaceutical industry. Marketing applications for avapritinib and pralsetinib are currently under review or planned ~~in the U. S. or~~ globally. To execute our business plan, in addition to successfully marketing and selling our approved drugs, we will need to successfully: ● **● gain regulatory acceptance for the development and commercialization of current or future drug candidates in our pipeline, including for additional indications or in additional geographies for marketed drugs in our portfolio; ● maintain our key collaborations; ● expand our global operations or enter into collaboration, partnerships or distribution arrangements in geographies where we may not have current operations or expertise; and ● manage our spending as costs and expenses increase due to clinical trials, marketing approvals, and commercialization.** If we are unsuccessful in accomplishing these objectives, we may not be able to successfully commercialize our current or future approved drugs, develop current or future drug candidates, expand our business or continue our operations. The commercial success of AYVAKIT / AYVAKYT ~~and GAVRETO~~, as well as any other drugs that we may bring to the market, will depend upon the degree of market acceptance by physicians, patients, third- party payors and others in the medical community. AYVAKIT / AYVAKYT ~~and GAVRETO~~, as well any other drugs that we may bring to the market, may not gain market acceptance by physicians, patients, third- party payors and others in the medical community. If these drugs do not achieve an adequate level of acceptance, we may not generate significant product revenues and may not become profitable. The degree of market acceptance for AYVAKIT / AYVAKYT ~~and GAVRETO~~, as well as any current or future drug candidates for which we receive marketing approval, will depend on a number of factors, including: ● the potential efficacy and potential advantages over alternative treatments; ● the prevalence and severity of any side effects, including any limitations or warnings contained in the drug' s approved labeling; ● the relative convenience and ease of administration; ● the willingness of eligible patients to try new therapies and of physicians to prescribe these therapies; ● the length of time that patients who are prescribed our drugs remain on treatment; ● the pricing of our drugs and any current or future drug candidates for which we receive marketing approval; ● publicity concerning our current and future drugs, or competing products and treatments; and ● sufficient third- party insurance coverage or reimbursement. Even if a drug candidate displays a favorable efficacy and safety profile in preclinical and clinical studies and the drug candidate receives marketing approval, market acceptance of the drug will not be known until after it is launched. Our efforts to educate the medical community and third- party payors on the benefits of our drugs may require significant resources, including more resources than those required for treatments marketed by competitors, and may never be successful. Any of these factors may cause our approved drugs, as well as any current or future drug candidates for which we receive marketing approval, to be unsuccessful or less successful than anticipated. If we are unable to establish additional commercial capabilities and infrastructure, we may be unable to generate sufficient revenue to sustain our business. We continue to build out our commercial capabilities and infrastructures and have been growing our sales and distribution experience and capabilities for marketing and market access. To successfully commercialize our approved ~~drugs~~ **45drugs** or any current or future drug candidates for which we receive marketing approval, we will need to continue to develop these capabilities and further expand our infrastructure to support commercial operations in the U. S., Europe and other regions, either on our own or with others. We may be competing with many companies that currently have extensive and well- funded marketing and sales operations. Without a significant internal team or the support of a third party to perform these functions, including marketing and sales functions, we may be unable to compete successfully against these more established companies. We cannot be sure that we will be able to or can successfully compete with other companies to recruit, hire and retain a sufficient number of sales representatives or that they will be effective at promoting our drugs. In addition, we will need to commit significant additional management and other resources to maintain and grow our sales organization. We may not be able to achieve the necessary development and growth in a cost- effective manner or realize a positive return on our investment. Factors that may inhibit our efforts to commercialize our drugs include: ● our inability to recruit, train and retain adequate numbers of sales and marketing personnel; ● the inability of sales personnel to obtain access to or to persuade adequate numbers of physicians to prescribe our drugs; ● unforeseen costs and expenses associated with maintaining an independent sales and marketing organization; and ● delays or disruptions to sales and marketing activities ~~, including due to the ongoing COVID- 19 pandemic~~ . ~~54In~~ **In** the event that we are unable to effectively deploy our sales organization or distribution strategy on a timely

and efficient basis, if at all, the commercialization of our drugs could be delayed which would negatively impact our ability to generate product revenues. If the market opportunities for our approved drugs or drug candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability will be adversely affected. The precise incidence and / or prevalence for SM, **chronic urticaria and other mast cell disorders** ~~RET- altered cancers, EGFR- mutated NSCLC~~ , CDK2- vulnerable cancers and GIST are unknown. Our projections of the number of people who have these diseases, the frequency of the genetic alterations targeted by our drugs and drug candidates and the subset of patients who have the potential to benefit from our treatment options are based on estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations or third- party market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these cancers and the number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for our approved drugs and drug candidates may be limited or may not be amenable to treatment with our precision therapies. Accordingly, the incidence and / or prevalence of the diseases we aim to address may not be otherwise amenable to treatment with our drugs, patients treated with our drugs and drug candidates may develop mutations that confer resistance to treatment or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business. We face substantial competition, which may result in others commercializing, developing or discovering drugs before or more successfully than we do. The development and commercialization of new drugs is highly competitive. We face competition with respect to our drugs and current clinical- stage drug candidates, and we will face competition with respect to any drugs and drug 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 drugs or are pursuing the development of therapies in **our areas 46of focus, including allergy / inflammation** the field of kinase inhibition for cancer and other diseases. Some of these competitive drugs 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. Specifically, there are a large number of companies developing or marketing treatments for cancer, including many major pharmaceutical and biotechnology companies. AYVAKIT / AYVAKYT **and elenestinib (BLU- 263)** ~~faces~~ **face** competition for advanced SM from Novartis AG' s midostaurin and imatinib, and may face competition from drug candidates in development, including that being developed by Cogent Biosciences, Inc. ~~If~~ **and Hoth Therapeutics.** ~~avapritinib~~ **Avapritinib** and elenestinib **may face** ~~are approved for~~ non- advanced SM ~~, they may face~~ competition from drug candidates in development, including those being developed by AB Science S. A., Allakos Inc. ~~and ,~~ Cogent Biosciences, Inc. ~~GAVRETO faces competition for RET fusion- positive NSCLC and RET- altered thyroid carcinoma~~ , ~~including MTC~~ **Hoth Therapeutics** , **Invea Therapeutics** ~~from Eli Lilly and Company' s selpercatinib. If pralsetinib receives marketing approval for patients with other solid tumors, it will also face competition from selpercatinib for these additional indications. In~~ **Inc** ~~addition~~ **.** , **and Theseus** ~~pralsetinib may face competition from other drug candidates in development for RET- altered cancers, including those being developed by AstraZeneca plc, Boston~~ Pharmaceuticals ~~,~~ Inc ~~., Eisai Inc., Exelixis, Inc., GlaxoSmithKline plc, Mirati Therapeutics, Inc., Novartis AG, Pfizer Inc., Stemline Therapeutics, Inc., and Turning Point Therapeutics, Inc., as well as several approved multi- kinase inhibitors with RET activity being evaluated in clinical trials, including alectinib, apatinib, cabozantinib, dovitinib, lenvatinib, sorafenib, sunitinib and vandetinib~~ . AYVAKIT / AYVAKYT may face competition from drug candidates in development for PDGFRA- driven GIST, including those being developed by AB Science S. A., ARIAD Pharmaceuticals, Inc., a wholly- owned subsidiary of Takeda Pharmaceutical Company Limited, AROG Pharmaceuticals, Inc., AstraZeneca plc, ~~Celldex Therapeutics, Inc.,~~ Cogent Biosciences, Inc., Deciphera Pharmaceuticals, LLC, Exelixis, Inc., Ningbo Tai Kang Medical Technology Co. Ltd. and Xencor, Inc. ~~55We are developing BLU- 525 and BLU- 945 for treatment- resistant EGFR- mutated NSCLC, which, if approved, will face competition from AstraZeneca plc' s osimertinib and aumolertinib, which is under collaboration between Jiangsu Hansoh Pharmaceutical Group Co., Ltd. and EQRx, Inc. and approved in China. In addition, BLU- 525 and BLU- 945 may face competition from drug candidates in development for EGFR- mutated NSCLC, including those being developed by Allist Pharmaceuticals, Arrivent Biopharma, Inc., Betta Pharmaceuticals, Black Diamond Therapeutics, Inc., Boehringer Ingelheim RCV GmbH & Co KG, Bridge Biotherapeutics, Inc., C4 Therapeutics, Inc., Daiichi Sankyo Company, Limited, Janssen Pharmaceuticals, Inc., J INTS Bio, Kanaph Therapeutics, RedCloud Bio, Theseus Pharmaceuticals, Inc., and Qilu Pharmaceutical. We are developing BLU- 451 for EGFR exon 20 insertion- positive NSCLC, which, if approved, will face competition from Janssen Pharmaceuticals, Inc. and Takeda Pharmaceuticals. In addition, BLU- 451 may face competition from drug candidates in development for EGFR exon 20 insertion- positive NSCLC, including those being developed by Abbisko Therapeutics Co., Ltd., Bayer AG, Cullinan Oncology, Inc., Daiichi Sankyo Company, Limited, Dizal Pharmaceutical Co. Ltd., Shenzhen Forward Pharmaceutical Co., Ltd., Shanghai Junshi Biosciences Co., Ltd., Orie Pharmaceuticals, Inc. and Scorpion Therapeutics, Inc.~~ We are developing BLU- 222 for cancers vulnerable to CDK2 inhibition, including **CCNE1- aberrant** cancers ~~with aberrant cyclin E~~ , which, if approved, will face competition from indication- specific therapies such as ~~Genentech~~ **AstraZeneca** ' s ~~bevacizumab~~ **capivasertib** , AstraZeneca and Merck' s olaparib, AstraZeneca and Daiichi Sankyo' s ~~Enhertu~~ **trastuzumab deruxtecan** , Clovis Oncology' s rucaparib, **Eisai' s lenvatinib, Genentech' s bevacizumab,** GSK' s niraparib, ~~Merck~~ **GSK** ' s ~~pembrolizumab~~ **dostarlimab** , Menarini Group & Stemline Therapeutics' ~~Elacestrant~~ **elacestrant** , **Merck** ~~and Eisai~~ ' s ~~lenvatinib~~ **pembrolizumab, and Novartis' alpelisib** . In addition, BLU- 222 may face competition from drug candidates in development, including those being developed by Acrivon Therapeutics, Allorion Therapeutics, Inc., Anrui Biomedical Technology, Arvinas, **AstraZeneca plc,** Aucentra Therapeutics **, Avenzo Therapeutics, Bayer, BeiGene** , BioTheryX, Inc., Cedilla Therapeutics, Inc., Cyclacel Pharmaceuticals Inc., Eli Lilly and ~~company~~ **Company**

, Ensem Therapeutics , Exelixis, Gilead Sciences, Inc., ~~Impact~~ **IMPACT** Therapeutics **, Inc.** , Incyclix Bio **, LLC** , Incyte Corporation, Monte Rosa Therapeutics, Inc., **Pfizer Inc., Plexium, Inc.,** Regor Therapeutics Inc., Relay Therapeutics, ~~Pfizer~~ Inc., ~~AstraZeneca plc~~ **Repare Therapeutics** , **Inc., Satya Pharma Innovations Pvt. Ltd., and** Zentalis Pharmaceuticals ~~, Inc. and Repare Therapeutics~~ , Inc. We are developing BLU- ~~852~~ **808** for ~~advanced cancers susceptible to MAP4K1 inhibition~~ **chronic urticaria and other allergy / inflammation disorders** , which ~~,~~ if approved, will face competition from ~~immuno~~ **omalizumab developed by Genentech and Novartis. In addition, BLU** - ~~oncology products~~ **808 may face competition from drug candidates in development for chronic urticaria** , including those developed by **Allakos** ~~Bristol- Myers Squibb Company, Merck & Co.,~~ Inc. **, Amgen Inc., AstraZeneca plc, Celldex Therapeutics, Inc., Escient Pharmaceuticals, Inc., Evommune, Inc, Incyte Corp., Jasper Therapeutics, Inc., Modulus Discovery Inc., Novartis AG** , Regeneron Pharmaceuticals, Inc., Sanofi S. A., **Third Harmonic Bio** ~~and AstraZeneca plc. In addition, BLU- 852 may face competition from drug candidates in development for advanced cancers susceptible to MAP4K1 inhibition, including those being developed by Treadwell Therapeutics~~ , Inc ~~.~~ , ~~BeiGene Ltd.~~ **Hangshou Highlightll Pharma** , ~~Nimbus Therapeutics~~ **Leo Pharma A / S** , ~~LLC and MingMed Biotechnology~~ **Acelyrin Inc., Taiho Pharmaceutical** Co., ~~Ltd~~ **LTD, and Enanta Pharmaceuticals, Inc** . Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early **-** stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we or our collaborators may develop. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we or our collaborators are able to enter the market. The key competitive factors affecting the success of all of our drug candidates, if approved, are likely to be their efficacy, safety, convenience, price, the ~~effectiveness of any related companion diagnostic tests, the~~ level of generic competition and the availability of reimbursement from government and other third- party payors. ~~56Product~~ **47Product** liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any of our approved drugs or drug candidates that we may develop. We face an inherent risk of product liability exposure related to the testing of our approved drugs and drug candidates in human clinical trials and use of our drug candidates through compassionate use programs, and an even greater risk in connection with our commercialization of our current and future drugs. If we cannot successfully defend ourselves against claims that any of our approved drugs or drug candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in: ● decreased demand for any of our approved drugs or drug candidates that we may develop and commercialize; ● 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 of approved drugs or drug candidates that we may develop. Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we may need to further increase our insurance coverage as we begin additional clinical trials or if we successfully commercialize additional drug candidates. 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. Increasing demand for compassionate use of our drug candidates could negatively affect our reputation and harm our business. We are developing drug candidates for the treatment of indications for which there are currently limited or no available therapeutic options. It is possible for individuals or groups to target companies with disruptive social media campaigns related to a request for access to unapproved drugs for patients with significant unmet medical need. If we experience a similar social media campaign regarding our decision to provide or not provide access to any of our current or future drug candidates under an expanded access policy, our reputation may be negatively affected and our business may be harmed. Media attention to individual patients' expanded access requests has resulted in the introduction and enactment of legislation at the local and national level referred to as " Right to Try " laws, such as the federal Right to Try Act of 2017, which are intended to allow patients access to unapproved therapies earlier than traditional expanded access programs. A possible consequence of both activism and legislation in this area may be the need for us to initiate an unanticipated expanded access program or to make our drug candidates more widely available sooner than anticipated. In addition, some patients who receive access to drugs prior to their commercial approval through compassionate use, expanded access programs or right to try access, collectively referred to as compassionate use programs, have life- threatening illnesses and have exhausted all other available therapies. The risk for serious adverse events in this patient population is high, which, if those adverse events are determined to be drug- related, could have a negative impact on the safety profile of our drug candidates if we were to provide them to these patients, which could cause significant delays or an inability to successfully commercialize our drug candidates and materially harm our business. If we were to provide patients with any of our drug candidates under a compassionate use program, our supply capabilities may limit the number of patients who are able to enroll in the program and we may in the future need to restructure or pause any compassionate use program in order to enroll sufficient numbers of patients in our controlled clinical trials required for regulatory approval and successful commercialization of our drug candidates, which could ~~57prompt~~ **48prompt** adverse publicity or other disruptions related to current or potential participants in such programs ~~. If we or our collaborators are unable to successfully develop and commercialize companion diagnostic tests for our drugs and drug candidates, or experience~~

~~significant delays in doing so we may not realize the full commercial potential of our drugs and drug candidates. Because we are focused on precision medicine, in which predictive biomarkers will be used to identify the right patients for our drugs and drug candidates, we believe that our success may depend, in part, on the development and commercialization of companion diagnostic tests. There has been limited success to date industry- wide in developing and commercializing these types of companion diagnostic tests. To be successful, we need to address a number of scientific, technical and logistical challenges. We have entered into agreements to develop and / or commercialize companion diagnostic tests with third parties, including for avapritinib in order to identify GIST patients with the PDGFRA D842V mutation, and pralsetinib in order to identify NSCLC patients with RET fusions and MTC patients with RET mutations. We have limited experience in the development and commercialization of companion diagnostic tests with third parties and may not be successful in developing and commercializing appropriate companion diagnostic tests with third parties to pair with our approved drugs or drug candidates that receive marketing approval. In addition, current commercially available diagnostic tests may become unavailable in the future. Companion diagnostic tests are subject to regulation by the FDA and similar regulatory authorities outside the U. S. as medical devices and require separate regulatory clearance or approval prior to commercialization. We are relying on third parties to design, manufacture, obtain regulatory clearance or approval for and commercialize the companion diagnostic tests, including for avapritinib and pralsetinib, and we expect to rely in whole or in part on third parties to design, manufacture, obtain regulatory clearance or approval for and commercialize any other companion diagnostic tests for current and future drug candidates. We and our collaborators may encounter difficulties in developing and obtaining clearance or approval for the companion diagnostic tests, including issues relating to selectivity / specificity, analytical validation, reproducibility, or clinical validation. In addition, our collaborators for any companion diagnostic test that we may seek to develop: ● may not perform their respective obligations as expected or as required under our agreements with them; ● may not pursue commercialization of a companion diagnostic test even if it receives any required regulatory clearances or approvals; ● may elect not to continue the development of a companion diagnostic test based on changes in their or other third parties' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities; ● may not commit sufficient resources to the marketing and distribution of a companion diagnostic test; and ● may terminate their relationship with us. Any delay or failure by us or our collaborators to develop or obtain regulatory clearance or approval of the companion diagnostic tests could delay, prevent or revoke approval of our drug candidates. If we, or any third parties that we have engaged or may in the future engage to assist us are unable to successfully develop and commercialize companion diagnostic tests for our drugs and drug candidates, or experience delays in doing so: ● the development of our approved drugs and drug candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials; ● our drug candidates may not receive marketing approval if safe and effective use of a therapeutic drug candidate depends on an in vitro diagnostic; ● regulatory authorities may impose post- marketing requirements regarding the development and commercialization of companion diagnostic tests for our drugs and drug candidates; and58 ● we may not realize the full commercial potential of any of our approved drugs or drug candidates that receive marketing approval if, among other reasons, we are unable to appropriately select patients who are likely to benefit from treatment with our drugs. As a result, our business may be materially harmed. In addition, third party collaborators may encounter production difficulties that could constrain the supply of the companion diagnostic tests, and both they and we may have difficulties gaining acceptance of the use of the companion diagnostic tests in the clinical community. If such companion diagnostic tests fail to gain market acceptance, it would have an adverse effect on our ability to derive revenues from sales of our current and future drugs. In addition, the diagnostic company with whom we contract may decide to discontinue selling or manufacturing the companion diagnostic test that we anticipate using in connection with development and commercialization of our approved drugs and drug candidates or our relationship with such diagnostic company may otherwise terminate. We may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our drugs and drug candidates or do so on commercially reasonable terms, which could adversely affect and / or delay the development or commercialization of our drugs and drug candidates~~ . Our reliance on single- source third- party suppliers could harm our ability to commercialize our drugs or any drug candidates that may be approved in the future. We do not currently own or operate manufacturing facilities for the production of our drugs or any drug candidates that may be approved in the future. We primarily rely on single- source third- party suppliers to manufacture and supply our drugs, which may not be able to produce sufficient inventory to meet commercial demand in a timely manner, or at all. Our third- party suppliers may not be required to provide us with any guaranteed minimum production levels or have dedicated capacity for our drugs. As a result, there can be no assurances that we will be able to obtain sufficient quantities of our drugs or any other drug candidates that may be approved in the future, which could have a material adverse effect on our business as a whole. If we are unable to **establish,** maintain and, if necessary, expand sales and marketing capabilities or enter into agreements with third parties to sell and market our drugs and drug candidates, we may not be successful in commercializing our drugs and drug candidates if and when they are approved. There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time- consuming and could delay any drug launch. If the commercial launch of a drug candidate or a new indication for a drug product for which we establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses, which may be costly. If we enter into arrangements with third parties to perform sales, marketing and distribution services, our drug revenues or the profitability of these drug revenues to us are likely to be lower than if we were to market and sell any current or future drugs ourselves. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our drugs effectively. In addition, we may not be successful in entering into arrangements with third parties to sell and market our current and future drugs or may be unable to do so on terms that are favorable to us. If we do not **establish,** maintain and, if necessary,

