Risk Factors Comparison 2024-02-20 to 2023-03-07 Form: 10-K

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Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report on Form 10- K, including our financial statements and the related notes and " Management' s Discussion and Analysis of Financial Condition and Results of Operations, " before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations, growth prospects and stock price. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Many of the following risks and uncertainties are, and will be, exacerbated by the COVID- 19 pandemic ~~or ,~~ the ongoing Ukraine- Russia conflict **, the Israel Hamas conflict, or banking sector volatility** and any worsening of the global business and economic environment as a result. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. Risks Related to Our Limited Operating History, Financial Condition and Capital Requirements We are an early- stage biopharmaceutical company with a limited operating history and no products approved for commercial sale. We have incurred significant losses since our inception, and we anticipate that we will continue to incur significant losses for the foreseeable future, which, together with our limited operating history, makes it difficult to assess our future viability. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We are an early- stage biopharmaceutical company, and we have only a limited operating history upon which you can evaluate our business and prospects. We currently have no products approved for commercial sale, have not generated any revenue from sales of products and have incurred losses in each year since our inception in June 2015. In addition, we have limited experience as a company and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical industry. ~~Three~~ **Four** of our product candidates, IDE397, darovasertib (IDE196) ~~and ,~~ IDE161 **and GSK101 (being developed by GSK under the Collaboration, Option and License Agreement with GSK)** , are currently in ongoing ~~or authorized~~ clinical trials ~~— one Phase 1 / 2 clinical trial to evaluate IDE397 for the treatment of patients having solid tumors with MTAP deletion that we initiated in April 2021, one ongoing Phase 1 / 2 clinical trial that we initiated in June 2019 to evaluate darovasertib in solid tumors harboring GNAQ or GNA11 hotspot mutations, one ongoing Phase 1 investigator sponsored clinical trial evaluating darovasertib as a potential neo- adjuvant and / or adjuvant therapy in primary, non- metastatic, uveal melanoma and one Phase 1 / 2 clinical trial to evaluate IDE161 for the treatment of patients having homologous recombination deficiencies (HRD) that has been authorized to proceed by the FDA and in which we are targeting initial dosing of our first patient in the first quarter of 2023~~ . We have had significant operating losses since our inception. Our net losses for the twelve months ended December 31, **2023 and** 2022 ~~and 2021~~ were $ **113. 0 million and $** 58. 7 million ~~and $ 49. 8 million~~ , respectively. As of December 31, ~~2022~~ **2023** , we had an accumulated deficit of $ ~~235~~ **348** . 4 million. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. ~~Our~~ **Three of our** product ~~candidate~~ **candidates are** ~~IDE397 is currently~~ in ~~a~~ **early** ~~Phase~~ **phase** ~~1 / 2~~ clinical ~~trial~~ **trials being conducted** ~~that we are conducting. Our product candidate darovasertib is currently in a Phase 1 / 2 clinical trial we are conducting. Our product candidate IDE161 is the subject of an IND, for a Phase 1 clinical trial that has been authorized to proceed~~ by **us** ~~the FDA and targeting initial dosing of our first patient in the first quarter of 2023~~ . We have multiple other product candidates in preclinical development, as well as early- stage research programs. Our product candidates will require substantial additional development time and resources before we will be able to apply for or receive regulatory approvals and, if approved, begin generating revenue from product sales. Furthermore, we expect to continue to incur additional costs associated with operating as a public company. We also do not yet have a sales organization or commercial infrastructure and, accordingly, we will incur significant expenses to develop a sales organization or commercial infrastructure in advance of regulatory approval and generating any commercial product sales. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will increase as we continue to develop IDE397, darovasertib, IDE161, our other product candidates and any future product candidates, conduct clinical trials and pursue research and development activities. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital. Our operating results may fluctuate significantly, which will make our future results difficult to predict and could cause our results to fall below expectations. Our quarterly and annual operating results may fluctuate significantly, which will make it difficult for us to predict our future results. These fluctuations may occur due to a variety of factors, many of which are outside of our control and may be difficult to predict, including: • the timing and cost of, and level of investment in, research, development and commercialization activities, which may change from time to time; • the timing and status of enrollment for our clinical trials; • the timing of regulatory approvals, if any, in the United States and internationally; • the cost of manufacturing, as well as building out our supply chain, which may vary depending on the quantity of productions, and the terms of any agreements we enter into with third- party suppliers; • timing and amount of any option exercise, milestone, royalty or other payments we may or may not receive pursuant to any current or future collaboration or license agreement, including under the Collaboration, Option and License Agreement with GSK; • timing and amount of any milestone, royalty or other payments due under any current or future collaboration or license agreement, including the License Agreement with Novartis or the Option and License Agreement with **CRT** ~~Cancer Research UK~~ and University of Manchester; • coverage and reimbursement policies with respect to any future

approved products, and potential future drugs that compete with our products; • expenditures that we may incur to acquire, develop or commercialize additional products and technologies; • the level of demand for any future approved products, which may vary significantly over time; • future accounting pronouncements or changes in our accounting policies; and • the timing and success or failure of preclinical studies and clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or collaboration partners. The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period- to- period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we may provide. We will require substantial additional financing to achieve our goals, and failure to obtain additional capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development programs, commercialization efforts or other operations. Since our inception, we have invested a significant portion of our efforts and financial resources in research and development activities for our precision medicine target and biomarker discovery platform and our initial preclinical and clinical product candidates. Preclinical studies and clinical trials and additional research and development activities will require substantial funds to complete. As of December 31, ~~2022~~ **2023**, we had cash, cash equivalents and marketable securities of $ ~~373~~ **632**. ~~1~~ **6** million. We believe that we will continue to expend substantial resources for the foreseeable future in connection with the research and development of our precision medicine target and biomarker discovery platform, clinical and preclinical product candidates, and any other future product candidates we may choose to pursue, as well as other corporate uses. Specifically, in the near term, we expect to incur substantial expenses as we advance our synthetic lethality product candidates through preclinical studies, advance darovasertib, IDE397 and IDE161 through clinical development, seek regulatory approval, prepare for and, if approved, proceed to commercialization, and continue our research and development efforts. These expenses will include our cost sharing obligations with GSK for research and development for our WRN program and our cost sharing obligations with Amgen for the Phase 1 / 2 clinical trial to evaluate IDE397 in combination with AMG 193. These expenditures will include costs associated with conducting preclinical studies and clinical trials, obtaining regulatory approvals, and manufacturing and supply, as well as marketing and selling any products approved for sale. In addition, other unanticipated costs may arise. Because the outcome of any preclinical study or clinical trial is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully develop and commercialize our product candidates or any future product candidates. We believe that our existing cash, cash equivalents and marketable securities will allow us to fund our planned operations for at least 12 months from the date of the issuance of the financial statements included in this Form 10- K. However, our operating plans and other demands on our capital resources may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other sources, such as strategic collaborations. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Such financing may result in dilution to stockholders, imposition of burdensome debt covenants and repayment obligations, or other restrictions that may adversely affect our business. If we raise additional funds through licensing or collaboration arrangements with third parties, we may have to relinquish valuable rights to our product candidates, or grant licenses on terms that are not favorable to us. Attempting to secure additional financing may also divert our management from our day- to- day activities, which may adversely affect our ability to develop our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Our future capital requirements will depend on many factors, including: • the scope, progress, results and costs of developing our product candidates or any other future product candidates, and conducting preclinical studies and clinical trials, including our ongoing **clinical trials for** IDE397 ~~Phase 1 / 2 clinical trial for the treatment of patients having solid tumors with MTAP deletion~~, ~~our ongoing~~ darovasertib ~~Phase 1 / 2 clinical trial in solid tumors harboring GNAQ or GNA11 mutations,~~ and ~~our~~ IDE161 ~~Phase 1 / 2 clinical trial for the treatment of patients having HRD~~; • the scope, progress, results and costs related to the research and development of our precision medicine target and biomarker discovery platform, including costs related to the development of our proprietary libraries and database of tumor genetic information and specific cancer- target dependency networks; • the timing of, and the costs involved in, obtaining regulatory approvals for our product candidates or any future product candidates, or any applicable diagnostics; • the number and characteristics of any additional product candidates we develop or acquire; • the cost of coordinating and / or collaborating with certain diagnostic companies for manufacturing and supply of companion diagnostics for biomarkers associated with our product candidates and any future product candidates; • our ability to maintain existing, and establish new, strategic collaborations, licensing or other arrangements and the financial terms of any such agreements, including the Collaboration, Option and License Agreement with GSK, the License Agreement with Novartis and the Option and License Agreement with Cancer Research ~~United Kingdom~~ **Technology Ltd.**, or **CRT** ~~Cancer Research UK~~, and University of Manchester; • the timing and amount of any option exercise, milestone, royalty or other payments we may or may not receive pursuant to any current or future collaboration or license agreement, including under the Collaboration, Option and License Agreement with GSK; • the timing and amount of any milestone, royalty or other payments we are required to make pursuant to any current or future collaboration or license agreement, including under the License Agreement with Novartis or the Option and License Agreement with **CRT** ~~Cancer Research UK~~ and University of Manchester; • potential delays in our ongoing clinical programs as a result of **any public health outbreaks, epidemics or pandemics (such as** the COVID- 19 pandemic **)**; • the cost of manufacturing our product candidates and any future products we successfully commercialize; • the cost of