expand sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our drugs and drug candidates, if approved. Further, our business, results of operations, financial condition and prospects will be materially adversely affected. 59Risks -- **Risks** Related to Drug Development and Regulatory ApprovalIf we are unable to advance our drug candidates to clinical development, obtain regulatory approval for our drug candidates, including for avapritinib and pralsetinib in additional indications or in additional geographies, and ultimately commercialize them, or experience significant delays in doing so, our business will be materially harmed. Our ability to generate substantial drug revenues, if ever, **material net cash inflows from our operations** will depend heavily on the successful development and commercialization of our drugs and drug candidates. Each of our drug candidates will require additional preclinical or clinical development, management of clinical, preclinical and manufacturing activities, regulatory approval in multiple jurisdictions, obtaining manufacturing supply, substantial investment and significant marketing efforts before we generate substantial revenues from sales for those drug candidates, if approved . In addition, for some of our drug candidates, in order to select patients most likely to respond to treatment and rapidly confirm mechanistic and clinical proof- of- concept, or to identify appropriate patients for our drugs or drug candidates for which we obtain approval, we may be required or we may seek to develop companion diagnostic tests, which are assays or tests to identify an appropriate patient population. Companion diagnostic tests are subject to regulation as medical devices and must themselves be cleared or approved for marketing by the FDA or certain other foreign regulatory agencies before we may commercialize our drug candidates . The success of our approved drugs and drug candidates will depend on several factors, including the following: ● successful enrollment in, and initiation and completion of, clinical trials, including our ongoing and planned clinical trials for our drugs and drug candidates as monotherapies and in combination with other agents; ● successful initiation and completion of preclinical studies for our other drug candidates; ● successful development of any companion diagnostic tests for use with our drugs and drug candidates; ● receipt of regulatory approvals from applicable regulatory authorities and transitioning any conditional marketing authorizations to full approvals; **49** ● in- house commercial manufacturing capabilities or arrangements with third- parties for clinical supply and commercial manufacturing, packaging and labeling and the receipt by such third- party manufacturers of requisite approvals to supply commercial inventories of our approved drugs and drug candidates; ● obtaining and maintaining patent and trade secret protection or regulatory exclusivity for our drugs and drug candidates; ● successful commercialization of our approved drugs and drug candidates, if and when approved, whether alone or in collaboration with others; ● acceptance of our approved drugs and drug candidates, if and when approved, by patients, the medical community and third- party payors; ● effectively competing with other therapies; ● obtaining and maintaining healthcare coverage and adequate reimbursement; ● enforcing and defending intellectual property rights and claims; and ● maintaining a continued acceptable safety profile of our drugs and drug candidates following approval. 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 drugs and drug candidates, which would materially harm our business. If we do not receive regulatory approvals for our drug candidates, we may not be able to continue our operations. 60If **If** we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented. We may not be able to initiate or continue clinical trials for our drug candidates , including avapritinib and pralsetinib for additional indications , if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the U. S. Because **because** the target patient populations for our drug candidates and approved drugs in clinical development for additional indications are relatively small, it may be difficult to successfully identify patients. Although we have entered into or plan to enter into agreements with third parties to develop companion diagnostic tests for use in some of our other current or future clinical trials in order to help identify eligible patients, we may experience delays in reaching, or fail to reach, agreement on acceptable terms to develop such companion diagnostic tests. Any third parties whom we engage to develop companion diagnostic tests may experience delays or may not be successful in developing such companion diagnostic tests, furthering the difficulty in identifying patients for our clinical trials. In addition, current commercially available diagnostic tests to identify appropriate patients for our clinical trials or any approved drug candidates may become unavailable in the future . In addition, we have experienced some delays or disruptions in enrollment in our ongoing clinical trials due to the COVID- 19 pandemic, and we anticipate we may experience additional delays or disruptions in the future due to the ongoing COVID- 19 pandemic and changes in local site or IRB policies availabilities of site staff reprioritization of hospital resources, restricted access to healthcare professionals and testing sites and other containment measures or concerns among patients about participating in clinical trials during a pandemic . Furthermore, some of our competitors have ongoing clinical trials for drug candidates that treat the same indications as our drug candidates and approved drugs in clinical development for additional indications, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' drug candidates. Patient enrollment may be affected by other factors including: ● the severity of the disease under investigation; ● the size of the target patient population; ● the eligibility criteria for the clinical trial; ● the availability of an appropriate genomic screening test; ● the perceived risks and benefits of the drug candidate under study; ● the efforts to facilitate timely enrollment in clinical trials; **50** ● the patient referral practices of physicians; ● the ability to monitor patients adequately during and after treatment; and ● the proximity and availability of clinical trial sites for prospective patients. Our inability to identify patients appropriate for enrollment in our clinical trials, or to enroll a sufficient number of patients in our clinical trials, would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our drug candidates , which would cause the value of our company to decline and limit our ability to obtain additional financing . If we are unable to include patients with the driver of the disease, including the applicable genomic alteration for diseases in genomically defined patient populations, this could compromise our ability to seek participation in the FDA' s expedited review and approval programs, including breakthrough therapy designation and fast track designation, or otherwise to seek to accelerate clinical development and regulatory timelines. 61If **If** we are not

able to obtain, or if there are delays in obtaining, required regulatory approvals for our drug candidates ~~and, if applicable, for any related companion diagnostic tests~~, we will not be able to commercialize, or may be delayed in commercializing, such drug candidates, and our ability to generate revenue will be materially impaired. Our drug candidates ~~and any companion diagnostic tests related to our approved drugs or drug candidates, including the companion diagnostic tests that we are developing or have developed for avapritinib in order to identify GIST patients with the PDGFRA D842V mutation, and pralsetinib in order to identify NSCLC patients with RET fusions and MTC patients with RET mutations,~~ and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export, are subject to comprehensive regulation by the FDA and other regulatory agencies in the U. S. and by comparable authorities in other countries. Before we can commercialize any of our drug candidates, we must obtain marketing approval ~~. We may also need marketing clearance or approval for any related companion diagnostic tests, including the companion diagnostic tests that we are developing for avapritinib and pralsetinib~~. We expect to rely on third- party CROs and / or regulatory consultants to assist us in filing and supporting the applications necessary to gain regulatory approvals. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the drug candidate' s safety and efficacy. Securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Should FDA determine that an inspection is necessary for approval of a marketing application and an inspection cannot be completed during the review cycle due to restrictions on travel, FDA has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, FDA may defer action on the application until an inspection can be completed. Our drug candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. The process of obtaining regulatory approvals, if approval is obtained at all, both in the U. S. and abroad is expensive, may take many years if additional clinical trials are required and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the drug candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted NDA for a drug candidate, pre- market approval **(** ~~, or~~ PMA **)** , ~~application for a companion diagnostic test~~ or equivalent application types, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. We currently have multiple marketing applications for our drug candidates under review across the world. Our drug candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following: ● the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials; ● we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a drug candidate is safe and effective for its proposed indication ~~or a related companion diagnostic test is suitable to identify appropriate patient populations~~ ; **51** ● the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval; ● we may be unable to demonstrate that a drug candidate' s clinical and other benefits outweigh its safety risks; ● the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials; ~~62~~ ● the data collected from clinical trials of our drug candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the U. S. or elsewhere; ● the FDA or comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes or facilities of third- party manufacturers with which we contract for clinical and commercial supplies; **and** ● the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval ~~; and ● delays or disruptions impacting the FDA or comparable foreign regulatory authorities due to the ongoing COVID- 19 pandemic. Moreover, during the COVID- 19 pandemic, a number of companies announced receipt of complete response letters due to the FDA' s inability to complete required inspections for their applications~~ . In addition, even if we were to obtain approval, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our drugs ~~and related companion diagnostic tests~~ , may grant approval contingent on the performance of costly post- marketing clinical trials or other post- marketing requirements, or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug candidate. Additionally, the receipt of regulatory approval for one indication does not ensure the likelihood of success for regulatory approval of expanded indications for a marketed product. Any of the foregoing scenarios could materially harm the commercial prospects for our drug candidates. If we experience delays in obtaining approval or if we fail to obtain approval of our ~~drug candidates and companion diagnostic tests related to our approved drugs and~~ drug candidates, the commercial prospects for our approved drugs or drug candidates may be harmed and our ability to generate revenues will be materially impaired. Inadequate funding for the FDA, the SEC and other government agencies, including from government shutdowns, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business. The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, the ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is

subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new drug candidates to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations. ~~Results~~ **52Results** from earlier stage trials may not be predictive of the results of later stage trials and interim and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available or as additional analyses are conducted and as the data are subject to audit and verification procedures that could result in material changes in the final data. The results of preclinical studies and early clinical trials of our drug candidates may not be predictive of the results of later- stage clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. There is typically an extremely high rate of attrition from the failure of drug candidates proceeding through clinical trials. Drug candidates in later stages of clinical trials may fail to show the desired safety and ~~63efficacy~~ -- **efficacy** profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or emergence of unacceptable safety issues, notwithstanding promising results in earlier trials. Most drug candidates that commence clinical trials are never approved as products and there can be no assurance that any of our future clinical trials will ultimately be successful or support further clinical development of any of our drug candidates. Drug candidates that appear promising in the early phases of development may fail to reach the market for several reasons, including: ● preclinical studies or clinical trials may show the drug candidates to be less effective than expected (e. g., a clinical trial could fail to meet its primary endpoint (s)) or to have unacceptable side effects or toxicities; ● failure to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful; ● failure to receive the necessary regulatory approvals; ● manufacturing issues, formulation issues, pricing or reimbursement issues or other factors that make a drug candidate uneconomical; and ● the proprietary rights of others and their competing products and technologies that may prevent one of our drug candidates from being commercialized. In addition, differences in trial design between early- stage clinical trials and later- stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their drug candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their products. Additionally, from time to time, we may publish interim or preliminary data from our clinical studies. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Material adverse changes between preliminary or interim data and final data could significantly harm our business prospects. Our drugs and drug candidates may cause undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, result in restrictive distribution or result in significant negative consequences following marketing approval, if any. Undesirable side effects caused by any of our approved drugs or drug candidates could cause us to interrupt, delay or halt preclinical studies or could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities. As is the case with all oncology drugs, it is likely that there may be side effects associated with the use of our drugs and drug candidates. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other 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 drugs or drug candidates for any or all targeted indications. The drug- related side effects could affect patient recruitment or the ability of enrolled ~~patients~~ **53patients** to complete clinical trials or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly. Further, our approved drugs and drug candidates could cause undesirable side effects in preclinical studies or clinical trials related to on- target toxicity. If on- target toxicity is observed, or if our drugs or drug candidates have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow 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. 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. ~~64Further~~ -- **Further** , clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients and limited duration of exposure, rare and severe side effects of our drugs or drug candidates may only be uncovered with a significantly larger number of patients exposed to the drugs or drug candidate. If we or others identify undesirable side effects caused by any of our approved drugs or drug candidates (or any other similar drugs) after marketing approval, a number of potentially significant negative consequences could result, including: ● regulatory authorities may withdraw or limit their approval of such drug; ● regulatory authorities may require the addition of labeling statements, such as a " boxed " warning or a contraindication; ● we may be required to create a medication guide outlining the risks of such side effects for distribution to patients; ● we may be required to change the way such drug is distributed or administered, conduct additional clinical trials or change the labeling of such drug; ● regulatory authorities may require a Risk Evaluation and Mitigation Strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools; ● we may be subject to regulatory investigations and government enforcement actions; ● we may decide to remove such drug from the marketplace; ● we could be sued and held liable for injury caused to individuals exposed to or taking our drugs and drug candidates; and ● our reputation may suffer. We

believe that any of these events could prevent us from achieving or maintaining market acceptance of the affected drugs or drug candidates and could substantially increase the costs of commercializing our approved drugs and drug candidates, if approved, and significantly impact our ability to successfully commercialize our approved drugs and drug candidates and generate revenues. We may seek designation for our discovery platform as a designated platform technology, but we might not receive such designation, and even if we do, such designation may not lead to faster drug development or a faster regulatory review or approval process. We may seek designation for our discovery platform as a designated platform technology. Under the Food and Drug Omnibus Reform Act of 2022 (FDORA), a platform technology incorporated within or utilized by a drug product is eligible for designation as a designated platform technology if (1) the platform technology is incorporated in, or utilized by, a drug approved under an NDA; (2) preliminary evidence submitted by the sponsor of the approved or licensed drug, or a sponsor that has been granted a right of reference to data submitted in the application for such drug, demonstrates that the platform technology has the potential to be incorporated in, or utilized by, more than one drug ~~without~~ **54without** an adverse effect on quality, manufacturing, or safety; and (3) data or information submitted by the applicable person indicates that incorporation or utilization of the platform technology has a reasonable likelihood to bring significant efficiencies to the drug development or manufacturing process and to the review process. A sponsor may request the FDA to designate a platform technology as a designated platform technology concurrently with, or at any time after, submission of an investigational new drug (IND) application for a drug that incorporates or utilizes the platform technology that is the subject of the request. If so designated, the FDA may expedite the development and review of any subsequent original NDA for a drug that uses or incorporates the platform technology. Even if we believe our discovery platform meets the criteria for such designation, the FDA may disagree and instead determine not to grant such designation. In addition, the receipt of such designation for a platform technology does not ensure that a drug will ~~65be~~ **be** developed or reviewed more quickly or receive FDA approval. Moreover, the FDA may revoke a designation if the FDA determines that a designated platform technology no longer meets the criteria for such designation. A fast track or breakthrough therapy designation by the FDA for our drug candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our drug candidates will receive marketing approval. We may seek fast track or breakthrough therapy designation for some of our current or future drug candidates. Fast track designation is designed for drug candidates intended for the treatment of a serious or life- threatening disease or condition, where nonclinical or clinical data demonstrate the potential to address an unmet medical need for this disease or condition. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life- threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as fast track or breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. The FDA ~~has~~ granted fast track designation to BLU- 782 for the treatment of FOP. ~~The FDA has granted breakthrough therapy designation to avapritinib for the treatment of moderate to severe indolent SM.~~ In addition, the FDA previously granted breakthrough **therapy** designation to our drugs, AYVAKIT and GAVRETO, for the treatment of certain patients with GIST, advanced SM, moderate to severe indolent SM and RET- altered cancers, respectively. Designation as a fast track or breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our drug candidates meets the criteria for designation as a fast track or breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a fast track or breakthrough therapy designation for a drug candidate may not result in a faster development process, review or approval compared to other drugs and does not assure ultimate approval by the FDA. In addition, even if one or more of our drug candidates qualify as fast track or breakthrough therapies, the FDA may later decide that the drugs no longer meet the conditions for qualification. We may seek approval of our drug candidates, where applicable, under the FDA' s accelerated approval pathway. A product may be eligible for accelerated approval if it is designed to treat a serious or life- threatening disease or condition and generally provides a meaningful advantage over available therapies. In addition, it demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality (IMM), that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of accelerated approval, the FDA likely would require that we perform adequate and well- controlled post- marketing clinical trials, and under FDORA the FDA is now permitted to require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if such post- approval studies fail to verify the product' s predicted clinical benefit. Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post- approval confirmatory study or submit timely reports to the agency on their progress. These confirmatory trials must be completed with due diligence. In addition, the FDA currently requires, unless otherwise informed by the agency, pre- approval of promotional materials for products receiving accelerated approval, which could adversely impact the timing of the commercial launch of the product. Thus, even if we seek to utilize the accelerated approval pathway, we may not be able to obtain accelerated approval and, even if we do, we may not experience a faster development, regulatory review or approval process for that product. In addition, receiving ~~accelerated~~ **55accelerated** approval does not assure that the product' s accelerated approval will eventually be converted to a traditional approval. **Additionally, if we are not able to obtain full approval of any accelerated approval product, including through the completion of post- marketing studies, we or our partners may decide to withdraw marketing of such products. Specifically, in June 2023, Roche voluntarily withdrew the indication of GAVRETO for the treatment of adult and pediatric patients 12 years of age and older with advanced or**