commercialization activities, including the cost of building a sales force in anticipation of product commercialization and distribution costs; • any product liability or other lawsuits related to our product candidates or future approved products; • the expenses needed to attract, hire and retain skilled personnel; • the costs associated with being a public company; • the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing our intellectual property portfolio; and • the timing, receipt and amount of sales of any future approved products, if any. Our ability to raise additional funds will depend on financial, economic and other factors, including the ongoing effects of the COVID- 19 pandemic ~~and~~ **,** the Ukraine- Russia conflict **, the Israel- Hamas conflict, and closure of or liquidity issues at financial institutions (including, for example, Silicon Valley Bank)** , many of which are beyond our control. Additional funds may not be available when we need them, on terms that are acceptable to us, **or at all. Furthermore, we maintain the majority of our cash and cash equivalents in accounts with major U. S. and multi- national financial institutions, and our deposits at certain of these institutions exceed insured limits. Market conditions can impact the viability of these institutions. In the event of failure of any of the financial institutions where we maintain our cash and cash equivalents, there can be no assurance that we would be able to access uninsured funds in a timely manner** or at all. If adequate funds are not available to us on a timely basis, we may be required to: • delay, limit, reduce or terminate preclinical studies, clinical trials or other research and development activities or eliminate one or more of our development programs altogether; or • delay, limit, reduce or terminate our efforts to establish manufacturing and sales and marketing capabilities or other activities that may be necessary to commercialize darovasertib, if approved, IDE397, if approved, IDE161, if approved, or any other future approved products, or reduce our flexibility in developing or maintaining our sales and marketing strategy. Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies. To date, we have primarily financed our operations through the sale of equity securities and payments received under our collaboration agreements. We will be required to seek additional funding in the future and currently intend to do so through collaborations, public or private equity offerings or debt financings, credit or loan facilities or a combination of one or more of these funding sources. If we raise additional funds by issuing equity securities, our stockholders may suffer dilution and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, is likely to involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of our equity securities received any distribution of our corporate assets. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights or jointly own some aspects of our technologies or product candidates that we would otherwise pursue on our own. Risks Related to Our Business We are early in our development efforts. Our business is dependent on the successful development of our product candidates, future product candidates, and companion diagnostics for biomarkers associated with our product candidates and future product candidates. Our current product candidates are in early stages of development and we are further developing our precision medicine target and biomarker discovery platform. We have no products approved for sale and our three most advanced product candidates, IDE397, darovasertib and IDE161, are in the early stages of clinical development and will require additional clinical development, regulatory review and approval in each jurisdiction in which we intend to market them, access to sufficient commercial manufacturing capacity, and significant sales and marketing efforts before we can generate any revenue from product sales ~~. IDE397 is currently being evaluated in an ongoing Phase 1 / 2 clinical trial to evaluate IDE397 for the treatment of patients with MTAP deletion. Darovasertib is currently being evaluated in an ongoing Phase 1 / 2 clinical trial in patients having tumors with GNAQ or GNA11 hotspot mutations, that we initiated in June 2019, including the combination arm with crizotinib that we initiated in December 2020. Darovasertib is also currently being evaluated in an ongoing Phase 1 investigator sponsored clinical trial as a potential neo- adjuvant and / or adjuvant therapy in primary, non- metastatic, uveal melanoma. IDE161 is the subject of an IND for a Phase 1 clinical trial to evaluate IDE161 for the treatment of patients with HRD that has been authorized to proceed by the FDA, and targeting initial dosing of our first patient in the first quarter of 2023~~ . Our other product candidates have not been tested in clinical trials. The success of our business, including our ability to finance our company and generate revenue in the future, will primarily depend on the successful development, regulatory approval and commercialization of our product candidates, which may never occur. In the future, we may also become dependent on other product candidates that we may develop or acquire; however, given our early stage of development, it may be many years, if at all, before we have demonstrated the safety and efficacy of a product candidate sufficient to support approval for commercialization. We have not previously submitted a new drug application, or NDA, to the FDA or similar approval filings to a comparable foreign regulatory authority, for any product candidate. An NDA or other relevant regulatory filing must include extensive preclinical and clinical data and supporting information to establish that the product candidate is safe and effective for each desired indication. The NDA or other relevant regulatory filing must also include significant information regarding the chemistry, manufacturing and controls for the product. We cannot be certain that our current or future product candidates will be successful in clinical trials or receive regulatory approval. Further, even if they are successful in clinical trials, our product candidates or any future product candidates may not receive regulatory approval. If we do not receive regulatory approvals for current or future product candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approval to market a product candidate, our revenue will depend, in part, upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights, as well as the availability of competitive products, whether there is sufficient third- party reimbursement and adoption by physicians. We plan to seek regulatory approval to commercialize our product candidates both in the United States and in select foreign countries. While the scope of regulatory approval generally is similar in other countries, in order to obtain separate regulatory approval in other countries we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy. Other countries also have their own regulations governing, among other things, clinical trials and commercial sales, as well as pricing and distribution of drugs, and we may be

required to expend significant resources to obtain regulatory approval and to comply with ongoing regulations in these jurisdictions. The clinical and commercial success of our current and any future product candidates will depend on a number of factors, including the following: • our ability to raise any additional required capital on acceptable terms, or at all; • our ability to develop and successfully utilize our precision medicine target and biomarker discovery platform; • timely and successful completion of our preclinical studies and clinical trials, which may be significantly slower or cost more than we currently anticipate and will depend substantially upon the performance of third- party contractors; • acceptance of INDs by the FDA, or similar regulatory filing by a comparable foreign regulatory authority for the conduct of clinical trials of our product candidates and our proposed design of future clinical trials; • whether we are required by the FDA or a comparable foreign regulatory agency to conduct additional clinical trials or other studies beyond those planned to support approval of our product candidates; • our ability to timely execute our ongoing clinical trials and enroll a sufficient number of patients on a timely basis ~~, particularly in light of the effects of the COVID- 19 pandemic,~~ to evaluate our product candidates in clinical development; • acceptance of our proposed indications and primary endpoint assessments of our product candidates by the FDA and comparable foreign regulatory authorities; • the availability or successful development of companion diagnostics for biomarkers associated with our product candidates or any other future product candidates; • our ability to make arrangements with third- party manufacturers for, or establish, commercial manufacturing capabilities, and to consistently manufacture our product candidates on a timely basis; • our ability, and the ability of any third parties with whom we contract, to remain in good standing with regulatory agencies and develop, validate and maintain commercially viable manufacturing processes that are compliant with current good manufacturing practices, or cGMPs, or similar foreign requirements; • our ability to demonstrate to the satisfaction of the FDA and comparable foreign regulatory authorities the safety, efficacy and acceptable risk- benefit profile of our product candidates; • the prevalence, duration and severity of potential side effects or other safety issues experienced with our product candidates, either as monotherapy or in combination with other drugs, or future approved products, if any; • the timely receipt of necessary marketing approvals from the FDA and comparable foreign regulatory authorities; • achieving and maintaining, and, where applicable, ensuring that our third- party contractors achieve and maintain, compliance with our contractual obligations and with all regulatory requirements applicable to our current product candidates or any future product candidates or approved products, if any; • the willingness of physicians, operators of hospitals and clinics and patients to use or adopt any approved products, as well as the willingness of physicians and other health- care providers to incorporate molecular diagnostics or genetic sequencing into their clinical practice; • our ability to successfully develop a commercial strategy and thereafter commercialize any approved products in the United States and internationally, whether alone or in collaboration with others; • the availability and level of coverage and adequate reimbursement from managed care plans, private insurers, government payors, such as Medicare and Medicaid, and other third- party payors for any of our product candidates that may be approved; • the convenience of our treatment or dosing regimen; • our ability to compete with other approved therapies, if any; • acceptance by physicians, payors and patients of the benefits, safety and efficacy of our product candidates or any future product candidates, if approved, including relative to alternative and competing treatments; • patient demand for any approved products; • our ability to establish and enforce intellectual property rights in and to our product candidates; and • our ability to avoid third- party patent interference, opposition, derivation, intellectual property challenges, intellectual property infringement claims or similar proceedings with respect to our intellectual property rights. These factors, many of which are beyond our control, could cause us to experience significant delays or an inability to obtain regulatory approvals or commercialize our current or future product candidates. Even if regulatory approvals are obtained, we may never be able to successfully commercialize any products. Accordingly, we cannot provide assurances that we will be able to generate sufficient revenue through the sale of products to continue our business or achieve profitability. In connection with the Collaboration, Option and License Agreement with GSK, if GSK terminates any development program under its collaborations with us, whether as a result of our inability to meet milestones or otherwise, any potential revenue from those collaborations will be significantly reduced or non- existent, and our results of operations and financial condition will be materially and adversely affected. We have invested a significant portion of our time and financial resources in the development of multiple product candidates that are included in our strategic partnership and collaboration with GSK, under the Collaboration, Option and License Agreement entered into on June 15, 2020, or the GSK Collaboration Agreement. The programs currently included in the GSK Collaboration Agreement are the Pol Theta ~~(POLQ)~~ and Werner Helicase (WRN) programs. Under the GSK Collaboration Agreement, we ~~are~~ **will be** eligible to receive from GSK future development and regulatory milestones of up to $ ~~485~~ **475 million for the Pol Theta and $ 482** . 0 million for **the** ~~each POLQ and~~ WRN product, and commercial milestones of up to $ 475 ~~. 0~~ million, with respect to ~~each POLQ~~ **the Pol Theta** and WRN product. Additionally, we are entitled to receive 50 % of U. S. net profits and tiered royalties on global non- U. S. net sales of WRN products by GSK, its affiliates and their sublicensees ranging from high single digit to sub- teen double digit percentages, subject to certain customary reductions. We are entitled to receive tiered royalties on global net sales of ~~POLQ~~ **Pol Theta** products by GSK, its affiliates and their sublicensees ranging from high single digit to sub- teen double digit percentages, subject to certain customary reductions. We have a right to opt- out of the 50 % U. S. net profit share and corresponding development cost share for the WRN program, and would be eligible to receive tiered royalties on U. S. net sales of WRN products by GSK, its affiliates and their sublicensees at the same royalty rates as for global non- U. S. net sales thereafter, with potential positive economic adjustments based on the stage of the WRN program, as applicable, at the time of opt- out. There is no guarantee that we will be able to successfully continue to advance the ~~POLQ~~ **Pol Theta** and WRN programs and receive regulatory filing milestone payments related to any ~~POLQ~~ **Pol Theta** or WRN product. GSK may terminate the entire GSK Collaboration Agreement or any collaboration program on a target- by- target basis for any or no reason upon written notice to us after expiration of a defined notice period. The GSK Collaboration Agreement or any program under the GSK Collaboration Agreement may also be terminated by either party for the other party' s insolvency or certain uncured breaches. We may terminate the GSK Collaboration Agreement if GSK or any of its sublicensees or affiliates challenge certain of our patents.

Depending on the timing of any such termination we may not be entitled to receive the option exercise fees, or potential milestone payments, as these payments terminate with termination of the GSK Collaboration Agreement. If GSK terminates its rights and obligations with respect to a program or the entire GSK Collaboration Agreement, then depending on the timing of such event: • the development of our product candidates subject to the GSK Collaboration Agreement may be terminated or significantly delayed; • our cash expenditures could increase significantly if it is necessary for us to hire additional employees and allocate scarce resources to the development and commercialization of product candidates that were previously funded by GSK; • we would bear all of the risks and costs related to the further development and commercialization of product candidates that were previously the subject of the GSK Collaboration Agreement, including the reimbursement of third parties; and • in order to fund further development and commercialization, we may need to seek out and establish alternative collaboration arrangements with third- party collaboration partners; this may not be possible, or we may not be able to do so on terms which are acceptable to us, in which case it may be necessary for us to limit the size or scope of one or more of our programs or increase our expenditures and seek additional funding by other means. Any of these events would have a material adverse effect on our results of operations and financial condition. As an organization, we have never completed a clinical trial, and may be unable to do so for any of our product candidates. We will need to successfully initiate and complete our own Phase 1 clinical trials and later- stage and pivotal clinical trials in order to obtain FDA or a comparable foreign regulatory body' s approval to market our product candidates. Carrying out clinical trials and the submission of regulatory filings is a complicated process. As an organization, we have not yet completed any clinical trials for any of our product candidates. ~~IDE397 is in a Phase 1 / 2 clinical trial that we are conducting, darovasertib, is in a Phase 1 / 2 clinical trial that we are conducting, and IDE161 is the subject of an IND for a Phase 1 clinical trial that has been authorized to proceed by the FDA, and targeting initial dosing of our first patient in the first quarter of 2023.~~ We have limited experience in preparing, submitting and prosecuting regulatory filings, and have not previously submitted any NDA or other comparable foreign regulatory submission for any product candidate. In addition, we have had limited interactions with the FDA and cannot be certain how many additional clinical trials of darovasertib, IDE397 or IDE161 or how many clinical trials of any of our other product candidates will be required or whether the FDA will agree with the design or implementation of our clinical trials. We are required to comply with certain regulatory requirements, and the FDA may identify specific clinical or other development- related requirements that we must satisfy, as a condition to initiating or continuing our clinical trials; if we fail to meet such a requirement, the FDA may issue a clinical hold or designate other conditions on our clinical trials. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to regulatory submission of a marketing application for, and approval of, darovasertib, IDE397, IDE161, or any of our other product candidates. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing darovasertib, IDE397, IDE161, or any other product candidate. The successful development of targeted therapeutics, including therapeutics involving direct targeting of an oncogenic pathway and synthetic lethality therapeutics, including our portfolio of synthetic lethality small molecule inhibitors, as well as any related diagnostics, is highly uncertain. Successful development of targeted therapeutics, including therapeutics involving direct targeting oncogenic pathways and synthetic lethality therapeutics, such as our portfolio of synthetic lethality small molecule inhibitors, as well as any related diagnostics, is highly uncertain and is dependent on numerous factors, many of which are beyond our control. Our precision medicine target and biomarker discovery platform is based on new technologies and methods relating to drug target and biomarker identification, screening and validation, including Dual CRISPR genetic screening and bioinformatics and we have not, to date, sought regulatory approval for any therapeutics developed through our precision medicine target and biomarker discovery platform. As such, it is difficult to accurately predict the developmental challenges we or our collaboration partners may incur for our current and future product candidates as we proceed through product discovery, identification, preclinical studies and clinical trials. Our precision medicine target and biomarker discovery platform is novel and may not be effective at identifying targets and / or biomarkers for product candidates. We therefore cannot provide any assurance that we will be able to successfully identify additional product candidates or biomarkers, advance any of these additional product candidates or diagnostics for their associated biomarkers through the development process. Additionally, particular patient genetic alterations, such as mutations, deletions or fusions may not be functionally active genetic drivers of the disease. Further, whether a genetic alteration is functionally active may be difficult to ascertain from preclinical cancer models, may be tissue- type dependent and may vary from patient to patient within a specific indication. If that was the case, we would need to functionally validate such genetic alterations, for example, using in vitro and in vivo models, potentially across more than one tumor- tissue type and across multiple cell lines. If some of the genetic alterations are not functionally validated, this would reduce the size of our addressable patient population. Even if genetic alterations are preclinically validated, the relevance of these alterations may not translate into a human clinical setting, which could adversely impact our clinical trial results and our commercial opportunities. Targeted therapeutics that appear promising in the early phases of development may fail to reach the market for several reasons, including: • research or preclinical studies may show our targeted small molecule inhibitors or antagonists to be less effective than desired or to have harmful or problematic side effects or toxicities; • failure to accurately identify, validate or develop clinically relevant biomarkers for our targeted therapeutic product candidates; • clinical trial results may show our targeted therapeutic small molecule inhibitors to be less effective than expected based on preclinical studies (e. g., a clinical trial could fail to meet its primary endpoint (s)) or to have unacceptable side effects or toxicities; • failure to receive the necessary regulatory approvals or a delay in receiving such approvals. Among other things, such delays may be caused by slow enrollment in clinical trials, patients dropping out of trials, length of time to achieve trial endpoints, additional time requirements for data analysis, IND preparation, discussions with the FDA or similar foreign regulatory authorities, an FDA or similar foreign regulatory authority request for additional preclinical or clinical data, or unexpected safety or manufacturing issues; • manufacturing costs,