metastatic RET- mutant MTC. The decision to withdraw the indication was made in consultation with the FDA, in accordance with the requirements of the FDA' s Accelerated Approval Program, with the official FDA withdrawal of the indication occurring on July 20, 2023. We may be unsuccessful in obtaining or may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity. The FDA has granted orphan drug designation to avapritinib for the treatment of GIST and the treatment of mastocytosis, to pralsetinib for the treatment of RET-rearranged NSCLC, JAK1 / 2- positive NSCLC or TRKC- positive ~~66NSCLC --~~ **NSCLC and to fisogatinib** for the treatment of HCC. In addition, the European Commission, or EC, has granted orphan medicinal product designation to avapritinib for the treatment of GIST and the treatment of mastocytosis. As part of our business strategy, we may seek orphan drug designation for some of our other drug candidates, and we may be unsuccessful. Regulatory authorities in some jurisdictions, including the U. S. and the EU, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200, 000 individuals annually in the U. S., or a patient population greater than 200, 000 in the U. S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U. S. In the U. S., orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user fee waivers. Similarly, in the EU, the European Commission grants orphan medicinal product designation after receiving the opinion of the European Medicines Agency' s, or EMA, Committee for Orphan Medicinal Products on an orphan medicinal product designation application. Orphan medicinal product designation is intended to promote the development of medicinal products that are intended for the diagnosis, prevention or treatment of life threatening or chronically debilitating conditions affecting not more than five (5) in ten thousand (10, 000) persons in the EU or for products intended for the diagnosis, prevention, or treatment of a life threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the product in the EU would generate sufficient return to justify the necessary investment in developing the product. In each case, there must be no satisfactory method of diagnosis, prevention, or treatment authorized for marketing in the EU (or, if such a method exists, the product would be of significant benefit to those affected by the condition). In the EU, orphan medicinal product designation entitles a party to financial incentives such as reduction of fees or fee waivers. Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the EC or the FDA from approving another marketing application for the same drug and indication for that time period, except in limited circumstances. The applicable period is seven years in the U. S. and ten years in the EU. The EU exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan medicinal product designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Even if we obtain orphan drug exclusivity for a drug, that exclusivity may not effectively protect the designated drug from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA' s preexisting regulatory interpretation, to require that a drug Sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The law reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. Moreover, in the Consolidated Appropriations Act of 2021, Congress did not further change this interpretation when it clarified that the interpretation codified in FDARA would apply in cases where FDA issued an orphan designation before the ~~enactment~~ **56enactment** of FDARA but where product approval came after the enactment of FDARA. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan drug exclusive marketing rights in the U. S. may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. While we intend to continue seek orphan drug designation for our drug candidates, we may never receive such designations. Even if we receive orphan drug designation for any of our drug candidates, there is no guarantee that we will enjoy the benefits of those designations. ~~67The --~~ **The** FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted. We may not be successful in our efforts to expand our pipeline of drug candidates. A key element of our strategy is to use our novel target discovery engine to identify kinases that are drivers of diseases in genomically defined patient populations with high unmet medical need in order to build a pipeline of drug candidates. Although our research and development efforts to date have resulted in a pipeline of drug candidates, we may not be able to continue to identify novel kinase drivers and develop drug candidates. We may also pursue opportunities to acquire or in-license additional businesses, technologies or drugs, form strategic alliances or create joint ventures with third parties to complement or augment our existing business. For example, in February 2022 we entered into a collaboration with Proteovant to research and advance novel targeted protein degrader therapies leveraging Proteovant' s artificial intelligence- enhanced targeted protein degradation platform and our small molecule precision medicine capabilities. However, we may not be able to identify

any drug candidates for our pipeline through such acquisition or in- license. Even if we are successful in continuing to build and expand our pipeline, the potential drug candidates that we identify may not be suitable for clinical development. For example, they may be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will be successful in clinical trials or receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize drug candidates, we will not be able to obtain drug revenues in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price. We may expend our limited resources to pursue a particular drug candidate or indication and fail to capitalize on drug candidates or indications that may be more profitable or for which there is a greater likelihood of success. Because we have limited human capital and financial resources, we focus on research programs and drug candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other drug 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 drugs or profitable market opportunities. Our spending on current and future research and development programs and drug candidates for specific indications may not yield any commercially viable drugs. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such drug candidate. At any time and for any reason, we may determine that one or more of our discovery programs or preclinical or clinical drug candidates or programs does not have sufficient potential to warrant the allocation of resources toward such program or drug candidate. Accordingly, we may choose not to develop a potential drug candidate or elect to suspend, deprioritize or terminate one or more of our discovery programs or preclinical or clinical drug candidates or programs. If ~~we~~ **57we** suspend, deprioritize or terminate a program or drug candidate in which we have invested significant resources, we will have expended resources on a program that will not provide a full return on our investment and may have missed the opportunity to have allocated those resources to potentially more productive uses, including existing or future programs or drug candidates. We intend to develop drug candidates in combination with other therapies, which exposes us to additional risks. We intend to develop, launch and commercialize BLU- 945, BLU- 525, BLU- 222 and potentially other drug candidates in combination with one or more approved or unapproved therapies. Even if any drug candidate we develop were to receive marketing approval for use in combination with other approved therapies, the FDA, the EMA or other regulatory authorities could still revoke approval of the therapy used in combination with our drug candidate. If the therapies used in combination with our drug candidates are replaced as the standard of care for the indications we choose for any of our drug candidates, the FDA, EMA or regulatory authorities may require us to conduct additional clinical trials which may experience complications surrounding trial execution, such as complexities surrounding trial design, establishing trial protocols and interpretability of results, clinical site access and initiation, patient recruitment and ~~68enrollment~~ -- **enrollment** , quality and supply of clinical doses, safety issues or a lack of clinically relevant activity. The uncertainty resulting for the use of our drug candidates in combination with other approved or unapproved therapies may make it difficult to accurately predict side effects in the future clinical trials. The occurrence of any of these risks could result in our own drug candidates, if approved, being removed from the market if they are not also approved as monotherapies or being less successful commercially. Further, we will not be able to market and sell any drug candidate we develop in combination with an unapproved therapy for a combination indication if that unapproved therapy does not ultimately obtain marketing approval either alone or in combination with our drug candidate. In addition, unapproved therapies face the same risks described with respect to our drug candidates currently in development and clinical trials, including the potential for serious adverse effects, delay in their clinical trials and lack of FDA approval. If the FDA, EMA or other regulatory authorities do not approve these other products or revoke their approval of, or if safety, efficacy, quality, manufacturing or supply issues arise with, the agents we choose to evaluate in combination with our drug candidates we may be unable to obtain approval of or market such combination therapy. Risks Related to Government Legislations and RegulationsWe are required to comply with comprehensive and ongoing regulatory requirements for any of our current or future approved drugs, including conducting confirmatory clinical trials for any drug that receives accelerated approval. In addition, our current or future approved drugs could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our drugs. **We have in the past and may in the future seek approval of current or future drug candidates, where applicable, under the FDA' s accelerated approval pathway.** Any current or future drug candidate for which we receive accelerated approval from the FDA ~~, including GAVRETO,~~ or similar conditional approval from the EMA, including AYVAKYT, or comparable regulatory authorities in other jurisdictions may be required to undergo one or more confirmatory clinical trials, as a condition of accelerated approval, be required to perform adequate and well- controlled post- marketing clinical trials to confirm the product' s clinical benefit. These post-market confirmatory trials must be completed according to timelines agreed upon with the FDA **, and if they are not completed in accordance with these timelines than it could result in withdrawal of the indication. For example, the voluntary withdrawal AcceleRET- MTC, a Phase 3 clinical trial required by the FDA to convert the accelerated approval of GAVRETO for MTC to a full approval, is no longer being pursued due to lack of feasibility** . If such drug candidate fails to meet its safety and efficacy endpoints in such confirmatory clinical trials, the regulatory authority may withdraw its approval. There is no assurance that any such drug candidate will successfully advance through its confirmatory clinical trial (s). Therefore, even if a drug candidate receives accelerated approval from the FDA or similar conditional approval from the EMA or comparable regulatory authorities, such approval may be withdrawn at a later date. In addition, under FDORA the FDA is now permitted to require, as appropriate, that post- marketing trials be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send ~~the~~ **58the** necessary updates to the FDA, or if such post- approval studies fail to verify the

product' s predicted clinical benefit. Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post- approval confirmatory study or submit timely reports to the agency on their progress. If the FDA or a comparable foreign regulatory authority approves any of our drug candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the drug will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post- marketing information and reports, registration requirements, as well as continued compliance with current Good Manufacturing Practices (cGMPs) and Good Clinical Practices (GCPs) for any clinical trials that we conduct post- approval. In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are subject to periodic unannounced inspections by the FDA and state agencies for compliance with cGMP requirements. For certain commercial prescription drug products, manufacturers and other parties involved in the supply chain must also meet chain of distribution requirements and build electronic, interoperable systems for product tracking and tracing and for notifying the FDA of counterfeit, diverted, stolen and intentionally adulterated products or other products that are otherwise unfit for distribution in the United States. Any regulatory approvals that we receive for our drug candidates may also be subject to limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post- marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the drug. Additionally, under FDORA, sponsors of approved drugs and biologics must provide 6 months' notice to the FDA of ~~69any~~ **any** changes in marketing status, such as the withdrawal of a drug, and failure to do so could result in the FDA placing the product on a list of discontinued products, which would revoke the product' s ability to be marketed. The FDA closely regulates the post- approval marketing and promotion of pharmaceutical and biological products to ensure such products are marketed only for the approved indications and in accordance with the provisions of the approved labeling. Later discovery of previously unknown problems with a drug, including adverse events of unanticipated severity or frequency, or with our third party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things: ● restrictions on the marketing or manufacturing of the drug, withdrawal of the drug from the market, " dear doctor " letters or drug recalls; ● fines, warning letters or holds on clinical trials; ● refusal by the FDA to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of marketing approvals; ● drug seizure or detention, or refusal to permit the import or export of drugs; and ● injunctions or the imposition of civil or criminal penalties. The FDA' s policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability. Regulatory agencies may also impose requirements for costly post- marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. The FDA and other agencies, including the Department of Justice (DOJ), closely regulate and monitor the post- approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed 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, or any future collaborators, do not market any of our products for which we, or they, receive marketing approval for only their approved indications, we, or they, may be subject to warnings or enforcement action for off- label marketing, government investigations, or litigation. Violation of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state healthcare fraud and abuse laws and state consumer ~~protection~~ **59protection** laws and could expose our company to substantial civil or criminal penalties. Even though we may have obtained approvals for certain of our products, such drug or drug candidate may become subject to unfavorable pricing regulations or third- party coverage and reimbursement policies, which would harm our business. The regulations that govern regulatory approvals, pricing and reimbursement for new drugs vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing 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 drug candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the drug candidate, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the drug candidate in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if our drug candidates obtain marketing approval. **See section entitled " Business – Coverage and Reimbursement ".** Our ability to commercialize any drugs and drug candidates successfully also will depend in part on the extent to which coverage and reimbursement for these drugs and drug candidates and related treatments will be available from government authorities, private health insurers and other organizations. ~~70In~~ **In** the U. S. and markets in other countries, patients generally rely on third- party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize additional products will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third- party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services (CMS), an agency within the U. S. Department of Health and Human Services (HHS). CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a

substantial degree. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments. Sales of these or other products that we may identify will depend substantially, both domestically and abroad, on the extent to which the costs of our products will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third- party payors. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our products. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. A primary trend in the U. S. healthcare industry and elsewhere is cost containment. Government authorities and other third- party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular drugs. Increasingly, third- party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs. We cannot be sure that coverage will be available for any drug candidate that we commercialize and, if coverage is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any drug candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any drug candidate for which we obtain marketing approval. ~~Further, due to the ongoing COVID- 19 pandemic, many individuals have lost or will be losing employer- based insurance coverage, which may adversely affect our ability to commercialize our products. It is unclear what effect, if any, American Rescue Plan and other government efforts to expand coverage will have on the number of covered individuals. See section entitled " Business – Coverage and Reimbursement. "~~ There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside the U. S. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on ~~reimbursement~~ **60reimbursement** levels already set for lower- cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U. S. Private third- party payors often rely upon Medicare coverage policy ~~and payment limitations~~ in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government- funded and private payors for any approved drugs that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize drugs and our overall financial condition. Healthcare legislative reform measures may have a material adverse effect on our business and results of operations. The United States has enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our current drug candidates or any future drug candidates, restrict or regulate post- approval activities and affect our ability to profitably sell any product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to ~~71product~~ **product** labeling; (iii) the recall or discontinuation of our products; or (iv) additional record- keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. ~~In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the ACA was passed, which substantially changes the way healthcare is financed by both governmental and private insurers, and significantly impacts the U. S. pharmaceutical industry. In August 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. The IRA includes several provisions that will impact our business to varying degrees, including provisions that create a $ 2, 000 out- of- pocket cap for Medicare Part D beneficiaries, impose new manufacturer financial liability on all drugs in Medicare Part D, allow the U. S. government to negotiate Medicare Part B and Part D pricing for certain high- cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for drug prices that increase faster than inflation, and delay the rebate rule that would require pass- through of pharmacy benefit manager rebates to beneficiaries. The effect of IRA on our business and the healthcare industry in general is not yet known.~~ See section entitled " Business – **Healthcare Reform** ~~Coverage and Reimbursement~~ . " At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. We may face competition in the U. S. for our development candidates and investigational medicines, if approved, from therapies sourced from foreign countries that have placed price controls on pharmaceutical products. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. **For example, by Executive Order, FDA works with states and Indian Tribes that propose to develop Section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003. FDA released implementing regulations on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. On January 5, 2024, FDA issued to Florida the first approval for a state importation plan. Colorado has a pending application. If successfully implemented, importation of drugs from Canada may materially and adversely affect the price we receive for any of our product candidates.** Legislation or regulations allowing the reimportation of drugs, if enacted, could decrease the price we receive for any products that we may develop and adversely affect our future revenues and prospects for profitability ~~. For example, on July 9, 2021, President Biden issued an executive order directing the FDA to, among other things, continue to clarify and improve the~~

~~approval framework for generic drugs and identify and address any efforts to impede generic drug competition which could adversely impact our business~~ . The Creating and Restoring Equal Access to Equivalent Samples Act, or the CREATES Act, was enacted in 2019 requiring sponsors of approved new drug applications and biologics license applications to provide sufficient quantities of product samples on commercially reasonable, market- based terms to entities developing generic drugs and biosimilar biological products. The law establishes a private right of action allowing developers to sue application holders that refuse to sell them product samples needed to support their applications. If we are required to provide product samples or allocate additional resources to respond to such requests or any legal challenges under this law, our business could be adversely impacted. **We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and / or impose price controls may adversely affect: • the demand for our product candidates, if we obtain regulatory approval; • our ability to set a price that we believe is fair for our approved products; • our ability to generate revenue and achieve or maintain profitability; • the level of taxes that we are required to pay; and • the availability of capital.** ~~Other 61~~**Other** legislative measures have also been enacted that may impose additional pricing and product development pressures on our business, and we expect that additional foreign, federal and state healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in limited coverage and reimbursement and reduced demand for our drugs and drug candidates, if approved, or additional pricing pressures. We are currently unable to predict what additional legislation or regulation, if any, relating to the health care industry may be enacted in the future or what effect recently enacted federal legislation or any such additional legislation or regulation would have on our business. The pendency or approval of such proposals or reforms could result in a decrease in our stock price or limit our ability to raise capital or to enter into collaboration agreements for the further development and commercialization of our approved drugs and drug candidates. Our relationships with customers and third- party payors will be subject to applicable anti- kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings. Our arrangements with third- party payors and customers expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, including but not limited to, the federal healthcare Anti- Kickback Statute, the False Claims Act, the federal Health Insurance Portability and Accountability Act of 1996 **(** ~~, or~~ HIPAA **), as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH)** , the Physician Payment Sunshine Act, ~~HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH,~~ the federal false statements statute, federal consumer protection and unfair competition laws ~~72and~~ -- **and** similar state and foreign laws and regulations that may regulate the business or financial arrangements and relationships through which we market, sell and distribute our drugs. The number and complexity of federal, state, and foreign laws continue to increase, and additional governmental resources are being used to enforce these laws and to prosecute companies and individuals who are believed to be violating them. See section entitled " Business – Other Healthcare Laws. " In the U. S., to help patients who have no or inadequate insurance access our drug, we have a patient assistance program that we administer in conjunction with our patient support program vendor. ~~If~~ **In addition, we have a copay support program for commercially insured patients. Government enforcement agencies have shown increased interest in pharmaceutical companies' product and patient assistance programs, including reimbursement support services, and a number of investigations into these programs have resulted in significant civil and criminal settlements. In addition, at least one insurer has directed its network pharmacies to no longer accept co- pay coupons for certain specialty drugs the insurer identified. Our co- pay coupon programs could become the target of similar insurer actions. In addition, in November 2013, the CMS issued guidance to the issuers of qualified health plans sold through the ACA' s marketplaces encouraging such plans to reject patient cost- sharing support from third parties and indicating that the CMS intends to monitor the provision of such support and may take regulatory action to limit it in the future. The CMS subsequently issued a rule requiring individual market qualified health plans to accept third- party premium and cost- sharing payments from certain government- related entities. In September 2014, the OIG of the HHS issued a Special Advisory Bulletin warning manufacturers that they may be subject to sanctions under the federal anti- kickback statute and / or civil monetary penalty laws if they do not take appropriate steps to exclude Part D beneficiaries from using co- pay coupons. Accordingly, companies exclude these Part D beneficiaries from using co- pay coupons. It is possible that changes in insurer policies regarding co- pay coupons and / or the introduction and enactment of new legislation or regulatory action could restrict or otherwise negatively affect these patient support programs, which could result in fewer patients using affected products, and therefore could have a material adverse effect on our sales, business, and financial condition. Third party patient assistance programs that receive financial support from companies have become the subject of enhanced government and regulatory scrutiny. The OIG has established guidelines that suggest that it is lawful for pharmaceutical manufacturers to make donations to charitable organizations who provide co- pay assistance to Medicare patients, provided that such organizations, among other things, are bona fide charities, are entirely independent of and not controlled by the manufacturer, provide aid to applicants on a first- come basis according to consistent financial criteria and do not link aid to use of a donor' s product. However, donations to patient assistance programs have received some negative publicity and have been the subject of multiple government enforcement actions, related to allegations regarding their use to promote branded pharmaceutical products over other less costly alternatives. Specifically, in recent years, there have been multiple settlements resulting out of government claims challenging the legality of their patient assistance programs under a variety of federal and state laws. It is possible that we may make grants to independent charitable foundations that help financially needy patients with their premium, co- pay, and co- insurance obligations. 62If** we or our vendors are deemed to fail to comply with relevant laws, regulations or