formulation issues, pricing or reimbursement issues, or other factors that may make our targeted therapeutic small molecule inhibitors uneconomical; and • proprietary rights of others and their competing products and technologies that may prevent our targeted therapeutic small molecule inhibitors, or the diagnostics for biomarkers associated with such small molecule inhibitors, from being commercialized. As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our precision medicine target and biomarker discovery platform will result in the identification, development, and regulatory approval of any products. The length of time necessary to complete clinical trials and to submit an application for marketing approval for a decision by a regulatory authority may be difficult to predict for targeted therapeutic small molecule inhibitors, in large part because of the limited regulatory history associated with them. The clinical trial requirements of the FDA and other comparable foreign regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the product candidate. Except for certain PARP inhibitors, no products based on synthetic lethality have been approved to date by regulators. As a result, the regulatory approval process for product candidates such as ours is uncertain and may be more expensive and take longer than the approval process for product candidates based on other, better known or more extensively studied technologies. It is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either the United States or other comparable regions of the world or how long it will take to commercialize our product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product candidate to market would adversely affect our business, financial condition, results of operations and prospects. Even if we are successful in obtaining regulatory approval, commercial success of any approved products will also depend in large part on the availability of insurance coverage and adequate reimbursement from third- party payors, including government payors, such as the Medicare and Medicaid programs, and managed care organizations, which may be affected by existing and future healthcare reform measures designed to reduce the cost of healthcare. Third- party payors could require us to conduct additional studies, including post-marketing studies related to the cost- effectiveness of a product, to qualify for reimbursement, which could be costly and divert our resources. If government and other healthcare payors were not to provide adequate insurance coverage and reimbursement levels for one any of our products once approved, market acceptance and commercial success would be limited. In addition, if any of our products is approved for marketing, we will be subject to significant regulatory obligations regarding the submission of safety and other post- marketing information and reports and registration, and will need to continue to comply (or ensure that our third- party providers comply) with cGMPs, or similar applicable foreign requirements and GCPs for any clinical trials that we conduct post- approval. In addition, there is always the risk that we or a regulatory authority might identify previously unknown problems with a product post- approval, such as adverse events, or AEs, of unanticipated severity or frequency. Compliance with these requirements is costly and any failure to comply or other post- approval issues with our product candidates could have a material adverse effect on our business, financial condition, results of operations and prospects. Preclinical and clinical drug development is a lengthy and expensive process with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any product candidates, which could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our business, financial condition, results of operations and prospects. Furthermore, results of earlier studies and trials may not be predictive of future trial results. Before we can initiate clinical trials for our product candidates, we must submit the results of preclinical studies to the FDA or a comparable foreign regulatory authority along with other information, including information about product candidate chemistry, manufacturing and controls, diagnostics for biomarkers for our product candidates and our proposed clinical trial protocol, as part of an IND application or similar regulatory filing. Before obtaining marketing approval from regulatory authorities for the sale of any products, we, or our collaboration partners must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Clinical trials are expensive and can take many years to complete, and their outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. In addition, we may rely in part on preclinical, clinical and quality data generated by contract research organizations, or CROs, and other third parties for regulatory submissions for our product candidates. While we have or will have agreements governing these third parties' services, we have limited influence over their actual performance. Further, pursuant to our license agreement with Novartis, we have a right of reference to certain data from Novartis' Phase 1 clinical trial data for our regulatory filings for darovasertib. If these third parties, including Novartis, fail to make data available to us, or, if applicable, make regulatory submissions in a timely manner, in each case pursuant to our agreements with them, our development programs may be significantly delayed and we may need to conduct additional studies or trials or collect additional data independently. In either case, our development costs would increase. Our clinical trial collaboration and supply agreements with Pfizer **, Amgen and Gilead** for the supply of crizotinib **, AMG 193 and Trodelvy, respectively** , support our plans to evaluate the safety and efficacy of darovasertib in combination with crizotinib **, IDE397 in combination with AMG 193, and IDE397 in combination with Trodelvy** . If ~~Pfizer~~ **any of these strategic collaborators** ~~delays~~ **delay** or ~~fails~~ **fail** to supply ~~crizotinib~~ **their compound** in support of ~~the~~ **these** combination ~~arms of~~ **trials, fail to sponsor or appropriately conduct** the **combination** ~~darovasertib clinical~~ trial **(in the case of Amgen),** or we fail to reach an agreement with ~~Pfizer~~ **any of these strategic collaborators** for the continued supply of ~~crizotinib~~ **their compound** beyond the terms of the current ~~clinical trial collaboration and~~ supply agreements, the development ~~program~~ **programs** as pertaining to **these** ~~combination~~ **combinations** ~~of darovasertib with a cMET inhibitor may be significantly delayed, and our development costs may increase. Subject to completion of and satisfactory results from preclinical studies, we may evaluate darovasertib in combination with one or more anti- cancer agent (s) in addition to crizotinib, such as a different inhibitor of cMET or an inhibitor of FAK, mTOR and / or CDK4 / 6, in a Phase 1 / 2 clinical trial in patients with metastatic uveal melanoma. Additionally, our clinical trial collaboration and supply agreement with Amgen for the clinical combination of IDE397 and AMG 193, supports our plans to evaluate the~~

~~safety and efficacy of the two compounds. If Amgen delays or fails to supply AMG 193 or to sponsor the combination arm of the IDE397 / AMG 193 clinical trial, the development program as pertaining to the combination~~ may be significantly delayed, and our development costs may increase. In each case, this may require us to establish additional supply agreements and rely upon third parties for supply of such combination agents, or if such combination agents are commercially available, in the absence of a supply agreement, we may incur the cost of purchasing such combination agents and may be at risk of having insufficient supply. We may initiate clinical trials in which our product candidates, including darovasertib, IDE397 or IDE161, are combined with one or more other pharmaceutical agents that have not yet been approved by the FDA or comparable foreign regulatory authorities; in such situations, we may be relying on third parties for obtaining appropriate regulatory approvals and we may have no or limited influence over whether or not such regulatory approvals are achieved for such combination agents. We and our strategic collaborators also may experience numerous unforeseen events during, or as a result of, any preclinical studies or clinical trials that could delay or prevent us or our strategic collaborators from successfully developing our product candidates, including: • we may be unable to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation of clinical trials; • the FDA or a comparable foreign regulatory authority disagreeing as to the design or implementation of our clinical trials; • delays in obtaining regulatory authorization to commence a clinical trial; • reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites; • obtaining IRB or ethics committee approval or positive opinion at each clinical trial site; • recruiting an adequate number of suitable patients to participate in a clinical trial, particularly **if any public health outbreak, epidemic or** ~~in light of the potential impact of the COVID- 19~~ pandemic **leads to** ~~on patient enrollment and~~ clinical site closures; • having patients complete a clinical trial or return for post-treatment follow- up; • clinical sites deviating from clinical trial protocol or dropping out of a clinical trial; • addressing subject safety concerns that arise during the course of a clinical trial; • adding a sufficient number of clinical trial sites; • obtaining sufficient quantities of product candidate for use in preclinical studies or clinical trials from third- party suppliers; or • accessing third- party products or product candidates for use in combination with our product candidates in preclinical studies or clinical trials, including third- party product candidates that have not yet been approved by the FDA or comparable foreign regulatory authorities. We and our strategic collaborators may experience numerous adverse or unforeseen events during, or as a result of, preclinical studies and clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including: • we may receive feedback from regulatory authorities that requires us to modify the design of our clinical trials; • clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon our development programs; • the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate; • we or our third- party contractors may fail to comply with regulatory requirements, fail to maintain adequate quality controls, or be unable to produce sufficient product supply to conduct and complete preclinical studies or clinical trials of our product candidates in a timely manner, or at all; • we or our investigators might have to suspend or terminate clinical trials of our product candidates for various reasons, including non- compliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics, or a finding that the participants are being exposed to unacceptable health risks; • the cost of clinical trials of our product candidates may be greater than we anticipate; • the quality of our product candidates or other materials necessary to conduct preclinical studies or clinical trials of our product candidates may be insufficient or inadequate; • regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and • collaborators may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us. If we or our strategic collaborators are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only moderately positive or if there are safety concerns, we may: • incur unplanned costs; • be delayed in obtaining marketing approval for our product candidates or not obtain marketing approval at all; • obtain marketing approval in some countries and not in others; • obtain marketing approval for indications or patient populations that are not as broad as intended or desired; • obtain marketing approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings; • be subject to additional post- marketing testing requirements, which could be expensive and time- consuming; or • have the treatment removed from the market after obtaining marketing approval. We and our strategic collaborators could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or another comparable foreign regulatory authority. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs or other foreign regulatory authorities or ethics committees for reexamination, which may impact the costs, timing or successful completion of a clinical trial. For example, in recent years the FDA has issued draft guidance and launched programs aiming to reform and modernize the dose optimization procedures used by clinical trial sponsors during the development of oncology drugs. Although these efforts have not yet resulted in any formal changes to the FDA' s regulations or policies, changes in the FDA' s thinking with respect to dose selection and optimization could require us to change the design of our planned or ongoing clinical trials or otherwise conduct additional preclinical, clinical or manufacturing studies beyond those