evolving government guidance in the operation of these programs, we could be subject to damages, fines, penalties or other criminal, civil or administrative sanctions or enforcement actions. We cannot ensure that our compliance controls, policies and procedures will be sufficient to protect against acts of our employees, business partners or vendors that may violate the laws or regulations of the jurisdictions in which we operate. Regardless of whether we have complied with the law, a government investigation could impact our business practices, harm our reputation, divert the attention of management, increase our expenses and reduce the availability of assistance to our patients. Ensuring that our future business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities to be conducted by our sales team, were to be found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government- funded healthcare programs, such as Medicare and Medicaid, 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. **If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects. We participate in the Medicaid Drug Rebate program, the 340B drug pricing program, and the Department of Veterans Affairs (VA)' s Federal Supply Schedule (FSS) pricing program. Under the Medicaid Drug Rebate program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for our drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data reported by us on a monthly and quarterly basis to CMS, the federal agency that administers the Medicaid Drug Rebate program. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the U. S. in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions. Our failure to comply with these price reporting and rebate payment obligations could negatively impact our financial results. The ACA made significant changes to the Medicaid Drug Rebate program. CMS issued a final regulation, which became effective on April 1, 2016, to implement the changes to the Medicaid Drug Rebate program under the ACA. The issuance of the final regulation has increased and will continue to increase our costs and the complexity of compliance, has been and will continue to be time- consuming to implement, and could have a material adverse effect on our results of operations, particularly if CMS challenges the approach we take in our implementation of the final regulation. Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the Public Health Service' s 340B drug pricing program in order for federal funds to be available for the manufacturer' s drugs under Medicaid and Medicare Part B. The 340B program requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B " ceiling price " for the manufacturer' s covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low- income patients. The 340B ceiling price is calculated using a statutory formula based on the average manufacturer price and Medicaid rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate program, and in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. Any additional future changes to the definition of average manufacturer price and the Medicaid rebate amount under the ACA, other legislation, or in regulation could affect our 340B ceiling price calculations and negatively impact our results of operations. The Health Resources and Services Administration, or HRSA, which administers the 340B program, issued a final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on 63manufacturers that knowingly and intentionally overcharge covered entities, which became effective on January 1, 2019. We also are required to report our 340B ceiling prices to HRSA on a quarterly basis. Implementation of the civil monetary penalties regulation and the issuance of any other final regulations and guidance could affect our obligations under the 340B program in ways we cannot anticipate. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in the inpatient setting. Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies and the courts. In the case of our Medicaid pricing data, if we become aware that our reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, we are obligated to resubmit the corrected data for up to three years after those data originally were due. Such restatements and recalculations increase our costs for complying with the laws and regulations governing the Medicaid Drug Rebate program and could result in an overage or underage in our rebate liability for past quarters. Price recalculations also may affect the ceiling price at which we are required to offer our products under the 340B program or could require us to issue refunds to 340B covered entities. Significant civil monetary penalties can be applied if we are found to have knowingly submitted any false pricing information to CMS, or if we fail to submit the required price data on a timely basis. Such conduct also could be grounds for CMS to terminate our Medicaid drug rebate agreement, in which case federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs. Significant civil monetary penalties also can be applied if**

we are found to have knowingly and intentionally charged 340B covered entities more than the statutorily mandated ceiling price. We cannot assure you that our submissions will not be found by CMS or HRSA to be incomplete or incorrect. In order to be eligible to have our products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies and grantees, as noted above, we participate in the VA' s FSS pricing program. As part of this program, we are obligated to make our products available for procurement on an FSS contract under which we must comply with standard government terms and conditions and charge a price that is no higher than the statutory Federal Ceiling Price, or FCP, to four federal agencies (the VA, U. S. Department of Defense, or DOD, Public Health Service, and the U. S. Coast Guard). The FCP is based on the Non- Federal Average Manufacturer Price, or Non- FAMP, which we calculate and report to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non- FAMP filing can subject a manufacturer to significant penalties for each item of false information. These obligations also contain extensive disclosure and certification requirements. We also participate in the Tricare Retail Pharmacy program, under which we pay quarterly rebates on utilization of innovator products that are dispensed through the Tricare Retail Pharmacy network to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non- FAMP and FCP. We are required to list our covered products on a Tricare Agreement in order for these products to be eligible for DOD formulary inclusion. If we overcharge the government in connection with our FSS contract or Tricare Agreement, whether due to a misstated FCP or otherwise, we are required to refund the difference to the government. Failure to make necessary disclosures and / or to identify contract overcharges can result in allegations against us under the FCA and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time- consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects. Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties. Our future profitability may depend, in part, on our ability to commercialize current or future drug candidates in foreign markets for which we may rely on collaboration with third parties. We are not permitted to market or promote any of our drug candidates before we receive regulatory approval from the applicable regulatory authority in that foreign market. To obtain separate regulatory approval in many other countries we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials, manufacturing, commercial sales, pricing and distribution of our drug candidates, and we cannot predict success in these jurisdictions. If we seek to develop our drug candidates or obtain approval of our drug candidates and ultimately ~~commercialize~~ **64commercialize** our drug candidates in foreign markets, we would be subject to additional risks and uncertainties, including: ● our customers' ability to obtain reimbursement for our drug candidates in foreign markets; ● our inability to directly control commercial activities because we are relying on third parties; ● the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements, including **, for example,** the European General Data Protection Regulation 2016 / 679, commonly referred to as GDPR; ● different medical practices and customs in foreign countries affecting acceptance in the marketplace; ● import or export licensing requirements; ● longer accounts receivable collection times; ● longer lead times for shipping; ~~73~~ ● language barriers for technical training; ● reduced protection of intellectual property rights in some foreign countries; ● the existence of additional potentially relevant third- party intellectual property rights; ● foreign currency exchange rate fluctuations; and ● the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute. Foreign sales of our drug candidates could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs. Governments outside the U. S. tend to impose strict price controls, which may adversely affect our revenues, if any. In some countries, particularly countries in the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost- effectiveness of our drug candidate to other available therapies. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed. If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business. We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate ~~coverage~~ **65coverage** against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials. Risks Related to Our Financial Position and Need for Additional CapitalWe are a precision therapy company in the process of growing our operations. We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future. We commenced operations in April 2011 and we have focused substantially all of our efforts and financial resources to date on organizing and staffing our company, business planning, raising capital, establishing our intellectual property building our discovery platform, including our proprietary compound library and new target discovery engine, identifying kinase drug targets and potential drug

candidates, conducting preclinical studies and clinical development for our drug candidates, commencing pre- commercial activities and the commercial launches for AYVAKIT / AYVAKYT and GAVRETO, and producing the active pharmaceutical ingredient, or API, drug substance and drug product material for use in preclinical studies and clinical trials for our drug candidates and commercial sale of our approved drugs. To date, we have financed our operations primarily through public offerings of our common stock, private placements of our convertible preferred and common stock, collaboration and license agreements, future royalty and revenue monetization, and a term loan. Through December 31, ~~2022~~ **2023**, we have received an aggregate of $ 3. ~~6~~ **7** billion from such transactions, including $ 1. 9 billion in aggregate gross proceeds from the sale of common stock in our initial public ~~74offering~~ -- **offering**, follow on public offerings, through our " at the market " stock offering program and the equity investment by Roche, $ 115. 1 million in gross proceeds from the issuance of convertible preferred stock, $ 175. 0 million in gross proceeds from our Royalty Purchase Agreement with Royalty Pharma, $ 250. 0 million in gross proceeds from our Future Revenue Purchase Agreement with Sixth Street Partners, $ 1. 0 billion in upfront payments and milestone payments under our collaborations with Roche, CStone and Zai Lab, our license agreement with Clementia and our former collaboration with Alexion Pharma Holding, or Alexion and $ ~~150~~ **250**. 0 million in gross proceeds from a term loan from Sixth Street Partners. In addition, since January 2020, we also have generated revenue through sales of our drug products. Since inception, we have incurred significant operating losses ~~, with the exception of~~ **. Our net loss was $ 507. 0 million for** the year ended December 31, ~~2020~~ **2023**. Our net losses were $ 557. 5 million and $ 644. 1 million for the years ended December 31, 2022 and 2021, respectively. **As of** ~~Our net income was $ 313. 9 million for the year ended~~ December 31, ~~2020~~ **2023** ~~primarily due to the collaboration revenue recorded under our collaboration with Roche for pralsetinib. As of December 31, 2022~~, we had an accumulated deficit of $ ~~1~~ **2**, ~~833~~ **339**. ~~0~~ **9** million. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from **selling,** general and administrative costs associated with our operations. We expect to continue to incur significant expenses and operating losses over the next few years. We anticipate that our expenses ~~will~~ **may** continue to increase in connection with our ongoing activities. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. We expect our research and development expenses to increase in connection with continuing our existing clinical trials and beginning additional clinical trials. In addition, we will incur significant sales, marketing and outsourced-manufacturing expenses in connection with the commercialization of any of our drugs or any drug candidates for which we may receive marketing approval. In addition, we have incurred and will continue to incur substantial costs associated with operating as a public company. Because of the numerous risks and uncertainties associated with developing pharmaceuticals, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis. Our ability to become profitable depends upon our ability to generate substantial revenue. Our ability to generate substantial revenue depends on a number of factors, including, but not limited to, our ability to: ● initiate and successfully complete clinical trials that meet their clinical endpoints; ● initiate and successfully complete all safety studies required to obtain U. S. and foreign marketing approval for our drug candidates, including for avapritinib ~~and pralsetinib for additional indications or~~ in additional geographies; ● continue to maintain and expand commercial manufacturing capabilities or make arrangements with third- party manufacturers to ensure clinical supply and commercial manufacturing; **66** ● maintain and, if necessary, expand a sales, marketing and distribution infrastructure to commercialize AYVAKIT / AYVAKYT and any current or future drug candidates for which we obtain marketing approval; ● achieve market acceptance in the medical community and with third- party payors for AYVAKIT / AYVAKYT ~~, GAVRETO~~ and any current or future drug candidates for which we receive marketing approval; and ● compete with companies that may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs. We expect to incur significant sales and marketing costs as we commercialize AYVAKIT / AYVAKYT ~~, jointly commercialize GAVRETO with Roche~~ and commercialize any current or future drug candidates for which we receive marketing approval. Even if we initiate and successfully complete pivotal clinical trials of our drug candidates, and our drug candidates are approved for commercial sale, and despite expending these costs, our drug candidates may not be commercially successful. We may not achieve profitability soon after generating drug sales, if ever. If we are unable to ~~75generate~~ -- **generate** ~~substantial drug revenue~~ **material net cash inflows from our operations**, we will not become profitable and may be unable to continue operations without continued funding. We may seek to raise additional funding from time to time. If we are unable to raise capital when needed, we may be forced to delay, reduce or eliminate some of our drug development programs or commercialization efforts. The development and commercialization of pharmaceuticals is capital ~~-~~intensive. We are currently advancing multiple drug candidates and development programs through clinical and preclinical development. **Our** ~~We expect our~~ expenses ~~to~~ **may** increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate or continue clinical trials of, and seek marketing approval for our drug candidates, including marketing approval for avapritinib ~~for additional indications or~~ in additional geographies ~~and for pralsetinib~~. In addition, we expect to incur additional significant commercialization expenses for AYVAKIT / AYVAKYT ~~, GAVRETO~~ and other drug candidates, if approved, related to drug sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of potential collaborators or licensors. We may also need to raise additional funds if we choose to pursue additional indications or geographies for any of our approved drugs or drug candidates or otherwise expand more rapidly than we presently anticipate. Our future capital requirements will depend on and ~~could~~ **may** increase ~~significantly~~ as a result of many factors, including: ● the success of our commercialization efforts and market acceptance for AYVAKIT / AYVAKYT ~~, GAVRETO~~ or any of our current or future drug candidates for which we receive marketing approval; ● the costs of maintaining, expanding or contracting for sales, marketing and distribution capabilities in connection with commercialization of AYVAKIT / AYVAKYT and any of our current or future drug candidates for which we

receive marketing approval; ● the costs of securing manufacturing, packaging and labeling arrangements for development activities and commercial production, including API, drug substance and drug product material for use in preclinical studies, clinical trials, our compassionate use program and for use as commercial supply, as applicable; ● the cost of purchasing quantities of agents for use in our clinical trials in connection with our efforts to develop our drugs and drug candidates, including for development as combination therapies; ● the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our approved drugs and drug candidates; ● the costs, timing and outcome of regulatory review of marketing applications for our drug candidates, including seeking marketing approval for avapritinib ~~and pralsetinib for additional indications or~~ in additional geographies; **67** ● the success of our collaborations with ~~Roche,~~ CStone ~~and Zai Lab~~ and our license agreements with Clementia and IDRx, as well as our ability to establish and maintain additional collaborations, partnerships or licenses on favorable terms, if at all; ● the achievement of milestones or occurrence of other developments that trigger payments under our existing collaboration or license agreements, our financing agreements, or any collaboration, partnership, financing or license agreements that we may enter into in the future; ● the extent to which we are obligated to reimburse, or entitled to reimbursement of, research and development, clinical or other costs under future collaboration agreements, if any; ● the extent to which we acquire or in- license other approved drugs, drug candidates or technologies and the terms of any such arrangements ~~; 76 ● the success of our current or future collaborations for the development and commercialization of companion diagnostic tests~~ ; ● the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property- related claims; and ● the costs of continuing to expand our operations. Accordingly, we may seek additional funding in connection with our continuing operations or business objectives. Any additional fundraising efforts may divert our management from their day- to- day activities, which may adversely affect our ability to develop and commercialize any of our approved drugs or drug candidates. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. We could also be required to seek funds through collaborations, partnerships, licensing arrangements or otherwise at an earlier stage than would be desirable and we may be required to relinquish rights to some of our technologies, drugs or drug candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects. If we are unable to obtain funding on a timely basis or on attractive terms, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any of our approved drugs or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations. Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or drug candidates. Until such time ~~, if ever~~ , as we can generate substantial drug revenues, we expect to finance our cash needs primarily through a combination of public and private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and future revenue monetizations. We do not have any committed external source of funds, other than our collaborations with Roche, CStone and Zai Lab and the license agreements with Clementia and IDRx, ~~the Royalty Purchase Agreement with Royalty Pharma,~~ and the Financing Agreement with Sixth Street Partners, which are limited in scope and duration and subject to the achievement of milestones or royalties on sales of licensed products, if any. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that materially adversely affect the rights of our common stockholders. Debt financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts or grant rights to develop and market drugs and drug candidates that we would otherwise prefer to develop and market ourselves. If we raise funds through additional collaborations, strategic alliances, licensing arrangements or future revenue monetizations with third parties, we may have to relinquish valuable rights to our intellectual property, future revenue streams, research programs, drugs or drug candidates or to grant licenses on terms that may not be favorable to us. Further, due to the uncertainty of pharmaceutical development, the high historical failure rates generally associated with ~~drug~~ **68drug** development and uncertainty of successful commercialization, we may not receive any regulatory, development, sales- based milestones or royalty payments under any such collaborations, strategic alliances, licensing arrangements or future revenue monetizations. **Our level** ~~In June 2022, we entered into a Royalty Purchase Agreement with Royalty Pharma, pursuant to which, we sold our right to receive all~~ of **indebtedness** ~~the royalties payable to the Company with respect to net sales by Roche, in all countries besides China, Hong Kong, Macau, Taiwan (collectively, " Greater China ")~~ and ~~the U. S., of GAVRETO under the Collaboration Agreement, dated July 13, 2020, by and between the Company and Roche, as amended. As consideration for the arrangement, we received $ 175. 0 million upfront in cash and may receive up to $ 165. 0 million in milestone payments. As a result, we will no longer derive cash from royalty payments from sales of GAVRETO in all countries 77besides Greater China and the U. S., other~~ -- **the terms** ~~than in the form~~ of ~~contingent milestone payments under the royalty purchase agreement with Royalty Pharma. In February 2023, Roche announced that it recorded a full impairment charge of the GAVRETO intangible asset during the fourth quarter of 2022 due to lower sales expectations. If specified net sales milestones are not achieved, we may not be eligible to receive certain milestone payments under the Royalty Purchase Agreement with Royalty Pharma and the Roche pralsetinib collaboration agreement. There are a number of factors that could materially affect the amount and timing of royalty payments to Royalty Pharma from Roche, and correspondingly, the amount of interest expense recorded by the Company, most of which are not within our control. Such factors include, but are not limited to, delays or~~

~~discontinuation of development of pralsetinib, regulatory approval, changing standards of care, the introduction of competing products, manufacturing or other~~ -- **the Financing** ~~delays, generic competition, intellectual property matters, adverse events that result in governmental health authority imposed restrictions on the use of the drug products, significant changes in foreign exchange rates as the royalties remitted to Royalty Pharm are made in U. S. dollars (USD) while the underlying sales of GAVRETO are made in currencies other than USD, and other events or circumstances that are not currently foreseen. Changes to any of these factors could result in increases or decreases to both royalty revenues and interest expense. In June 2022, we entered into a Future Revenue Purchase~~ Agreement with Sixth Street Partners ~~, the~~ **could adversely affect our operations and limit our ability to plan for or respond to changes in our business. If we are unable to comply with restrictions in** ~~other~~ -- **the Financing Agreement** ~~purchasers from time to time party thereto~~ , ~~and~~ **the repayment of our existing indebtedness could be accelerated. Under the Financing Agreement with** Sixth Street Partners ~~as representative for the purchasers, pursuant to which, we sold our right to receive future royalty payments at a rate of 9. 75 % on up to $ 900 million each year of (i) aggregate worldwide annual net product sales of AYVAKIT / AYVAKYT (avapritinib) and (ii) if it is approved, aggregate worldwide annual net product sales of elecestinib, but excluding sales in Greater China, subject to a cumulative cap of 1. 45 times the upfront invested capital or a total of $ 362. 5 million. In the event that certain revenue targets are not achieved by specified dates, the royalty rate and cumulative cap shall be increased to 15 % and 1. 85 times the invested capital (or $ 462. 5 million), respectively. As consideration for the arrangement, we received $ 250. 0 million in cash in July 2022 upon the transactions closing. Our level of indebtedness and the terms of the Sixth Street financing agreement could adversely affect our operations and limit our ability to plan for or respond to changes in our business. If we are unable to comply with restrictions in the financing agreement, the repayment of our existing indebtedness could be accelerated. Under the Financing Agreement by and among the Company, the other lenders from time to time party thereto and Tao Talents, LLC, as the administrative agent for the lenders,~~ we have incurred a substantial amount of debt, which could adversely affect our business. In July 2022, we drew down the senior secured term loan of $ 150. 0 million. The facility also includes a senior secured delayed draw term loan of up to $ 250. 0 million to be funded in two tranches: (i) a tranche A delayed draw loan in an aggregate principal amount of $ 100. 0 million and (ii) a tranche B delayed draw term loan in an aggregate principal amount of up to $ 150. 0 million. We may also at any time request an incremental term loan in an amount not to exceed $ 260. 0 million on terms to be agreed and subject to the consent of the lenders providing such incremental term loan **. In August 2023, we received the first tranche of the senior secured delayed draw term loan facility in the amount of $ 100. 0 million in gross proceeds** . Our level of indebtedness could affect our business in the following ways, among other things: make it more difficult for us to satisfy our contractual and commercial commitments; require us to use a substantial portion of our cash flow from operations to pay interest and principal, which would reduce funds available for working capital, capital expenditures and other general corporate purposes; limit our ability to obtain additional financing for working capital, capital expenditures, acquisitions and other investments or general corporate purposes; heighten our vulnerability to downturns in our business, our industry or in the general economy; place us at a disadvantage compared to those of our competitors that may have proportionately less debt; limit management' s discretion in operating our business; and limit our flexibility in planning for, or reacting to, changes in our business, the industry in which we operate or the general economy. The ~~financing~~ **Financing** ~~agreement~~ **Agreement** requires us to make certain payments of principal and interest over time and contains several other restrictive covenants. Among other requirements of the ~~financing~~ **Financing** ~~agreement~~ **Agreement** , we and our subsidiaries party to the ~~financing~~ **Financing** ~~agreement~~ **Agreement** must maintain a minimum consolidated liquidity of $ 80. 0 million. These and other terms in the ~~Sixth Street~~ Financing Agreement could restrict our ability to grow our business or enter into transactions that we believe would be beneficial to our business. Our business may not generate cash flows from operations in the future that are sufficient to service our debt ~~78and~~ -- **and** support our growth strategies. If we are unable to generate such cash flows, we may be required to adopt one or more alternatives, such as obtaining additional equity capital on terms that may be onerous or highly dilutive, selling assets, or restructuring debt. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations. Risks Related to Our Dependence on Third PartiesWe have entered into collaborations and licenses with our partners for the development and commercialization of several of our drugs and drug candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these drugs and drug candidates. We have entered into collaborations and licenses with ~~Roche,~~ CStone, Zai Lab, Proteovant, Clementia and IDRx for the development and commercialization of several of our drugs and drug candidates, and may enter into additional collaborations and licenses with other third parties in the future. The success of these arrangements will depend heavily on the efforts and activities of our collaborators and licensing partners. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. In some situations, we may not be able to influence our collaboration partners' decisions regarding the development and collaboration of our partnered drugs and drug candidates, and as a result, our collaboration partners may not pursue or prioritize the development and commercialization of those partnered drugs and drug candidates in a manner that is in our best interest. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable drug candidate and, in some cases, termination of the collaboration arrangement or result in litigation or arbitration, which would be time- consuming ~~and~~ **69and** expensive. Licensors generally have sole discretion in determining the efforts and resources that they will apply to the licensed products. Collaborations and licenses with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. ~~For example, in the fourth quarter of 2017, Alexion terminated our collaboration related to fibrodysplasia ossificans progressiva for convenience following a strategic review by Alexion of its research and development portfolio.~~ Any termination or expiration of our collaboration or license agreements with ~~Roche,~~ CStone, Zai Lab, Proteovant, Clementia or IDRx, or of any future collaboration or license

agreement, could adversely affect us financially or harm our business reputation **. For example, in February 2023, Roche provided written notice of its election to terminate for convenience our collaboration agreement for the development and commercialization of GAVRETO worldwide, excluding the CStone Territory. While we will regain rights to the development and commercialization of GAVRETO following the effective date of such termination, there can be no assurance that we will be able to successfully enter into a new arrangement with a third party to collaborate on the development and commercialization or GAVRETO. Further, following the termination of such collaboration agreement, we have not otherwise met the net sales milestone thresholds under the Royalty Purchase Agreement with Royalty Pharma and are no longer be eligible to receive any of the contingent milestone payments under the Royalty Purchase Agreement. However, the failure to meet such milestone thresholds shall not affect the $ 175. 0 million upfront payment received** . We rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our drug candidates and our business could be substantially harmed. We do not have the ability to independently conduct clinical trials. We rely on medical institutions, clinical investigators, CROs, contract laboratories and other third parties to conduct or otherwise support clinical trials for our approved drugs and drug candidates. We rely heavily on these parties for execution of clinical trials for our drugs and drug candidates and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on CROs will not relieve us of our regulatory responsibilities. For any violations of laws and regulations during the conduct of our clinical trials, we could be subject to warning letters or enforcement action that may include civil penalties up to and including criminal prosecution. We and our CROs are required to comply with regulations, including GCPs, for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for any drugs in clinical development. The FDA enforces GCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will ~~79determine~~ -- **determine** that our current or future clinical trials comply with GCPs. In addition, our clinical trials must be conducted with drug candidates produced under cGMPs regulations. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government- sponsored database, ClinicalTrials. gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. Although we intend to design and sponsor the clinical trials for our approved drugs and drug candidates, CROs will conduct all of our clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct current or future clinical trials will also result in less direct control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may: ● have staffing difficulties; ● fail to comply with contractual obligations; **70** ● experience regulatory compliance issues; ● undergo changes in priorities or become financially distressed; or ● form relationships with other entities, some of which may be our competitors. Some of these factors may be beyond our control ~~. For example, the performance of our CROs may also be delayed or disrupted by the ongoing COVID- 19 pandemic, including due to travel or quarantine policies, availabilities of staff, exposure of CRO staff to COVID- 19 or re- prioritization of CRO resources as a result of the pandemic~~ . These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. If the CROs do not perform clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our approved drugs for additional indications and our drug candidates may be delayed, we may not be able to obtain regulatory approval and commercialize our drug candidates, or our development program materially and irreversibly harmed. If we are unable to rely on clinical data collected by our CROs, we could be required to repeat, extend the duration of, or increase the size of any clinical trials we conduct and this could significantly delay commercialization and require significantly greater expenditures. If any of our relationships with these third- party CROs terminate, we may not be able to enter into arrangements with alternative CROs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any clinical trials such CROs are associated with may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our drug for additional indications or our drug candidates. As a result, we believe that our financial results and the commercial prospects for our drugs or our drug candidates in the subject indication would be harmed, our costs could increase and our ability to generate substantial revenue could be delayed. We contract with third parties for the manufacture of our approved drugs and drug candidates, including for preclinical, clinical and commercial supply. This reliance on third parties increases the risk that we will not have sufficient quantities of our approved drugs or drug candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts. We do not currently own or operate, nor do we have any plans to establish in the future, any manufacturing facilities or personnel. We rely, and expect to continue to rely, primarily on third parties for the manufacture of our drug candidates for preclinical development

and clinical testing, as well as for the commercial manufacture of our current and future drugs. This reliance on third parties increases the risk that we will not have sufficient quantities of our drugs or drug candidates or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development ~~80or~~ **or** commercialization efforts. The facilities used by our contract manufacturing organizations (CMOs) to manufacture our drugs and drug candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our marketing applications to the FDA. We do not control the manufacturing process of, and will be completely dependent on, our CMOs for compliance with cGMPs in connection with the manufacture of our drugs and drug candidates. Manufacturers and manufacturers' facilities are required to comply with extensive FDA, and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations and applicable product tracking and tracing requirements. If our CMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and / or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our CMOs to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our drugs and drug candidates ~~or is unable to conduct inspections necessary to approve these facilities due to delays or disruptions caused by the ongoing COVID- 19 pandemic~~ , or if the FDA or a comparable regulatory authority withdraws any such approval in the future, we may be delayed in obtaining approval of these facilities for the manufacture of our drugs and drug candidates or need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our drug candidates, if approved, and could require comparability studies for the setup of manufacturing operations at alternative facilities. If any CMO with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different CMO, which we may not be able to do on reasonable terms, if at all. In either scenario, our ~~clinical~~ **71clinical** trials supply or commercial distribution could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or drug candidates may be unique or proprietary to the original CMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back- up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our drug candidate according to the specifications previously submitted to or approved by the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to develop drug candidates or commercialize our products in a timely manner or within budget. Furthermore, a CMO may possess technology related to the manufacture of our drug candidate that such CMO owns independently. This would increase our reliance on such CMO or require us to obtain a license from such CMO in order to have another CMO manufacture our drug products or drug candidates. In addition, in the case of the CMOs that supply our drug candidates, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials. Further, our failure, or the failure of our third- party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of drug candidates or drugs, if approved, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business and supplies of our drugs and drug candidates ~~. Since March 2020 when foreign and domestic inspections of facilities were largely placed on hold, the FDA has been working to resume pre- pandemic levels of inspection activities, including routine surveillance, bioresearch monitoring and pre- approval inspections on a prioritized basis. Since April 2021, the FDA has conducted limited inspections and employed remote interactive evaluations, using risk management methods, to meet user fee commitments and goal dates. Ongoing travel restrictions and other uncertainties continue to impact oversight operations both domestic and abroad and it is unclear when standard operational levels will resume. The FDA is continuing to complete mission- critical work, prioritize other higher- tiered inspectional needs (e. g., for- cause inspections), and carry out surveillance inspections using risk- based approaches for evaluating public health. Should the FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be adequate, the agency has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. During the COVID- 19 pandemic, a number of companies announced receipt of 81complete response letters due to the FDA' s inability to complete required inspections for their applications. Regulatory authorities outside the U. S. may adopt similar restrictions or other policy measures in response to the ongoing COVID- 19 pandemic and may experience delays in their regulatory activities~~ . We do not have long- term supply agreements with all of our CMOs, and may purchase our required drug supply, including the API, drug product and drug substance used in our drugs and drug candidates, on a purchase order basis with certain CMOs. In addition, we may be unable to establish or maintain any agreements with third- party manufacturers or to do so on acceptable terms. Even if we are able to establish and maintain agreements with third- party manufacturers, reliance on third- party manufacturers entails additional risks, including: ● reliance on the third party for regulatory compliance and quality assurance; ● the possible breach of the manufacturing agreement by the third party; ● the possible misappropriation of our proprietary information, including our trade secrets and know- how; and ● the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us. Any of our drugs and drug candidates that we may develop may compete with other approved drugs and drug candidates 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. In March 2020, the U. S. enacted the CARES Act in response to the U. S. COVID- 19 pandemic. Throughout the ~~ongoing~~ COVID- 19 pandemic, there **was** ~~has been~~ public concern over the availability and accessibility of critical medical products, and the CARES Act ~~enhances~~ **enhanced** FDA' s existing authority with respect to drug shortage measures. Under the CARES Act, we must have in place a risk management plan in place that identifies and evaluates the risks to the supply of approved drugs for certain serious diseases or conditions for each establishment where the drug or API is manufactured. The risk management plan will be subject to FDA review during an inspection. If we experience shortages in the supply of our marketed products, our results could be materially impacted. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply for all of our bulk drug substances. If our current **CMOs** ~~contract manufacturers~~ cannot perform as agreed, we may experience shortages that require reporting to the FDA or foreign regulatory authorities and may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our approved drugs and drug candidates, we may incur added costs and delays in identifying and qualifying any such replacement. ~~Our~~ **72Our** current and anticipated future dependence upon others for the manufacture of our drugs or drug candidates could result in significant delays or gaps in availability of such drugs or drug candidates and may adversely affect our future profit margins and our ability to commercialize any drugs that receive marketing approval on a timely and competitive basis. The third parties upon whom we rely for the supply of the API, drug substance and drug product used in avapritinib ~~and pralsetinib~~ are our sole source of supply, and the loss of any of these suppliers could significantly harm our business. The API, drug substance and drug product used in our drug and drug candidates are supplied to us primarily from single- source suppliers. Our ability to successfully develop our drug candidates, supply our drug candidates for clinical trials and to ultimately supply our commercial drugs in quantities sufficient to meet the market demand, depends in part on our ability to obtain the API, drug substance and drug product for these drugs in accordance with regulatory requirements and in sufficient quantities for clinical testing and commercialization. Although we have entered into arrangements to establish redundant or second- source supply of some of the API, drug product or drug substance for avapritinib ~~and pralsetinib~~ , if any of our suppliers ceases its operations for any reason or is unable or unwilling to supply API, drug product or drug substance in sufficient quantities or on the timelines necessary to meet our needs ~~, including as a result of the ongoing COVID- 19 pandemic~~ , it could significantly and adversely affect our business, the supply of our drug candidates or approved drugs and our financial condition. For all of our drug candidates, we may from time to time explore opportunities to identify and qualify additional manufacturers to provide such API, drug substance and drug product prior to submission of an NDA to the FDA and / or an MAA to the EMA. We are not certain that our single- source suppliers will be able to meet our demand for their products, either because of the nature of our agreements with those suppliers, our limited experience with those suppliers or our relative importance as a customer to those suppliers. It may be difficult for us to assess their ability to timely meet our demand in the future based on past performance. While our suppliers have generally met our demand for their products on a timely basis in the past, they may subordinate our needs in the future to their other customers. In addition, we currently have sufficient supply or plans for supply to meet our anticipated global commercial and clinical development needs for our approved drugs and clinical- stage drug candidates through ~~2022~~ **2023** ~~. However, the ongoing COVID- 19 pandemic could adversely impact our suppliers and result in delays or disruptions in our current or future supply chain~~ . Establishing additional or replacement suppliers for the API, drug substance and drug product used in our drug candidates or approved drugs, if required, may not be accomplished quickly. If we are able to find a replacement supplier, such replacement supplier would need to be qualified and may require additional regulatory approval, which could result in further delay. While we seek to maintain adequate inventory of the API, drug substance and drug product used in our drug candidates and approved drugs, any interruption or delay in the supply of components or materials, or our inability to obtain such API, drug substance and drug product from alternate sources at acceptable prices in a timely manner could impede, delay, limit or prevent our development efforts, which could harm our business, results of operations, financial condition and prospects. Certain of our research and development, clinical trials and manufacturing and supply for certain raw materials used in our drugs and our drug candidates takes place in China through third- party CROs, collaborators or manufacturers. A significant disruption in the operation of those CROs, collaborators or manufacturers, could materially adversely affect our business, financial condition and results of operations. We have relied on certain third parties located in China to manufacture and supply certain raw materials used in our drugs and our drug candidates, and we expect to continue to use such third **-** party manufacturers for such purposes. In addition, certain of our drug candidates are being evaluated at clinical trial sites in China under our collaboration with CStone and through CROs located in China. A natural disaster, epidemic or pandemic disease outbreaks, ~~including the ongoing COVID- 19 pandemic,~~ trade war, political unrest or other events in China could disrupt the business or operations of CROs, collaborators, manufacturers or other third parties with whom we conduct business now or in the future. Any disruption in China that significantly impacts such third parties, including services provided by CROs for our research and development programs, clinical trial operations conducted by CROs or our collaborators, or our manufacturers ability to produce raw materials in adequate quantities to meet our needs could impair our ability to operate our business on a day- to- day basis and impede, delay, limit or prevent the research, development or commercialization of our current and future approved drugs or drug candidates. In addition, for any activities conducted in China, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the policies of the U. S. or Chinese governments, political unrest or unstable economic conditions in China, and we may be exposed to fluctuations in the value of the local currency in China for goods and services. Our costs for any of these services or activities could also increase as a result of future ~~appreciation~~ **73appreciation** of the local currency in China or increased labor costs if the demand for skilled laborers increases in China and the availability of skilled labor declines in China. Risks Related to Intellectual Property If we are unable to adequately protect our proprietary technology or obtain and maintain patent protection for our technology and drugs or if the scope of the patent protection obtained is not sufficiently broad, our competitors could

develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology and drugs may be impaired. Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection in the U. S. and other countries for our drugs and drug candidates and our core technologies, including our novel target discovery engine, our proprietary compound library, targeted protein degrader platform and other know- how. We seek to protect our proprietary and intellectual property position by, among other methods, filing ~~83patent~~ **patent** applications in the U. S. and abroad related to our proprietary compounds, as well as the use of these compounds in the treatment of diseases, formulations, solid forms, and manufacturing processes and other technologies, inventions and improvements that are important to the development and implementation of our business. We also rely on copyright, trade secrets, know- how and continuing technological innovation to develop and maintain our proprietary and intellectual property position. The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. The degree of patent protection we require to successfully commercialize any of our approved drugs and drug candidates may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our patents have, or that any of our pending patent applications that mature into issued patents will include, claims with a scope sufficient to protect our drugs and drug candidates. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the U. S. Furthermore, patents have a limited lifespan. In the U. S., the natural expiration of a patent is generally twenty years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing drugs similar or identical to our drugs and drug candidates, including generic versions of such drugs or drug candidates. Other parties have developed technologies that may be related or competitive to our own, and such parties may have filed or may file patent applications, or may have received or may receive patents, claiming inventions that may overlap or conflict with those claimed in our own patent applications or issued patents, with respect to either the same methods or formulations or the same subject matter, in either case, that we may rely upon to dominate our patent position in the market. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U. S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first- to- file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights cannot be predicted with any certainty. For example, we are aware of a patent owned by third parties that has generic method of treatment claims that may cover pralsetinib. If the claims of this third- party patent are asserted against us, we do not believe pralsetinib or our proposed activities related to such compound would be found to infringe any valid claim of this patent. While we may decide to initiate proceedings to challenge the validity of these patents in the future, we may be unsuccessful, and courts or patent offices in the U. S. and abroad could uphold the validity of any such patents. If we were to challenge the validity of any issued U. S. patent in court, we would need to overcome a statutory presumption of validity that attaches to every U. S. patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent' s claims. In addition, the patent prosecution process is expensive and time- consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Patent prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the U. S. Patent and ~~Trademark~~ **74Trademark** Office, or USPTO, have been significantly narrowed by the time they issue, if at all. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, there may be circumstances, when we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Even if we acquire patent protection that we expect should enable us to maintain such competitive advantage, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the U. S. and abroad. For example, we may be subject to a third- party submission of prior art to the USPTO challenging the priority of an invention claimed within one of our patents, which submissions may also be made prior to a patent' s issuance, precluding the granting of any of our pending patent applications. We may become involved in opposition, ~~84derivation~~ **derivation**, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others from whom we have obtained licenses to such rights. Competitors may claim that they invented the inventions claimed in our issued patents or patent applications prior to us or may file patent applications before we do. Competitors may also claim that we are infringing on their patents and that we therefore cannot practice our technology as claimed under our patents, if issued. Competitors may also contest our patents, if issued, by showing the patent examiner that the invention was not original, was not novel or was obvious. In litigation, a competitor could claim that our patents, if issued, are not valid for a number of reasons. If a court agrees, we would lose our rights to those challenged patents, and if our patents are successfully challenged, we may face generic competition prior to the expiration dates of our U. S. Orange Book listed patents. In addition, we may in the future be subject to claims by our former employees, consultants, advisors, and other third parties who have access to our proprietary know- how asserting an ownership right in our patents or patent applications, as a result of the work they performed on our behalf. Although we generally require all of our employees, consultants and advisors and any other third parties who have access to our