we currently anticipate, which could increase our costs and / or delay the development of our product candidates. As another example, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the **EU** Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application for multi- center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state' s decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR foresees a three- year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the **EU** Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the EU Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third- party service providers, such as CROs, may impact our developments plans. Further, conducting clinical trials in foreign countries, as we may do for certain of our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the possibility that we could be required to conduct additional preclinical studies before initiating any clinical trials, the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with comparable foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries. Principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or a regulatory authority concludes that the financial relationship may have affected the interpretation of the clinical trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of the marketing application we submit. Any such delay or rejection could prevent or delay us from commercializing our current or future product candidates. If any of our preclinical studies or clinical trials of our product candidates are delayed or terminated, the commercial prospects of our product candidates may be harmed, and our ability to ultimately generate revenues from any of these product candidates will be delayed or not realized at all. In addition, any delays in completing our clinical trials may increase our costs, slow down our product candidate development and regulatory approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may significantly harm our business, financial condition, results of operations and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. If our product candidates and any future product candidates prove to be ineffective, unsafe or commercially unviable, our entire platform and approach would have little, if any, value, which would have a material adverse effect on our business, financial condition, results of operations and prospects. Furthermore, the results of preclinical studies and clinical trials of our product candidates may not be predictive of the results of later- stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy despite having progressed through preclinical studies and initial clinical trials. Furthermore, for some of our programs, in the future we intend to conduct basket trials, which will be designed to include multiple clinically defined populations under one investigational protocol, although each population is enrolled and analyzed separately. A basket trial design could potentially decrease the time to study new populations by decreasing administrative burden, however, these trials may not provide opportunities for accelerated regulatory pathways, and do not overcome limitations to extrapolating data from the experience in one disease to other diseases, because safety and efficacy results in each indication are analyzed separately. Accordingly, clinical success in a basket trial, or any trial in one indication, may not predict success in another indication. In contrast, in the event of an adverse safety issue, clinical hold, or other adverse finding in one or more indications being tested, such event could adversely affect our trials in the other indications and may delay or prevent completion of the clinical trials. A number of companies in the pharmaceutical, biopharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials for similar indications that we are pursuing due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies, and we cannot be certain that we will not face similar setbacks. Even if our clinical trials are completed, the results may not be sufficient to obtain regulatory approval of any products. Synthetic lethality represents an emerging class of precision medicine targets, and negative perceptions of the efficacy, safety or tolerability of this class of targets, including any that we develop, could adversely affect our ability to conduct our business, advance our product candidates or obtain regulatory approvals. Aside from PARP inhibitors, such as Lynparza, Rubraca, Zejula and Talzenna, no synthetic lethality small molecule inhibitor therapeutics have been approved to date by the FDA or other comparable regulators. AEs in future clinical trials of our product candidates or in clinical trials of others developing similar products and the resulting publicity, as well as any other AEs in the field of synthetic lethality, or other products that are perceived to be similar to synthetic lethality, such as those related to gene therapy or gene editing, could result in a decrease in the perceived benefit of one or more of our programs, increased regulatory scrutiny, decreased confidence by patients and CROs in our product candidates, and less demand for any product that we may develop. Our substantial pipeline of synthetic lethality small molecule inhibitor product candidates could result in a greater quantity of reportable AEs or other reportable negative clinical outcomes, manufacturing reportable events or material clinical events that could lead to clinical delays or holds by the FDA or applicable regulatory authority or other clinical delays,

any of which could negatively impact the perception of one or more of our synthetic lethality programs, as well as our business as a whole. In addition, responses by U. S. federal, state or foreign governments to negative public perception may result in new legislation or regulations that could limit our ability to develop any product candidates or commercialize any approved products, obtain or maintain regulatory approval, or otherwise achieve profitability. More restrictive statutory regimes, government regulations, or negative public opinion would have an adverse effect on our business, financial condition, results of operations, and prospects, and may delay or impair the development of our product candidates and commercialization of any approved products or demand for any products we may develop. Tissue- type agnostic basket trials are an emerging clinical approach that may result in delays in clinical development, additional regulatory requirements and delays in, or the prevention of, our ability to obtain regulatory approval or commercialize our product candidates. We initiated a Phase 1 / 2 tissue- type agnostic basket trial with darovasertib in June 2019, and may also utilize a basket trial approach in clinical trials for other product candidates. Basket trials allow us to evaluate the safety and efficacy of a product candidate in a variety of tumor types with a specific molecular profile. We believe that this clinical approach provides many benefits, however, there are limited precedents, and as a result, there a number of inherent risks. There is limited precedent for the FDA and foreign regulatory authorities to review and grant tissue- type agnostic approvals. Furthermore, as clinical trials increasingly use classification of tumors by molecular profiling, the FDA or other regulatory authority may change or issue guidance or adopt a policy that adversely affects requirements for basket trials. In the event that such guidance or policy has an effect on any of our protocols or trials, as the case may be, it may result in the delay of clinical development, or require us to conduct additional preclinical studies or clinical trials. Even if we obtain a tissue- type agnostic approval for one or more of our product candidates, there is limited precedent for obtaining reimbursement. Third- party payors may reimburse at different levels across tumor tissue types and indicates, or not at all. We may find it difficult to enroll patients in our clinical trials given the limited number of patients who have the diseases for which our product candidates are being developed. If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our and our collaboration partners' ability to enroll a sufficient number of patients who remain in the clinical trial until its conclusion. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The enrollment of patients depends on many factors, including: • the patient eligibility and exclusion criteria defined in the protocol; • the size and nature of the patient population required for analysis of the clinical trial' s primary endpoints; • the proximity of patients to clinical trial sites; • the design of the clinical trial; • the risk that enrolled patients will not complete a clinical trial; • our ability to recruit clinical trial investigators with the appropriate competencies and experience; • clinical trial investigators' willingness to continue enrolling patients and patients ~~'~~ **'** willingness to complete protocol assessments during ~~the COVID- 19~~ **any public health outbreak, epidemic or** pandemic; • clinicians' and patients' perceptions as to the safety of the product candidate; • clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new therapies that may be approved for the indications we are investigating as well as any drugs under development; and • our ability to obtain and maintain patient consents. We will be required to identify and enroll a sufficient number of patients for each of our clinical trials. Potential patients for any planned clinical trials may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for such trials. We also may encounter difficulties in identifying and enrolling patients with a stage of disease appropriate for our planned clinical trials and monitoring such patients adequately during and after treatment. We may not be able to initiate or continue clinical trials if we are unable to locate a sufficient number of eligible patients to participate in the clinical trials required by the FDA or a comparable foreign regulatory authority. In addition, the process of finding and diagnosing patients may prove costly. In addition, our clinical trials may compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. As a result of **any public health outbreak** ~~the COVID- 19 pandemic~~ , competition for potential patients in our trials ~~is~~ **may be** further exacerbated as a result of ~~multiple~~ **any** clinical site closures. Since the number of qualified clinical investigators is already limited, we may conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site. Furthermore, certain conditions for which we plan to evaluate our current development candidates are rare diseases, such as metastatic uveal melanoma, with limited patient pools from which to draw for clinical trials. For example, one of our product candidates, darovasertib, is currently being evaluated in a Phase 1 / 2 basket trial that we initiated in June 2019 to evaluate darovasertib in solid tumors harboring GNAQ / GNA11 hotspot mutations in metastatic uveal melanoma. The timing of our clinical trials depends, in part, on the speed at which we can recruit patients to participate in our trials, as well as completion of required follow- up periods. The eligibility criteria of our clinical trials, once established, will further limit the pool of available trial participants. In addition, our clinical trials may be affected by **any public health outbreak, epidemic or pandemic. Clinical site initiation and patient enrollment may be delayed. For example, as a result of** the COVID- 19 pandemic **,** ~~. Clinical site initiation and patient enrollment may be delayed. Several~~ **several** of our sites halted new enrollment for several months in 2020 before resuming enrollment. Some patients may not be able or willing to comply with clinical trial protocols, and data collected may be incomplete, if quarantines impede patient movement or interrupt healthcare services. Similarly, the ability to recruit and retain patients, and principal investigators and site staff who, as healthcare providers, may have heightened exposure to **infectious diseases** ~~COVID- 19~~ , may be delayed or disrupted, which may adversely impact our clinical trial operations. If patients are unwilling to participate in our clinical trials for any reason, including the existence of other approved therapies or concurrent clinical trials for similar patient populations, if they are unwilling to enroll in a clinical trial with a placebo- controlled design, or we otherwise have difficulty enrolling a sufficient number of patients, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of our product candidates may be delayed. Our