proprietary know- how, information or technology to assign or grant similar rights to their inventions to us, we cannot be certain that we have executed such agreements with all parties who may have contributed to our intellectual property, nor can we be certain that our agreements with such parties will be upheld in the face of a potential challenge, or that they will not be breached, for which we may not have an adequate remedy. An adverse determination in any such submission or proceeding may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and drugs, without payment to us, or could limit the duration of the patent protection covering our technology, drugs and drug candidates. Such challenges may also result in our inability to manufacture or commercialize our drugs or drug candidates, if approved, without infringing third- party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future drugs and drug candidates. Even if they are unchallenged, our issued patents and our pending ~~patents~~ **patent** applications, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent our owned or licensed patents by developing similar or alternative technologies or drugs in a non-infringing manner. For example, a third party may develop a competitive drug that provides benefits similar to one or more of our drugs and drug candidates but that has a different composition that falls outside the scope of our patent protection. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our drugs and drug candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our drugs or drug candidates, if approved, could be negatively affected, which would harm our business. Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our current and future drugs and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by ~~extensive~~ **75extensive** and frequent litigation regarding patents and other intellectual property rights. We may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our drugs, drug candidates and technology, including interference proceedings before the USPTO. Our competitors or other third parties may assert infringement claims against us, alleging that our drugs are covered by their patents. Given the vast number of patents in our field of technology, we cannot be certain that we do not infringe existing patents or that we will not infringe patents that may be granted in the future. Many companies have filed, and continue to file, patent applications related to small molecule therapeutics. Some of these patent applications have already been allowed or issued, and others may issue in the future. For example, we are aware of a patent owned by a third party that has generic method of treatment claims that may cover pralsetinib. If the claims of this third- party patent are asserted against us, we do not believe pralsetinib or our proposed activities related to such compound would be found to infringe any valid claim of this patent. While we may decide to initiate proceedings to challenge the validity of these patents in the future, we may be unsuccessful, and courts or patent offices in the U. S. and abroad could uphold the validity of any such patents. If we were to challenge the validity of any issued U. S. patent in court, we would need to overcome a statutory presumption ~~85of~~ **of** validity that attaches to every U. S. patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent' s claims. Since this area is competitive and of strong interest to pharmaceutical and biotechnology companies, there will likely be additional patent applications filed and additional patents granted in the future, as well as additional research and development programs expected in the future. Furthermore, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our drugs and drug candidates. If a patent holder believes any of our approved drugs or drug candidate infringes on its patent, the patent holder may sue us even if we have received patent protection for our drugs, drug candidates and technology. Moreover, we may face patent infringement claims from non- practicing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect. If we are found to infringe a third party' s intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our drug candidates and technology. 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 such a license, it could be granted on non- exclusive terms, thereby providing our competitors and other third parties access to the same technologies licensed to us. Without such a license, we could be forced, including by court order, to cease developing and commercializing the infringing technology, drugs or drug candidates. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed such third- party patent rights. A finding of infringement could prevent us from commercializing our current and future drugs or force us to cease some of our business operations, which could materially harm our business. We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time- consuming and unsuccessful. Competitors and other third parties may infringe, misappropriate or otherwise violate our patents and other intellectual property rights. To counter infringement or unauthorized use, including against ANDA filers, we may be required to resort to litigation, that includes infringement claims. A court may disagree with our allegations, however, and may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the third- party technology in question. Further, such third parties could counterclaim that we infringe their intellectual property or that a patent we have asserted against them is invalid or unenforceable. In patent litigation in the U. S., defendant counterclaims challenging the validity, enforceability or scope of asserted patents are commonplace. In addition, third parties may initiate legal proceedings against us to assert such challenges to our intellectual property rights. The outcome of any such proceeding is generally unpredictable. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements,

including lack of novelty, obviousness or non- enablement. Patents may be unenforceable if someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. It is possible that prior art of which we and the patent examiner were unaware during prosecution exists, which could render our patents invalid. Moreover, it is also possible that prior art may exist that we are aware of but do not believe is relevant to our current or future patents, but that could nevertheless be determined to render our patents invalid. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. If a defendant were to prevail on a legal assertion of invalidity or unenforceability of our patents ~~covering~~ **76covering** any of our approved drugs or drug candidates, we would lose at least part, and perhaps all, of the patent protection covering such drug or drug candidate. Competing drugs may also be sold in other countries in which our patent coverage might not exist or be as strong. If we lose a foreign patent lawsuit, alleging our infringement of a competitor' s patents, we could be prevented from marketing our drugs in one or more foreign countries. Any of these outcomes would have a materially adverse effect on our business. Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities. Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time- consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk ~~86that~~ -- **that** some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating or from successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. If we are not able to obtain, or in applicable cases maintain, patent term extension or non- patent exclusivity in the United States under the Hatch- Waxman Act and in foreign countries under similar legislation, thereby potentially extending the marketing exclusivity term of our products or product candidates, our business may be materially harmed. Depending upon the timing, duration and specifics of FDA marketing approval of our products or product candidates, one of the U. S. patents covering each of such products or product candidates or the use thereof may be eligible for up to five years of patent term extension under the Hatch- Waxman Act. The Hatch- Waxman Act allows a maximum of one patent to be extended per FDA approved product as compensation for the 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 and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension also may be available in certain foreign countries upon regulatory approval of our product candidates. Nevertheless, we may not be granted patent term extension either in the United States or in any foreign country because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority 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 request, the period during which we will have the right to exclusively market our product may be shortened and our competitors may obtain approval of competing products following our patent expiration sooner, and our revenue could be reduced, possibly materially. It is possible that we will not obtain patent term extension under the Hatch- Waxman Act for a U. S. patent covering a product candidate even where that patent is eligible for patent term extension, or if we obtain such an extension, it may be for a shorter period than we had sought. Further, for certain of our licensed patents, we do not have the right to control prosecution, including filing with the USPTO, an application for patent term extension under the Hatch- Waxman Act. Thus, if one of our licensed patents is eligible for patent term extension under the Hatch- Waxman Act, we may not be able to control whether an application to obtain a patent term extension is filed, or an extension obtained, from the USPTO. ~~Also~~ **77Also** , there are detailed rules and requirements regarding the patents that may be submitted to the FDA for listing in the Approved Drug Products with Therapeutic Equivalence Evaluations, or the Orange Book. We may be unable to obtain patents covering our product candidates that contain one or more claims that satisfy the requirements for listing in the Orange Book. Even if we submit a patent for listing in the Orange Book, the FDA may decline to list the patent, or a manufacturer of generic drugs may challenge the listing. If a patent covering one of our approved products is not listed in the Orange Book, a manufacturer of generic drugs would not have to provide advance notice to us of any abbreviated new drug application, or ANDA, filed with the FDA to obtain permission to sell a generic version of such product. Depending upon the timing and specifics of marketing approval of our products, the FDA and other applicable regulatory authorities may grant certain non- patent exclusivities. However, we may be unable to secure or maintain additional non- patent exclusivity for our products or maintain any non- patent exclusivity. Similarly, although we intend to seek new chemical entity exclusivity, and potentially other exclusivities, for product candidates we are developing, we ~~87may~~ -- **may** not be successful in doing so. Moreover, these non- patent exclusivities, if granted, are limited and other companies may be able to submit marketing applications and receive approval earlier than we anticipate. Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental

patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance fees on issued patents often must be paid to the USPTO and foreign patent agencies over the lifetime of the patent. While an unintentional lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non- compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non- payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our drugs, drug candidates or procedures, we may not be able to stop a competitor from marketing drugs that are the same as or similar to our drugs or drug candidates, which would have a material adverse effect on our business. We may not be able to effectively enforce our intellectual property rights throughout the world. Filing, prosecuting and defending patents on our drugs and drug candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. In addition, the patent laws of some foreign countries do not afford intellectual property protection to the same extent as the laws of the U. S. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U. S. Competitors may use our drugs, drug candidates and technologies in jurisdictions where we have not obtained patent protection to develop their own drugs and, further, may export otherwise infringing drugs to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities is inadequate. These drugs may compete with our drugs and drug candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in the major markets for our drugs and drug candidates, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our drug candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. ~~We~~ **78We** depend on intellectual property licensed from third parties and termination of any of these licenses could result in the loss of significant rights, which would harm our businessUnder our current license agreements, we may not have the final or sole decision on whether we are able to opt out certain of our in- licensed European patents and patent applications from the recently created Unified Patent Court (UPC) for the European Union, that **was** ~~is expected to be fully~~ ratified ~~in~~ **on June 1,** 2023. Our licensors may decide to not opt out the of the UPC, which would subject our in- licensed European patents and patent applications to the jurisdiction of the UPC. Furthermore, even if our licensors decide to opt out of the UPC, we cannot guarantee that our licensors will comply with the legal formalities and requirements for properly opting out of the UPC. Thus, we cannot be certain that our in- licensed European patents and patent applications will not fall under the jurisdiction of the UPC. Under the UPC, a single European patent would be valid and enforceable in numerous European countries. A challenge to the validity of a European patent under the UPC, if successful, could result in a loss of patent protection in numerous European countries which could have a material adverse impact on our business and our ability to commercialize or license our technology ~~88and~~ -- **and** product candidates. Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or the USPTOOur European patents and patent applications could be challenged in the recently created ~~Unified Patent Court (~~UPC ~~)~~ for the European Union, that **was** ~~is expected to be fully~~ ratified ~~in~~ **on June 1,** 2023. We may decide to opt out our European patents and patent applications from the UPC. However, if certain formalities and requirements are not met, our European patents and patent applications could be challenged for non- compliance and brought under the jurisdiction of the UPC. We cannot be certain that our 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. Although such patent rights would apply to numerous European countries, a successful challenge to a European patent under the UPC could result in loss of patent protection in numerous European countries. Accordingly, a single proceeding under the UPC addressing the validity and infringement of the European patent could result in loss of patent protection in numerous European countries rather than in each validated 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 or license our technology and product candidates. Changes to the patent law in the U. S. and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our drugs and drug candidates. As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity and is therefore costly, time- consuming and inherently uncertain. Recent patent reform legislation in the U. S. and other countries, including the Leahy- Smith America Invents Act, or **the** Leahy- Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy- Smith Act includes a number of significant changes to U. S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost- effective avenues for competitors to challenge the validity of patents. In addition, the Leahy- Smith Act has transformed the U. S. patent system into a " first- to- file " system. The first- to- file provisions,

however, only became effective on March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy- Smith Act will have on the operation of our business. However, the Leahy- Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations and financial condition. The U. S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition, there have been recent proposals for additional changes to the patent laws of the U. S. and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U. S. Congress, the U. S. courts, the USPTO and the relevant law- making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. ~~If~~ **79If** we are unable to protect the confidentiality of our trade secrets, our business and competitive position may be harmed. In addition to the protection afforded by patents, we rely upon unpatented trade secret protection, unpatented know- how and continuing technological innovation to develop and maintain our competitive position. With respect to the building of our proprietary compound library and targeted degrader platform, we consider trade secrets and know- how to be our primary intellectual property. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our collaborators, scientific advisors, employees and consultants, and invention assignment agreements with our consultants and employees. We may not be able to prevent the unauthorized disclosure or use of our technical know- how or other trade secrets by the parties to these agreements, however, despite the existence generally of confidentiality agreements and other contractual restrictions. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees and consultants who are parties to these ~~89agreements~~ -- **agreements** breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result. Enforcing a claim that a third party illegally obtained and is using our trade secrets, like patent litigation, is expensive and time- consuming, and the outcome is unpredictable. In addition, courts outside the U. S. are sometimes less willing to protect trade secrets. Our trade secrets could otherwise become known or be independently discovered by our competitors. Competitors could purchase our drugs and drug candidates and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around our protected technology or develop their own competitive technologies, drugs, and drug candidates that fall outside of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If our trade secrets are not adequately protected so as to protect our market against competitors' drugs, our competitive position could be adversely affected, as could our business. We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of our competitors or are in breach of non- competition or non- solicitation agreements with our competitors. We could in the future be subject to claims that we or our employees have inadvertently or otherwise used or disclosed alleged trade secrets or other proprietary information of former employers or competitors. Although we try to ensure that our employees and consultants do not use the intellectual property, proprietary information, know- how or trade secrets of others in their work for us, we may in the future be subject to claims that we caused an employee to breach the terms of his or her non- competition or non- solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and could be a distraction to management. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our drugs or drug candidates if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. An inability to incorporate such technologies or features would have a material adverse effect on our business and may prevent us from successfully commercializing our drugs and drug candidates, if approved. In addition, we may lose valuable intellectual property rights or personnel as a result of such claims. Moreover, any such litigation or the threat thereof may adversely affect our ability to hire employees or contract with independent sales representatives. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our drugs and drug candidates, if approved, which would have an adverse effect on our business, results of operations and financial condition. Risks Related to Our Business, including Employee Matters, Managing Growth and OthersOur ~~business, results of operations and future growth prospects could be materially and adversely affected by the ongoing COVID- 19 pandemic. Due to the continued evolution and uncertain global impacts of the ongoing COVID- 19 pandemic and the identification of new variants of COVID- 19, we cannot precisely determine or quantify the impact this pandemic will have on our business, operations and financial performance. The extent to which the ongoing COVID- 19 pandemic may impact our business, results of operations and future growth prospects will depend on a variety of factors and future developments, which are highly uncertain and cannot be predicted with confidence, including the duration, scope and severity of the pandemic, the duration and extent of travel restrictions and social distancing in the U. S. and other countries, business closures or business disruptions and the effectiveness of actions taken in the U. S. and other countries to contain and treat COVID- 19. For example, public health actions being undertaken globally in response to the ongoing COVID- 19 pandemic, including quarantines, stay- at- home, executive and similar government orders and the prioritization of healthcare resources, could adversely impact our business, results of operations and future growth prospects. For ongoing and planned clinical trials, we anticipate and have experienced some temporary delays or disruptions due to the COVID- 19 pandemic, including limited or reduced patient access to trial investigators, hospitals and trial sites, delayed~~

~~initiation of new clinical trial sites and limited on- site personnel support at various trial sites, which could adversely impact our development plans, including the initiation of planned clinical trials, the rate of enrollment and our ability to conduct 90ongoing clinical trials. There may also be local orders affecting one or more trial sites, which may trigger mandated changes to our clinical trial protocols or temporary suspensions in the affected trial sites. In addition, quarantines, stay- at- home, executive and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations have occurred and could continue to occur or be expanded in scope or duration, which could adversely impact: ● ongoing and planned clinical trials; ● our employees and business operations; ● personnel at our third- party suppliers and other vendors in the U. S. and other countries; ● the availability, cost or supply of materials, which may cause delays or disruptions to development plans for our drug candidates or clinical or commercial supply chains for our current or future approved drugs and drug candidates; and ● sales and marketing activities related to AYVAKIT / AYVAKYT, GAVRETO and any drug candidates for which we may receive marketing approval in the U. S. or other geographies in the future. To the extent the ongoing COVID- 19 pandemic adversely affects our business, results of operations and future growth prospects, it may also have the effect of heightening many of the other risks described in this " Risk Factors " section. Our~~ future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel. We are highly dependent on the research and development, clinical, commercial, business development, financial and legal expertise of our executive officers, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment agreements with our executive officers, each of ~~our~~ **80our** executive officers may terminate their employment with us at any time. In addition, insurance coverage is increasingly expensive, including with respect to directors and officers liability insurance, or D & O insurance. We may not be able to maintain D & O insurance at a reasonable cost or in an amount adequate to satisfy any liability that may arise. An inability to secure and maintain D & O insurance may make it difficult for us to retain and attract talented and skilled directors and officers to serve our company, which could adversely affect our business. We do not maintain " key person " insurance for any of our executives or other employees. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited. We expect to continue hiring qualified development personnel. Recruiting and retaining qualified scientific, clinical, regulatory, manufacturing and sales and marketing personnel is critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing key employees and executive officers may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize drugs. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel. ~~91We~~ **We** will need to develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations. As of January 31, ~~2023~~ **2024**, we had ~~641~~ **655** full- time and part- time employees, and we expect to continue to increase our number of employees and expand the scope of our operations. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Also, our management may need to divert a disproportionate amount of its attention away from its day- to- day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Physical expansion of our operations in the future may lead to significant costs, including capital expenditures, and may divert financial resources from other projects, such as the development of our drug candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our drug candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company. Unfavorable global economic or political conditions could adversely affect our business, financial condition or results of operations. Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the ~~ongoing~~ COVID- 19 pandemic ~~has~~ caused extreme volatility and disruptions in the capital and credit markets. In addition, geopolitical developments, such as the **Israeli- Palestinian conflict,** Russian invasion of Ukraine or deterioration in the bilateral relationship between the U. S. and China could contribute to disruption, instability and volatility in the global markets, as well as an increased inflation, which in turn could adversely impact our operations and those of third parties upon which we rely. **Geopolitical conflicts could also have an adverse impact on third parties located in the involved jurisdictions, which could in turn have an adverse impact on our business. For example, certain of our distributors are located in Israel, and may be adversely impacted by the Israeli- Palestinian conflict.** Related sanctions, export controls or other actions that may be initiated by nations including the U. S., the EU **, Israel** or Russia (e. g., potential cyberattacks, disruption of energy flows) could adversely affect our business, our supply ~~chain~~ **81chain**, CROs, CMOs, clinical trial sites, collaborative partners, **distributors** or other third parties with which we conduct business. There can be no assurance that further deterioration in credit

and financial markets and confidence in economic conditions will not occur. A severe or prolonged economic downturn could result in a variety of risks to our business, including ~~,~~ weakened demand for our drug candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Political ~~development~~ **developments** can also lead to uncertainty around regulations and rules that may materially affect our business. For example, as the UK regulatory system is now independent from the EU, a long ~~-~~ term effect of Brexit could be that the UK significantly alters its regulations affecting the clearance or approval of our drug or drug candidates that are developed in the UK. Any new regulations could add time and expense to the conduct of our business, as well as the process by which our drug candidates receive regulatory approval in the UK, as compared to the EU and elsewhere ~~. Geopolitical risks associated with the Russian invasion of Ukraine could have an adverse impact on our business, financial condition and results of operations, including our clinical trials. On February 24, 2022, Russian forces invaded Ukraine, which has resulted in conflict and disruption in the region. In response to this action taken by Russia, the U. S. and other countries immediately imposed various economic sanctions against Russia. In the event Russia' s invasion continues or geographically expands, additional governmental sanctions may be enacted. The uncertain nature of this evolving situation, including the potential effects of sanctions limitations, retaliatory cyber- attacks on the world economy and markets, have also contributed to increased market volatility and uncertainty, which could have an adverse impact on macroeconomic factors that affect our business and operations. Additionally, the ongoing conflict in Ukraine may disrupt the ability of our commercial research organizations, or CROs, to conduct clinical trials at certain sites in Ukraine. Moreover, enrollment and retention of clinical trial participants may be adversely affected. The overall impact of this conflict on our ability to conduct clinical trials at certain sites in future periods is hard to predict. However, interruptions of our clinical trials could significantly delay our clinical 92development plans and potential authorization or approval of our product candidates, which could increase our costs and impact our timelines for commercializing certain of our product candidates~~ . Rising inflation rates could negatively impact our revenues and profitability if increases in the prices of our products or a decrease in spending on products in the biopharmaceutical industry in general results in lower sales by us or those who we collaborate with. In addition, if our costs increase and we are not able to correspondingly adjust our commercial relationships to account for this increase, our net income would be adversely affected, and the adverse impact may be material. Inflation rates, particularly in the U. S., have increased recently to levels not seen in years. Increased inflation may result in decreased demand for our products, increased operating costs (including our labor costs), reduced liquidity, and limitations on our ability to access credit or otherwise raise debt and equity capital. In addition, the United States Federal Reserve has raised, and may again raise, interest rates in response to concerns about inflation. Increases in interest rates, especially if coupled with reduced government spending and volatility in financial markets, may have the effect of further increasing economic uncertainty and heightening these risks. In an inflationary environment, we may be unable to raise the sales prices of our products at or above the rate at which our costs increase, which could reduce our profit margins and have a material adverse effect on our financial results and net income. We also may experience lower than expected sales and potential adverse impacts on our competitive position if there is a decrease in spending on products in the biopharmaceutical industry in general or a negative reaction to our pricing or the pricing of those we do, or will collaborate with. A reduction in our revenue would be detrimental to our profitability and financial condition and could also have an adverse impact on our future growth. Foreign currency exchange rates fluctuations could have an adverse impact on our operating results. From time to time, we contract with vendors that are located in Asia and Europe, which are denominated in foreign currencies. We are subject to fluctuations in foreign currency rates in connection with these agreements. If the U. S. dollar weakens against a specific foreign currency, our revenues will increase, having a positive impact on net income, but our overall expenses will increase, having a negative impact. Conversely, if the U. S. dollar strengthens against a specific foreign currency, our revenues will decrease, having a negative impact on net income, but our overall expenses will decrease, having a positive impact. Continued fluctuations in foreign exchange rates can impact our operating results and financial condition. We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster. Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as clinical trial sites or the manufacturing facilities of our third- party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, could have a material adverse effect on our business. ~~Our~~ **82Our** internal computer systems, or those of our third- party collaborators, service providers, contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our drugs' and drug candidates' development programs and have a material adverse effect on our reputation, business, financial condition or results of operations. Our internal computer systems and those of our current or future third- party collaborators, service providers, contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Attacks on information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and they are being conducted by increasingly sophisticated and organized groups and individuals with a wide range of motives and expertise. In addition to extracting sensitive information, such attacks could include the deployment of harmful malware, ransomware, denial- of- service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and ~~93availability~~ -- **availability** of information **. Cyber- attacks also could include phishing attempts or e- mail fraud to cause payments or information to be transmitted to an unintended**

recipient and could include the use of artificial intelligence, or AI, and machine learning to launch more automated, targeted and coordinated attacks on targets . The prevalent use of mobile devices also increases the risk of data security incidents. While we have not experienced any material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations or the operations of third- party collaborators, service providers, contractors and consultants, it could result in a material disruption of our drugs' and drug candidates' development programs and significant reputational, financial, legal, regulatory, business or operational harm. For example, the loss of clinical trial data for our drugs or drug candidates 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 other data or applications relating to our technology or drug candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our drug candidates could be delayed. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyberattacks and other related breaches. Any failure or perceived failure by us or any third- party collaborators, service providers, contractors or consultants to comply with our privacy, confidentiality, data security or similar obligations to third parties, or any data security incidents or other security breaches that result in the unauthorized access, release or transfer of sensitive information, including physician data, patient data, or any personally identifiable information, may result in governmental investigations, enforcement actions, regulatory fines, litigation or public statements against us, could cause third parties to lose trust in us or could result in claims by third parties asserting that we have breached our privacy, confidentiality, data security or similar obligations, any of which could have a material adverse effect on our reputation, business, financial condition or results of operations. Moreover, data security incidents and other security breaches can be difficult to detect, and any delay in identifying them may lead to increased harm. While we have implemented data security measures intended to protect our information technology systems and infrastructure, there can be no assurance that such measures will successfully prevent service interruptions or data security incidents. **Similarly, the increasing use of AI, and machine learning technology in the biopharmaceutical industry presents new risks and challenges. The use of AI based software may lead to the inadvertent release of confidential or proprietary information, which may adversely impact our ability to realize the benefit of our intellectual property, cause us to incur liabilities as the result of any breaches of confidentiality or impact our ability to comply with data security and privacy laws. Further, as the regulatory framework for these technologies evolves, it is possible that new laws and regulations will be adopted, or that existing laws and regulations may be interpreted in ways that would affect our business, including as a result of the cost to comply with such laws or regulations.** Interruptions in the availability of server systems or communications with Internet or cloud- based services, or failure to maintain the security, confidentiality, accessibility or integrity of data stored on such systems, could harm our business. We rely upon a variety of Internet service providers, third- party hosting facilities and cloud computing platform providers to support our business. Failure to maintain the security, confidentiality, accessibility or integrity of data stored on such systems could damage our reputation in the market, cause us to lose revenue or market share, increase our service costs, cause us to incur substantial costs, subject us to liability for damages and / or fines and divert our resources from other tasks, any one of which could materially adversely affect our business, financial condition, results of operations and prospects. Any damage to, or failure of, such systems, or communications to and between such systems, ~~could~~ **83could** result in interruptions in our operations. If our security measures or those of our third- party data center hosting facilities, cloud computing platform providers, or third- party service partners, are breached, and unauthorized access is obtained to our data or our information technology systems, we may incur significant legal and financial exposure and liabilities. We do not have control over the operations of the facilities of our cloud service providers and our third- party providers may be vulnerable to damage or interruption from natural disasters, cybersecurity attacks, terrorist attacks, power outages and similar events or acts of misconduct. In addition, any changes in our cloud service providers' service levels may adversely affect our ability to meet our requirements and operate our business. Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could have a material adverse effect on our business, financial condition or results of operations. Privacy and data security have become significant issues in the U. S., Europe and in many other jurisdictions where we conduct or may in the future conduct our operations. The regulatory framework for the collection, use, safeguarding, sharing and transfer of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. Notably, for example, **in Europe** ~~on May 25, 2018~~ , the European General Data Protection Regulation 2016 / 679, which is commonly referred to as GDPR ~~, took effect. The GDPR~~ applies to any company established in the European Economic Area, or EEA, as well as any company outside the EEA that collects or otherwise processes personal data in connection with the offering goods or services to individuals in the EEA or the monitoring of their behavior. The GDPR ~~enhances~~ **imposes** data protection obligations ~~for~~ **on** processors and controllers of personal ~~94data~~ -- **data** , including, for example, ~~expanded~~ disclosures about how personal information is to be used, **having** ~~ensuring we have~~ a valid legal basis to process personal data, maintaining records of our processing activities and ~~to document~~ **documenting** data protection impact assessments where there is high risk processing, limitations on retention of information, mandatory data breach notification requirements, ensuring appropriate technical and organizational measures **are** ~~to be~~ put in place to safeguard personal data and onerous ~~new~~ obligations on services providers. ~~The~~ **Penalties under the** GDPR ~~imposes additional obligations and risk upon our business and substantially increase the penalties to which we could be subject in the event of any non- compliance, including~~ **include** fines of up to € 20 million or 4 % of total worldwide annual turnover, whichever is higher **. EEA Member States have adopted national laws to implement the GDPR which may partially deviate from the GDPR. Further, competent authorities in the EEA Member States may interpret GDPR obligations slightly differently from country to country. For these reasons, we do not expect to operate**

in a uniform legal landscape in the EEA . Further to the UK' s exit from the European Union on January 31, 2020, the ~~GDPR ceased to apply in the~~ UK ~~at the end of the transition period on December 31, 2020. However, as of January 1, 2021, the UK' s European Union (Withdrawal) Act 2018~~ incorporated the GDPR (as it existed on December 31, 2020 but subject to certain UK specific amendments) into UK law (referred to as the ~~"~~ UK GDPR ~~"~~). The UK GDPR and the UK Data Protection Act 2018 set out the UK' s data protection regime, which is independent from but **currently still** aligned to the EU' s data protection regime. Non- compliance with the UK GDPR may result in monetary penalties of up to £ 17. 5 million or 4 % of worldwide revenue, whichever is higher. ~~In this document~~ **Although the UK is regarded as a third country under the EU' s GDPR** , **the European Commission has issued a decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EEA to the UK remain unrestricted. Likewise The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing. The UK Government has introduced a Data Protection and Digital Information Bill (** " **UK Bill ") into the UK legislative process. The aim of the UK Bill is to reform the UK' s data protection regime following Brexit. If passed, the final version of the UK Bill may have the effect of further altering the similarities between the UK and EEA data protection regime and threaten the UK Adequacy Decision from the European Commission (" EC "). This may lead to additional compliance costs and could increase our overall risk. The respective provisions and enforcement of the EU** GDPR ~~" refers to both the EU~~ and ~~the~~ UK GDPR ~~, unless specified otherwise~~ **may further diverge in the future and create additional regulatory challenges and uncertainties** . Given the breadth and depth of changes in data protection obligations, preparing for and complying with the GDPR requirements has required and will continue to require significant time, resources and a review of our technologies, systems and practices, as well as those of any third- party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the **UK or** EEA ~~. EEA Member States have adopted national laws to implement the GDPR which may partially deviate from the GDPR. Further, competent authorities in the EEA Member States may interpret GDPR obligations slightly differently from country to country. For these reasons, we do not expect to operate in a uniform legal landscape in the EEA. In addition, the UK has announced plans to reform the country' s data protection legal framework in its Data Reform Bill, but these have been put on hold~~ . Further, European data protection laws also ~~prohibit~~ **regulates** the transfer of personal data from the EEA **, the UK** and Switzerland to third countries that are not considered to provide adequate protections **to** ~~are provided for~~ personal data **. On June 4** , ~~including~~ **2021,** ~~the~~ **84the European Commission (** ~~U. S. With regard to transfers of personal data from the EEA, transfers to third countries that have not been approved as~~ " ~~adequate~~ **EC** " **) issued new** ~~are prohibited unless an appropriate safeguard specified by the GDPR is implemented, such as the~~ Standard Contractual Clauses ~~, or~~ **(" "** SCCs **")** ~~, approved by the European Commission, or~~ **for** ~~EC, or binding corporate rules, or a derogation applies. In the past, companies in the U. S. were able to rely upon the Privacy Shield framework to legitimize~~ data transfers from **controllers or processors in** the EEA ~~to the U. S. In July 2020, the Court of Justice of the European Union, or CJEU, in Case C- 311 / 18~~ (**or otherwise subject to the EU GDPR) to controllers or processors established outside the EEA (and not subject to the EU GDPR). The new SCCs replace the SCCs that were adopted previously under the** Data Protection **Directive** ~~Commissioner v Facebook Ireland and Maximillian Schrems, or Schrems II) invalidated the EU- U. S. Privacy Shield on the grounds that the Privacy Shield failed to offer adequate protections to EU personal data transferred to the U. S~~ . The **UK** ~~CJEU, in the same decision, deemed that the Standard Contractual Clauses, or SCCs, published by the EC are valid. However, the CJEU ruled that transfers made pursuant to the SCCs need to be assessed on a case- by- case basis to ensure the law in the recipient country provides " essentially equivalent " protections to safeguard the transferred personal data as the EEA, and required businesses to adopt supplementary measures if such standard~~ is not **subject to** ~~met. On June 4, 2021,~~ the ~~European Commission issued~~ **EC' s** new SCCs ~~that account for the CJEU' s decision and other developments, which need to be put in place for new contracts involving the transfer of personal data from the EEA to a third country since September 27, 2021, and incorporated into existing contracts since December 27, 2022. The New SCCs do not apply to the UK,~~ but ~~the UK Information Commissioner' s Office~~ has published its own ~~transfer mechanism~~ **standard clauses** , the International Data Transfer Agreement, **which enables transfers from the UK. We will be required to implement these new safeguards when conducting restricted data transfers under the EU GDPR and UK GDPR and doing so will require significant effort and cost. Where relying on the SCCs** or UK IDTA ~~, which entered into force~~ -- **for** ~~on 21 March 2022, and enables~~ data transfers **, we may also be** ~~originating from the UK. It requires~~ **required** ~~a similar assessment of the data protection provided in the importer' s country. The UK IDTA needs~~ to **carry out** ~~be concluded in new contracts involving the~~ transfer ~~of~~ **impact assessments to assess whether the recipient is subject to local laws which allow public authority access to** personal data ~~from the UK as of 22 September 2022. Organizations have until 21 March 2024 to update existing agreements~~ . On ~~March 25~~ **July 10** , ~~2022~~ **2023** , the ~~EC~~ **EU adopted** ~~and~~ **an adequacy decision for** ~~the US announced to have reached a political agreement on~~ a new " ~~Trans- Atlantic~~ Data Privacy Framework **,** " ~~,~~ which ~~will replace~~ **replaces** the ~~invalidated~~ Privacy Shield ~~and on December 13~~ , **which the European Court of Justice invalidated in** ~~2022~~ **2020 for personal data transferred from the EU to the U. S. On July 17, 2023 the U. S. Department of Commerce released registration means and requirements for U. S. companies to register** . The ~~EC published a draft adequacy decision~~ **Framework provides additional certification mechanisms to provide for UK and Swiss data transfers. We have registered and have active membership under the Framework, allowing for transfer of HR and** ~~on~~ **non** ~~the Trans- Atlantic~~ **HR** ~~Data~~ **data** ~~Privacy Framework~~ **from Switzerland and EEA member states** . We will be required to ~~implement~~ **maintain** these new safeguards when conducting restricted cross- border data transfers and doing so will require significant effort and cost. These and other future developments regarding the flow of data across borders could increase the cost and complexity of delivering our services in some markets and may lead to governmental enforcement actions, litigation, fines, and penalties or adverse publicity, which could adversely affect our business and financial position. ~~95Although the UK is regarded as a third country under the EU' s GDPR, the EC has issued a decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data~~