inability to enroll a sufficient number of patients for any of our future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. In addition, we expect to rely on CROs and clinical trial sites to ensure proper and timely conduct of our future clinical trials and, while we intend to enter into agreements governing their services, we will have limited influence over their actual performance. We cannot assure you that we will not experience delays in enrollment, which would result in the delay of completion of such trials beyond our expected timelines. Our product candidates or any future product candidates may be associated with undesirable side effects or AEs that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any. As with most pharmaceutical products, use of our product candidates could be associated with side effects or AEs which can vary in severity from minor reactions to death and in frequency from infrequent to prevalent. Undesirable side effects or unacceptable toxicities caused by our product candidates 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 a comparable foreign regulatory authority. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of these or other side effects. Furthermore, certain of our product candidates may be co- administered with third-party approved or experimental therapies, such as darovasertib with crizotinib in the combination arms of our Phase 1 / 2 clinical trial or IDE397 with ~~Pemetrexed or~~ PRMT5 inhibitors in the combination arms of our Phase 1 / 2 clinical trial. These combinations may have additional side effects. The uncertainty resulting from the use of our product candidates in combination with other therapies may make it difficult to accurately predict side effects in future clinical trials. To date, only ~~two~~ **three** of our product candidates, IDE397 ~~and ,~~ darovasertib, **and IDE161** have been tested in clinical trials ~~, including an ongoing Phase 1 / 2 clinical trial of IDE397 and an ongoing Phase 1 / 2 clinical trial of darovasertib~~ , and they have been observed to be generally well tolerated, with certain drug- related SAEs and AEs being reported for darovasertib, as monotherapy and in combination with crizotinib **, for IDE397, and for IDE161** . If unacceptable side effects arise in the further development of darovasertib, including in combination with crizotinib, in the further development of IDE397, including in combination with ~~Pemetrexed, texanes or~~ PRMT5 inhibitors, in the further development of IDE161, or in the development of any of our other product candidates, we, the FDA or comparable foreign regulatory authorities, or the IRBs at the institutions in which the clinical trials are being conducted could suspend or terminate our clinical trials or the FDA or a comparable foreign regulatory authority could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete any of our clinical trials or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition, results of operations and prospects significantly. In addition, even if we successfully advance our product candidates or any future product candidates into and through clinical trials, such trials will likely only include a limited number of patients and limited duration of exposure to our product candidates. As a result, we cannot be assured that adverse effects of our product candidates will not be uncovered when a significantly larger number of patients are exposed to the product candidate. Further, any clinical trials may not be sufficient to determine the effect and safety consequences of taking our product candidates over a multi- year period. If any of our product candidates receives marketing approval and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including: • regulatory authorities may withdraw their approval of the product; • we may be required to recall a product or change the way such product is administered to patients; • additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof; • regulatory authorities may require the addition of labeling statements, such as a " black box " warning or a contraindication; • we may be required to implement a Risk Evaluation and Mitigation Strategy, or REMS, or create a Medication Guide outlining the risks of such side effects for distribution to patients or similar risk management measures; • we could be sued and held liable for harm caused to patients; • the product may become less competitive; and • our reputation may suffer. Any of the foregoing events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and result in the loss of significant revenues to us, which would adversely affect our business, financial condition, results of operations and prospects. In addition, if one or more of our product candidates prove to be unsafe, our entire technology platform and pipeline could be affected, which would have a material adverse effect on our business, financial condition, results of operations and prospects. If we are unable to successfully develop molecular diagnostics for biomarkers that enable patient selection and / or that demonstrate drug- target interaction, or experience significant delays in doing so, we may not realize the full commercial potential of our product candidates. A key component of our strategy includes the use of molecular diagnostics to guide patient selection and / or to confirm target engagement of our product candidates. In some cases, a diagnostic may be commercially available, for example, on a tumor- profiling panel. If not already commercially available, we may collaborate with diagnostic companies for the development of biomarkers associated with our product candidates. We may have difficulty in establishing or maintaining such development relationships, and we will face competition from other companies in establishing these collaborations. There are also several risks associated with biomarker identification and validation. We, in collaboration with any diagnostic partners, may not be able to identify predictive biomarkers or pharmacodynamic biomarkers for one or more of our programs. We may not be able to validate potential biomarkers (e. g., certain genetic mutations) or their functional relevance preclinically in relevant in vitro or in vivo models. Data analytics and information from databases that we rely on for identifying or validating some of our biomarker- target relationships may not accurately reflect potential patient populations. Potential biomarkers, even if validated preclinically, may not be functionally effective or validated in human clinical trials. If we, in collaboration with these parties, are unable to successfully develop companion diagnostics for our product candidates, or

experience delays in doing so, the development of our product candidates may be adversely affected. The development of companion diagnostic products requires a significant investment of working capital, and may not result in any future income. This could require us to raise additional funds, which could dilute our current investors or impact our ability to continue our operations in the future. There are also risks associated with diagnostics that are commercially available, including that we may not have access to reliable supply for such diagnostics. The failure to obtain required regulatory approvals or certification for any companion diagnostic tests that we may pursue may prevent or delay approval of our product candidates. Moreover, the commercial success of any of our product candidates may be tied to the regulatory approval or certification, market acceptance and continued availability of a companion diagnostic. The FDA regulates in vitro companion diagnostics as medical devices that will likely be subject to and require prospective validation in clinical trials in conjunction with the clinical trials for our product candidates, and which will require regulatory clearance or approval prior to commercialization. We plan to collaborate with third parties for the development, testing and manufacturing of these companion diagnostics, the application for and receipt of any required regulatory clearances or approvals, and the commercial supply of these companion diagnostics. Our third- party collaborators may fail to obtain the required regulatory clearances or approvals, which could prevent or delay approval of our product candidates. In addition, the commercial success of any of our product candidates may be tied to and dependent upon the receipt of required regulatory clearances or approvals of the companion diagnostic. Even if a companion diagnostic is approved, we will rely on the continued ability of any third- party collaborator to make the companion diagnostic commercially available to us on reasonable terms in the relevant geographies. Furthermore, if commercial tumor profiling panels are not able to be updated to include additional tumor- associated genes, or if clinical oncologists do not incorporate molecular or genetic sequencing into their clinical practice, we may not be successful in developing or commercializing our existing product candidates or any future product candidates. Further, approval, clearance or certification of companion diagnostics may be subject to further legislative or regulatory reforms notably in the EU. On May 25, 2017, the new In Vitro Medical Devices Regulation, or IVDR, entered into force. The IVDR repeals and replaces the EU In Vitro Diagnostic Medical Devices Directive. Unlike directives, which must be implemented into the national laws of the EU member states, regulations are directly applicable, i. e., without the need for adoption of EU member states laws implementing them, in all EU member states and are intended to eliminate current differences in the regulation of medical devices among EU member states. The IVDR, among other things, is intended to establish a uniform, transparent, predictable and sustainable regulatory framework across the EU for in vitro diagnostic medical devices and ensure a high level of safety and health while supporting innovation. The IVDR became applicable on May 26, 2022. However **,** on October 14, 2021, the European Commission had proposed a " progressive " roll- out of the IVDR to prevent disruption in the supply of in vitro diagnostic medical devices. Therefore, the IVDR applies since May 26, 2022 but there is a tiered system extending the grace period for many in vitro diagnostic medical devices (depending on their risk classification) before they have to be fully compliant with the ~~regulation~~ **Regulation** . The regulation of companion diagnostics is subject to further requirements since the IVDR became applicable as it introduced a new classification system for companion diagnostics which are now specifically defined as diagnostic tests that support the safe and effective use of a specific medicinal product, by identifying patients that are suitable or unsuitable for treatment. Companion diagnostics will have to undergo a conformity assessment by a notified body. Before it can issue an EU certificate, the notified body must seek a scientific opinion from the EMA on the suitability of the companion diagnostic to the medicinal product concerned if the medicinal product falls exclusively within the scope of the centralized procedure for the authorization of medicines, or the medicinal product is already authorized through the centralized procedure, or a marketing authorization application for the medicinal product has been submitted through the centralized procedure. For other substances, the notified body can seek the opinion from a national competent authorities or the EMA. These modifications may make it more difficult and costly for us to obtain regulatory clearances, approvals or certifications for our companion diagnostics or to manufacture, market or distribute our products after clearance, approval or certification is obtained. Interim, " topline " and preliminary data from our clinical trials may differ materially from the final data. From time to time, we may publicly disclose preliminary or " topline " data from our clinical trials, which are based on a preliminary analysis of then- available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same clinical trials, or different conclusions or considerations may qualify such topline results, once additional data have been received and fully evaluated. Topline 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, topline data should be viewed with caution until the final data ~~are~~ **is** available. From time to time, we may also disclose interim data from our clinical trials. Interim data from clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business, financial condition, results of operations and prospects. Others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and the value of our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is typically a summary of extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product, product candidate or our business. If the topline data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates

may be harmed, which could harm our business, financial condition, operating results and prospects. We may be unable to obtain regulatory approval for our product candidates or any future product candidates. The denial or delay of such approval would prevent or delay commercialization of our product candidates and adversely impact our business, financial condition, operating results and prospects. The process of obtaining regulatory approval is expensive, often takes many years following the commencement of clinical trials and can vary substantially based upon the type, complexity and novelty of the product candidates involved, as well as the target indications and patient population. Approval policies or regulations may change, and the FDA or comparable foreign regulatory authorities have substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed. Neither we nor any collaborator or any future collaborator, is permitted to market any of our product candidates in the United States or abroad until we receive approval of an NDA from the FDA or similar regulatory approvals from comparable foreign regulatory authorities. Prior to obtaining approval to commercialize a product candidate in the United States, we or our collaborators must demonstrate with substantial evidence from adequate and well- controlled clinical trials, and to the satisfaction of the FDA, that such product candidates are safe and effective for their intended uses. Foreign regulatory authorities may require a similar demonstration before we can obtain approval to commercialize a product candidate abroad. Results from preclinical studies and clinical trials can be interpreted in different ways. Even if we believe the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA or comparable foreign regulatory authorities. The FDA or a comparable foreign regulatory authority, as the case may be, may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post- approval, or may object to elements of our clinical development program. The FDA or a comparable foreign regulatory authority can delay, limit or deny approval of a product candidate for many reasons, including: • such authorities may disagree with the design or implementation of our clinical trials; • negative or ambiguous results from our clinical trials, or results may not meet the level of statistical significance required by the FDA or a comparable foreign regulatory agency for approval; • serious and unexpected drug- related side effects may be experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates; • the population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval; • such authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the United States; • we are unable to demonstrate that a product candidate' s clinical and other benefits outweigh its safety risks; • the FDA' s or the applicable comparable foreign regulatory agency' s non-approval of the formulation, labeling or specifications of our product candidates or any of our future product candidates; • such authorities may disagree with our interpretation of data from preclinical studies or clinical trials; • such authorities could question the integrity of data obtained in our current or future clinical trials, for example, due to missed protocol procedures ~~due to the impact of the COVID- 19 pandemic~~ ; • such authorities may not agree that the data collected from clinical trials of our product candidates are acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere, and such authorities may impose requirements for additional preclinical studies or clinical trials; • such authorities may disagree regarding the formulation, labeling and / or the specifications of our product candidates; • such authorities may only approve indications that are significantly more limited than what we apply for and / or with other significant restrictions on distribution and use; • such authorities may find deficiencies in the manufacturing processes or facilities of our third- party manufacturers with which we or any of our collaborators or any potential future collaborators, contract for clinical and commercial supplies; and • the approval policies or regulations of such authorities may significantly change in a manner rendering our or any of our collaborators' clinical data insufficient for approval. With respect to foreign markets, approval procedures vary among countries and, in addition to the foregoing risks, may involve additional product testing, administrative review periods and agreements with pricing authorities. In addition, events raising questions about the safety of certain marketed pharmaceuticals may result in increased cautiousness by the FDA and comparable foreign regulatory authorities in reviewing new drugs based on safety, efficacy or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us or any of our collaborators or any potential future collaborators, from commercializing any products. Of the large number of drugs in development, only a small percentage successfully complete the FDA or comparable foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects. Even if we eventually complete clinical trials and receive approval of an NDA or foreign marketing application for a product, the FDA or a comparable foreign regulatory authority may grant approval contingent on the performance of costly additional clinical trials, including Phase 4 clinical trials, and / or the implementation of a REMS, which may be required to ensure safe use of the drug after approval. The FDA or a comparable foreign regulatory authority also may approve a product candidate for a more limited indication or patient population than we originally requested, and the FDA or a comparable foreign regulatory authority may not approve the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects. We may develop our product candidates and future product candidates in combination with other therapies, and safety or supply issues with combination- use products may delay or prevent development and approval of our product candidates. We may develop our product candidates in combination with one or more cancer therapies, both approved and unapproved. Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or similar regulatory authorities outside of the United States could revoke approval of the therapy used in combination with our

product candidates or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies. Combination therapies are commonly used for the treatment of cancer, and we would be subject to similar risks if we develop any of our product candidates for use in combination with other drugs or for indications other than cancer. Similarly, if the therapies we use in combination with our product candidates are replaced as the standard of care for the indications we choose for any of our product candidates, the FDA or similar regulatory authorities outside of the United States may require us to conduct additional clinical trials. The occurrence of any of these risks could result in our own products, if approved, being removed from the market or being less successful commercially. We may also evaluate our product candidates in combination with one or more cancer therapies that have not yet been approved for marketing by the FDA or a similar regulatory authority outside of the United States. We may be unable to effectively identify and collaborate with third parties for the evaluation of our product candidates in combination with their therapies. We will not be able to market and sell any product candidate we develop in combination with any such unapproved cancer therapies that do not ultimately obtain marketing approval. The regulations prohibiting the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA and other foreign government agencies. In addition, there are additional risks similar to the ones described for our products currently in development and clinical trials that result from the fact that such cancer therapies are unapproved, such as the potential for serious adverse effects, delay in their clinical trials and lack of FDA or comparable foreign regulatory authorities approval. If the FDA or a similar regulatory authority outside of the United States does not approve these other drugs or revokes approval of, or if safety, efficacy, manufacturing, or supply issues arise with, the drugs we choose to evaluate in combination with any product candidate we develop, we may be unable to obtain approval of or market such product. Although we may apply for orphan drug designation for our product candidates, we may not receive the designation or we may be unable to obtain the benefits associated with such designation, including the potential for marketing exclusivity Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. In the United States, 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 in the United States, or a patient population greater than 200, 000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding, tax credits for certain clinical trial costs and user- fee waivers. If a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same drug and indication for seven years, except in limited circumstances. In the EU, the European Commission grants orphan designation on the basis of the EMA' s Committee for Orphan Medicinal Products opinion. A medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life- threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10, 000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment, of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. In the EU, orphan designation entitles a party to financial incentives such as reduction of fees or fee waivers, protocol assistance, and access to the centralized marketing authorization procedure. Moreover, upon grant of a marketing authorization and assuming the requirement for orphan designation are also met at the time the marketing authorization is granted, orphan medicinal products are entitled to a ten- year period of market exclusivity for the approved therapeutic indication. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed Pediatric Investigation Plan, or PIP. Although we may apply for orphan drug designation for our product candidates, we may not receive the designation we apply for. Even if we received orphan drug designation for one or more of our product candidates, which we have received for darovasertib in uveal melanoma, there is no guarantee that we will obtain approval or orphan drug exclusivity for the product. Even if we obtain approval and orphan drug exclusivity for any of our product candidates, that exclusivity may not effectively protect the product candidate from competition because different therapies can be approved for the same condition and the same therapy could be approved for different conditions. 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 provide greater safety, greater effectiveness or a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. In the EU, during the exclusivity period, marketing authorizations may be granted to a similar medicinal product with the same orphan indication if: (i) the applicant can establish that the second medicinal product, although similar to the orphan medicinal product already authorized is safer, more effective or otherwise clinically superior to the orphan medicinal product already authorized; (ii) the marketing authorization holder for the orphan medicinal product grants its consent; or (iii) if the marketing authorization holder of the orphan medicinal product is unable to supply sufficient quantities of product. The European exclusivity period can be reduced to six years, if, at the end of the fifth year a drug no longer meets the criteria for orphan drug designation (i. e. the prevalence of the condition has increased above the orphan designation threshold or it is judged that the product is sufficiently profitable so as not to justify maintenance of market exclusivity). 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 may seek additional orphan drug designations for applicable indications for our current and any future product candidates, we may never receive such designations. Even if we do receive such designations, there is no