~~originating in the EEA to the UK remain unrestricted. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing.~~ While we have taken steps to mitigate the impact on us with respect to transfers of data, such as **registering with the U. S. governing bodies managing the Data Privacy Framework, and** implementing the SCCs **where necessary** in new contracts with our service providers, customers, subsidiaries ~~, and are updating existing contracts with the new SCCs in anticipation of the December 2022 deadline~~ , the validity of these transfer mechanisms remains uncertain **. The previous data transfer mechanisms providing adequacy to enable cross-border transfers between the US and the EEA have been invalidated, and the Data Privacy Framework has already been challenged in several jurisdictions** . Complying with this guidance as it exists today and evolves will be expensive and time consuming and may ultimately prevent us from transferring personal data outside **Europe** ~~the EEA,~~ which would cause significant business disruption for ourselves and our customers and potentially require the changes in the way our products are configured, hosted and supported. In addition, we are subject to Swiss data protection laws, including the Federal Act on Data Protection, or FADP. While the FADP provides broad protections to personal data, on September 25, 2020, the Swiss federal Parliament enacted a revised version of the FADP, which is anticipated to become effective in September 2023. The new version of the FADP aligns Swiss data protection law with the GDPR **. We have updated our agreements to reflect the new requirements per the FADP, but further modifications or changes may require revisiting these agreements** . Further, in addition to existing European data protection law, the European Union also is considering another draft data protection regulation. The proposed regulation, known as the Regulation on Privacy and Electronic Communications (ePrivacy Regulation), would replace the current ePrivacy Directive. ~~The Draft Regulation is still the subject of negotiations between the Council of the European Union and the European Parliament.~~ It is unclear **whether and / or** when the Draft Regulation will enter into force ~~. New rules related to the ePrivacy Regulation are likely to include enhanced consent requirements in order to use communications content and communications metadata, as well as obligations and restrictions on the processing of data from an end- user' s terminal equipment, which may negatively impact our product offerings and our relationships with our customers~~ . Preparing for and complying with the evolving application of the GDPR, national laws in Switzerland and the UK, as well as ePrivacy Regulation (if and when it becomes effective) has required and will continue to require us to incur substantial operational costs and may require us to change our business practices. Despite our efforts to bring practices into compliance with the GDPR, appliable national data protection laws and before the effective date of the ePrivacy Regulation, we may not be successful either due to internal or external factors such as resource allocation limitations. Non- compliance could result in proceedings, fines or penalties against us by governmental entities, customers, data subjects, consumer associations or others. In addition to European data protection requirements, we are subject to the California Consumer Privacy Act, or CCPA, which took effect on January 1, 2020 and imposes sweeping privacy and security obligations on many companies doing business in California and provides for substantial fines for non- compliance and, in some cases, a private right of action to consumers who are victims of data breaches involving their unredacted or unencrypted personal information. While there is currently an exception for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact our business activities. The CCPA became enforceable as of ~~July~~ **85July** 1, 2020, but there continues to be uncertainty about how the law will be interpreted and enforced. **The CCPA was amended by** ~~Additionally, a new California ballot initiative,~~ the California Privacy Rights Act **(,** ~~or~~ CPRA **) which** ~~, was passed in November 2020 and~~ became effective on January 1, 2023. The CPRA imposes additional obligations on companies covered by the legislation and ~~will~~ significantly ~~modify~~ **modified** the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also ~~creates~~ **created** a new state agency that **is** ~~will be~~ vested with authority to implement and enforce the CCPA ~~and the CPRA~~ . The effects of the CCPA ~~and the CPRA~~ are potentially significant and may require us to modify our data collection or processing practices and policies and to incur substantial costs and expenses in an effort to comply and increase our potential exposure to regulatory enforcement and / or litigation. ~~Also, on March 2, 2021, Virginia enacted the Consumer Data Protection Act, or CDPA. The CDPA became effective on January 1, 2023. The CDPA regulates how businesses, which the CDPA refers to as " controllers ", collect and share personal information. The law applies to companies that conduct business in Virginia or product products or 96services that are targeted to residents of Virginia and either: (1) annually control or process personal data of at least 100, 000 Virginia residents; or (2) control or process the personal data of at least 25, 000 Virginia residents and derive over 50 % of gross revenue from the sale of personal data. While the CDPA incorporates many similar concepts of the CCPA and CPRA, there are also several key differences in the scope, application, and enforcement of the law that will change the operational practices of controllers. The CDPA regulates impact how controllers collect and process personal sensitive data, conduct data protection assessments, transfer personal data to affiliates, and respond to consumer rights requests.~~ In addition **to** ~~, on July 8, 2021, Colorado' s governor signed~~ the ~~Colorado Privacy Act, or CPA~~ **CCPA** ~~, into law. The CPA is rather similar to the Virginia' s CPDA but also contains additional requirements. The~~ new ~~measure applies to companies conducting business in Colorado or who produce or deliver commercial products or services intentionally targeted to its residents of the state and that either: (1) control or process the personal data of at least 100, 000 Colorado residents during a calendar year; or (2) derive revenue or receive a discount on the price of goods or services from the sale of personal data and process or control the personal data of at least 25, 000 Colorado residents. Moreover, on March 24, 2022, Utah' s governor signed the Utah Consumer Privacy Act, or UCPA, into law. The UCPA will take effect on December 31, 2023. Also, in 2022, Connecticut Governor Lamont signed the Connecticut Data Privacy Act, or CTDPA, into laws. The UCPA and CTDPA draw heavily upon their predecessors in Virginia and Colorado. With the CTDPA, Connecticut became the fifth state to enact a comprehensive privacy law.~~ New privacy and data security laws have been ~~proposed~~ **enacted** in **numerous** ~~more than half of the states in the U. S. and in the U. S. Congress. With bills proposed in many other jurisdictions, it remains quite possible that~~ other states **and have been** ~~will follow suit. Such~~ proposed **in even more states as well as in the U. S. Congress, reflecting a trend toward more stringent**

privacy legislation ~~, if enacted, may add additional complexity, variation~~ in ~~requirements~~ **the U. S.** , ~~restrictions~~ **which may accelerate. Furthermore, a smaller number of states have passed or are considering laws that are specifically focused upon health privacy, such as Washington' s My Health My Data Act. The effects of state and federal privacy laws are potentially significant and may require us to modify our data processing practices and policies and to incur substantial costs** and potential ~~legal risk~~ **liability in an effort to comply with such legislation. Additionally** , **the Federal Trade Commission (FTC) has focused enforcement actions in the healthcare space. Multiple enforcement actions around how healthcare companies collect, notice and share personal data have provided important signals on points of emphasis for us to focus our compliance efforts. We have taken necessary steps to comply with guidance to date, however guidance and enforcement actions may** require additional investment of resources in compliance programs ~~, impact strategies and the availability of previously useful data and could result in increased compliance costs~~ and / or changes in business practices and policies. **On October 30, 2023, President Biden issued an Executive Order on Safe, Secure, and Trustworthy Artificial Intelligence which provided a framework for and a call for Congress to enact laws establishing the appropriate development and use of artificial intelligence (AI.)** The ~~existence~~ **widespread use** of ~~comprehensive privacy~~ **generative AI and natural language processing tools have significant risk when used in the healthcare space. We are exposed to risks associated with employees utilizing generative AI in methods and ways that are contrary to the framework laid out by the Executive Order or the subsequent complementary** laws **. We** ~~in different states in the country~~ will ~~make~~ **need to invest resources to ensure appropriate development and use of any generative AI,** ~~our~~ **or like- technology, and to develop internal** compliance ~~obligations more complex~~ **policies and procedures addressing this use. Cybersecurity presents** ~~and~~ **an** ~~costly~~ **ongoing risk vector for our company. A cybersecurity incident impacting our internal systems or network could compromise sensitive information of patients** and **employees, requiring additional resources to enable us to ensure remediation and proper notification. Additionally, we rely on vendors to provide** ~~may~~ **many** ~~increase~~ **services where** ~~the~~ **they** ~~likelihood~~ **collect, use or process sensitive data on our behalf or jointly. An incident compromising the databases of our internal network or our vendor' s information may materially impact our ability to continue development of our products or have appropriate data to complete FDA submissions. If data related to drug development is compromised, the integrity of** that ~~we may~~ **data might** be ~~subject~~ **impacted in such a way** to ~~enforcement actions~~ **render it unusable or potentially modified to a degree it will not be reliable. This type of attack may have material financial impacts resulting from a cybersecurity incident disclosing or making unavailable IP related to** ~~or~~ **our** ~~otherwise incur~~ **drug development through a ransomware attack or similar method. The continued development and management of our Information Security function may require additional investment of resources to mature our** ~~liability~~ -- **ability** ~~for noncompliance~~ **to prevent and respond to cybersecurity incidents** . The increasing number and complexity of regional, country and U. S. state data protection laws, and other changes in laws or regulations across the globe, especially those associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could lead to government enforcement actions and significant penalties against us and could have a material adverse effect on our business, financial condition or results of operations. Our employees, principal investigators, CROs and consultants may engage in misconduct or other improper activities, including non- compliance with regulatory standards and requirements and insider trading. We are exposed to the risk that our employees, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and / or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of the FDA and other regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; healthcare fraud and abuse laws and regulations in the U. S. and abroad; or laws that require the reporting of financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare ~~industry~~ **86industry** are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self- dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws ~~or regulations~~ **orregulations** . In addition, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and ~~97curtailment~~ - **curtailment** of our operations, any of which could adversely affect our ability to operate our business and our results of operations. We may acquire or in- license businesses, technologies or platforms, approved drugs, drug candidates or discovery- stage programs, or form strategic alliances, collaborations or partnerships, in the future, and we may not realize the benefits of such acquisitions, in- licenses, alliances, collaborations or partnerships. We may acquire or in- license additional businesses, technologies or platforms, approved drugs, drug candidates or discovery- stage programs, or form strategic alliances, collaborations or partnerships that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new drugs or drug candidates resulting from a strategic alliance, collaboration,

partnership or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. In addition, we cannot assure you that, following any such transaction, we will achieve the expected synergies to justify the transaction. We may be subject to adverse legislative or regulatory tax changes that could negatively impact our financial condition. The rules dealing with U. S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the IRS and the U. S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect our stockholders or us. We assess the impact of various tax reform proposals and modifications to existing tax treaties in all jurisdictions where we have operations to determine the potential effect on our business and any assumptions we have made about our future taxable income. We cannot predict whether any specific proposals will be enacted, the terms of any such proposals or what effect, if any, such proposals would have on our business if they were to be enacted. For tax years beginning after December 31, 2021, the Tax Cuts and Jobs Act of 2017 **(TCJA)** eliminates the once available option to deduct research and development expenditures currently and requires taxpayers to amortize specified research expenditures attributable to domestic research over a period of five years and fifteen years for research activities attributable to foreign research. As of December 31, ~~2022~~ **2023**, the U. S. Congress has not passed legislation that would defer the amortization requirement to future periods and as such the inability to deduct research and development expenditures in their entirety in ~~2022~~ **2023** had a material impact on the carryover of taxable losses used to offset future taxable income, and in turn will impact our cash flows in future years. Risks Related to Our Common StockThe price of our common stock has been and may in the future be volatile and fluctuate substantially. Our stock price has been and may in the future be subject to substantial volatility. For example, our stock traded within a range of a high price of $ 125. 61 and a low price of $ 13. 04 per share for the period beginning on April 30, 2015, our first day of trading on The Nasdaq Global Select Market, through February ~~15~~ **13**, ~~2023~~ **2024**. As a result of this volatility, our stockholders could incur substantial losses. ~~The~~ **87The** stock market in general has recently experienced relatively large price and volume fluctuations ~~, particularly in response to the COVID- 19 outbreak~~. In particular, the market prices of securities of Nasdaq listed and biopharmaceutical companies have experienced extreme fluctuations that often have been unrelated or disproportionate to the operating results of these companies. Continued market fluctuations could result in extreme volatility in the price of our common stock, which could include a decline in the value of our common stock. In addition, the market price for our common stock may be influenced by many factors, including: ● the success of commercialization of our drugs and drug candidates, if approved; ● the success of competitive drugs or technologies; ● results of clinical trials of our drug candidates or those of our competitors; ● regulatory or legal developments in the U. S. and other countries; ~~98~~ ● 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 drug candidates or clinical development programs; ● the results of our efforts to discover, develop, acquire or in- license additional drug candidates or drugs; ● actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts; ● variations in our financial results or those of companies that are perceived to be similar to us; ● changes in the structure of healthcare payment systems; ● market conditions in the pharmaceutical and biotechnology sectors; ● natural disasters, epidemic or pandemic disease outbreaks, including the COVID- 19 pandemic, trade wars, political unrest or other similar events; ● general economic, industry and market conditions; and ● the other factors described in this " Risk Factors " section. Future sales or issuances of common stock or other equity related securities may also adversely affect the market price of our common stock. In February 2022, we entered into a new sales agreement with Cowen and Company, LLC through which we may, from time to time, issue and sell shares of our common stock having an aggregate offering price of up to $ 300. 0 million, subject to the terms and conditions of the sales agreement. We did not sell any shares of common stock under this sales agreement during the year ended December 31, ~~2022~~ **2023**. If we seek authorization to sell shares of common stock under the new sales agreement, enter into new " at the market " stock offering programs, or conduct a public offering or private offering through other means, it could lead to additional dilution for our stockholders and may impact our stock price adversely. These and other market and industry factors may cause the market price and demand for our common stock to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from readily selling their shares of common stock and may otherwise negatively affect the liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert the time and attention of our management. ~~We~~ **88We** have in the past relied in part on sales of our common shares through our at- the- market (ATM) offering program to raise capital. Increased volatility and decreases in market prices of equity securities generally and of our common shares in particular may have an adverse impact on our willingness and / or ability to continue to sell our common shares through our ATM offering. Decreases in these sales could affect the cost or availability of equity capital, which could in turn have an adverse effect on our business, including current operations, future growth, revenues, net income and the market prices of our common shares. In February 2022, we commenced a new at- the- market, or ATM, program to raise capital. Under our ATM program, we have entered into a sales agreement to sell common shares, up to a maximum aggregate market value of $ 300. 0 million, through one or more at- the- market offerings. Given volatility in the capital markets, we may not be willing or able to continue to raise equity capital through our ATM program. We may, therefore, need to turn to other sources of funding that may have terms that are not favorable to us, or reduce our business operations given capital constraints. Alternative financing arrangements, if we pursue any, could involve issuances of one or more types of securities, including common stock, preferred stock, convertible debt, warrants to acquire common stock or other ~~99securities~~ **securities**. These securities could be issued at or below the then prevailing market price for our common shares. In addition, if we issue debt securities, the holders of the debt would have a claim to our assets that would be superior to the rights of stockholders until the principal, accrued and unpaid interest and any premium or make- whole has been paid. In addition, if we borrow funds and / or issue debt securities through a subsidiary, the lenders and / or holders of those debt securities would have

a right to payment that would be effectively senior to the company' s equity ownership in the subsidiary, which would adversely affect the rights of holders of both the company' s equity securities and its debt and debt securities. Interest on any newly- issued debt securities and / or newly- incurred borrowings would increase our operating costs and increase our net loss, and these impacts may be material. If the issuance of new securities results in diminished rights to holders of our common stock, the market price of our common shares could be materially and adversely affected. Should the financing we require to sustain our working capital needs be unavailable or prohibitively expensive when we require it, the consequences could result in a material adverse effect on our business, operating results, financial condition and prospects. If equity research analysts publish negative evaluations of or downgrade our common stock, the price of our common stock could decline. The trading market for our common stock relies in part on the research and reports that equity research analysts publish about us or our business. We do not control these analysts. If one or more of the analysts covering our business downgrade their evaluations of our common stock, the price of our common stock could decline. If one or more of these analysts cease to cover our common stock, we could lose visibility in the market for our common stock, which in turn could cause our common stock price to decline. Our executive officers, directors, principal stockholders and their affiliates maintain the ability to exercise significant influence over our company and all matters submitted to stockholders for approval. Our executive officers, directors and stockholders who own more than 5 % of our outstanding common stock, together with their affiliates and related persons, beneficially own shares of common stock representing a significant percentage of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to influence our management and affairs and the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation, or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire. In addition, this concentration of ownership might adversely affect the market price of our common stock by: ● delaying, deferring or preventing a change of control of us; ● impeding a merger, consolidation, takeover or other business combination involving us; ~~or~~ **or89** ● discouraging a potential acquiror from making a tender offer or otherwise attempting to obtain control of us. Anti- takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management. Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders, enhanced procedural mechanics and disclosure requirements in connection with stockholder nominations and submissions of stockholder proposals, and the ability of our board of directors to issue preferred stock without stockholder approval. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15 % of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring ~~100potential~~ **potential** acquirors to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, 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, which is responsible for appointing the members of our management. Our bylaws contain exclusive forum provisions, which may limit a stockholder' s ability to bring a claim in a judicial forum it finds favorable and may discourage lawsuits with respect to such claims. Our amended and restated bylaws, ~~as amended,~~ or bylaws, provide that unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for state law claims for (1) any derivative action, (2) any claim of breach of fiduciary duty, (3) any claim against a current or former director, officer, employee or stockholder, and (4) any action against our company governed by the internal affairs doctrine, which we refer to collectively as the Delaware forum provision. The Delaware forum provision does not apply to any claims arising under the Securities Exchange Act of 1934 or the Securities Act of 1933, as amended, or the Securities Act. Our bylaws further provide that, unless we consent in writing to an alternative forum, the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, which we refer to as the federal forum provision. We have chosen the federal district courts of the United States as the exclusive forum for such Securities Act causes of action. In addition, our bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the Delaware forum provision and the federal forum provision. In addition, our bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the Delaware forum provision and the federal forum provision. The Delaware forum provision and the federal forum provision may impose additional litigation costs on stockholders who assert the provision is not enforceable and may impose more general additional litigation costs in pursuing any such claims, particularly if the stockholders bringing a claim that is covered by the Delaware forum provision do not reside in or near the State of Delaware. In addition, these forum selection clauses in our bylaws may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. The federal forum provision may also impose additional litigation costs on stockholders who assert the provision is not enforceable or invalid. Alternatively, if the federal forum provision is found inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could have an adverse effect on our business, financial condition or results of operations. The Court of Chancery of the State of Delaware and the federal district courts of the United States may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

~~Future~~ **90Future** sales of our common stock, including by us or our directors and executive officers or shares issued upon the exercise of currently outstanding options, could cause our stock price to decline. A substantial portion of our outstanding common stock can be traded without restriction at any time. In addition, a portion of our outstanding common stock is currently restricted as a result of federal securities laws, but can be sold at any time subject to applicable volume limitations. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, by us or others, could reduce the market price of our common stock or impair our ability to raise adequate capital through the sale of additional equity securities. In addition, we have a significant number of shares that are subject to outstanding options. The exercise of these options and the subsequent sale of the underlying common stock could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. We cannot predict the number, timing or size of future issuances or the effect, if any, that any future issuances may have on the market price for our common stock. ~~101We~~ **We** have incurred and will continue to incur substantial costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives and corporate governance practices. As a public company, we have incurred and expect to continue to incur significant legal, accounting and other expenses. In addition, the Sarbanes- Oxley Act of 2002 and rules subsequently implemented by the Securities and Exchange Commission ~~, or~~ **(the** SEC ~~,~~**)** and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and make some activities more time- consuming and costlier. Pursuant to Section 404 of the Sarbanes- Oxley Act of 2002 **(** ~~, or~~ Section 404 ~~,~~**)** we are required to furnish an annual report by our management on our internal control over financial reporting. To achieve compliance with Section 404 within the prescribed period, we have been and will continue to be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that in the future neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404 or that we will not be able to comply with the requirements of Section 404 in a timely manner. If this were to occur, the market price of our stock could decline and we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources. Furthermore, investor perceptions of our company may suffer if deficiencies are found, and this could cause a decline in the market price of our stock. Irrespective of compliance with Section 404, any failure of our internal control over financial reporting could have a material adverse effect on our stated operating results and harm our reputation. If we are unable to implement these requirements effectively or efficiently, it could harm our operations, financial reporting, or financial results and could result in an adverse opinion on our internal control over financial reporting from our independent registered public accounting firm. Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be the sole 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, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future. **91** ~~Repurchases of our capital stock may be subject to additional tax. Congress recently enacted a new 1 % excise tax on certain stock repurchases (or similar transactions) effected by publicly traded domestic corporations such as Blueprint. This tax could make stock repurchases less desirable (and therefore less likely) as compared with other possible uses of our funds, and could reduce the amount of cash available if we do determine to pursue a stock repurchase. 102~~