guarantee that we will enjoy the benefits of those designations. We may seek and fail to obtain fast track or breakthrough therapy designations for our current or future product candidates. Even if we are successful, these programs may not lead to a faster development or regulatory review process, and they do not guarantee we will receive approval for any product candidate. If a product is intended for the treatment of a serious or life- threatening condition and preclinical or clinical data demonstrate the potential to address an unmet medical need for this condition, the product sponsor may apply for fast track designation. The sponsor of a fast track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the product candidate may be eligible for priority review. A fast track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted. The FDA has broad discretion whether or not to grant fast track designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Although the FDA has granted fast track designation to darovasertib in combination with crizotinib for treatment of adult patients with MUM and **to IDE161 for treatment of adult patients with breast cancer or ovarian cancer and** we may seek additional designation for other product candidates in the future, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may rescind the fast track designation if it believes that the designation is no longer supported by data from our clinical development program. We may also seek breakthrough therapy designation for any product candidate that we develop. 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 currently approved therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Product candidates designated as breakthrough therapies by the FDA may also be eligible for priority review. Like fast track designation, breakthrough therapy designation is within the discretion of the FDA. Accordingly, even if we believe a product candidate we develop meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to drugs developed under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if a product candidate we develop qualifies as a breakthrough therapy, the FDA may later decide that the drug no longer meets the conditions for qualification and rescind the designation. We may attempt to secure approval from the FDA through the use of the accelerated approval pathway. If we are unable to obtain such approval, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post- marketing requirements, the FDA may seek to withdraw any accelerated approval we have obtained. We may in the future seek accelerated approval for our one or more of our product candidates. Under the accelerated approval program, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life- threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is contingent on the sponsor' s agreement to conduct, in a diligent manner, additional post- approval confirmatory studies to verify and describe the drug' s clinical benefit. If such post- approval studies fail to confirm the drug' s clinical benefit or are not completed in a timely manner, the FDA may withdraw its approval of the drug on an expedited basis. In addition, in December 2022, President Biden signed an omnibus appropriations bill to fund the U. S. government through fiscal year 2023 which included the Food and Drug Omnibus Reform Act of 2022, or FDORA. Among other things, the legislation introduced reforms intended to expand the FDA' s ability to regulate products receiving accelerated approval, including by increasing the FDA' s oversight over the conduct of confirmatory trials; however, the ultimate impact of these reforms remains unclear. Prior to seeking accelerated approval for any of our product candidates, we intend to seek feedback from the FDA and will otherwise evaluate our ability to seek and receive accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA for accelerated approval or any other form of expedited development, review or approval. Furthermore, if we decide to submit an application for accelerated approval for our product candidates, there can be no assurance that such application will be accepted or that any expedited review or approval will be granted on a timely basis, or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for a product candidate would result in a longer time period to commercialization of such product candidate, if any, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace. We face significant competition in an environment of rapid technological and scientific change, and our failure to effectively compete may prevent us from achieving significant market

penetration. Most of our competitors have significantly greater resources than we do and we may not be able to successfully compete. The biotechnology and pharmaceutical industries in particular are characterized by rapidly advancing technologies, intense competition and a strong emphasis on developing proprietary therapeutics. We compete with a variety of multinational biopharmaceutical companies and specialized biotechnology companies, as well as technology being developed at universities and other research institutions. Our competitors have developed, are developing or will likely develop product candidates and processes competitive with our product candidates. Competitive therapeutic treatments include those that have already been approved and accepted by the medical community and any new treatments that enter the market. We believe that a significant number of product candidates are currently under development, and may become commercially available in the future, for the treatment of diseases and other conditions for which we may try to develop product candidates. Our competitors may obtain regulatory approval of their products more rapidly than we may or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidates. We believe that while our precision medicine target and biomarker discovery platform and our scientific and technical know- how give us a competitive advantage in this space, competition from many sources remains. Our competitors include larger and better funded biopharmaceutical, biotechnological and oncology therapeutics companies, as well as universities and other research institutions. Our commercial opportunity and success will be reduced or eliminated if competing products emerge that are safer, more effective, or less expensive than the therapeutics we develop. Our competitors may develop drugs that are more effective, more convenient, more widely used and less costly or have a better safety profile than our products and these competitors may also be more successful than us in manufacturing and marketing their products. For darovasertib, we are not aware of other companies actively developing clinical- stage therapeutics directed to PKC as a target for solid tumors. MingSight is developing a PKC beta inhibitor in chronic lymphocytic leukemia **, or CLL,** and diabetic macular edema, both in Phase 1 studies. Varian Biopharmaceuticals is advancing a preclinical- stage atypical PCK iota inhibitor, including as a dermatologic gel formulation for potential topical treatment of Basal Cell Carcinoma, or BCC. Exscientia is developing a PKC theta inhibitor in inflammatory diseases in Phase 1 studies. ~~HotSpot Therapeutics~~ **Varsity Pharma** is ~~advancing~~ **developing** a ~~program targeting~~ PKC ~~- theta~~ **inhibitor in CLL** . We are aware of other companies that are conducting research and development of potential therapies for primary UM or for MUM based on other targets and approaches. For example, Aura Biosciences is developing AU- 011 a virus-like drug conjugate (VDC) as local treatment for early- stage choroidal melanoma. Immunocore is developing and commercializing Tebentafusp, also known under its branded name as ~~Kimmtrakfor --~~ **Kimmtrak for** the treatment of adult patients with HLA- A * 02: 01- positive unresectable or metastatic uveal melanoma. Novartis is developing DYP688, an antibody- drug- conjugate, or ADC, with a GNAQ- 11 inhibitor payload in a Phase 1 / 2 clinical trial in MUM. For IDE397, Servier Pharmaceuticals, LLC, or Servier, is ~~preclinically~~ evaluating a small molecule MAT2A inhibitor designated as S95035 ~~. Servier is also clinically evaluating~~ **in a Phase 1 trial and Insilico Medicine has** a small molecule MAT2A inhibitor ~~designated as S95033, and formerly designated as AG270,~~ in **IND** ~~patients having tumors with MTAP deletion, following its acquisition of the Agios Pharmaceuticals', or Agios', commercial, clinical and research~~ **enabling studies** ~~stage oncology portfolio, including AG270~~ . For IDE161, we are not aware of any other clinical- stage therapies targeting PARG. Several companies are conducting preclinical research to develop PARG inhibitors, including ~~Sumitomo,~~ Nodus Oncology **, SynRx, 858 Therapeutics** and Satya Pharma Innovations **. For GSK101 (IDE705)** , ~~and based on information and belief~~ **Artios Pharma is developing two clinical-stage therapies targeting Pol Theta** , ~~potentially NeoMed Institute and 858~~ **both in Phase 1 / 2 studies. Additionally, Repare** Therapeutics **and Breakpoint Therapeutics have Pol Theta inhibitors in IND- enabling studies** . For our preclinical pipeline of synthetic lethality therapeutics, potential competition includes established companies as well as earlier- stage emerging biotechnology companies. Multiple established companies have been involved with research and development in synthetic lethality, such as AstraZeneca (Lynparza), Pfizer (Talzenna), GSK (Zejula) and Roche. Additionally, several other early- stage companies, including 858 Therapeutics, Anticancer Bioscience, Artios, Breakpoint Therapeutics, ~~Cyteir, Foghorn Therapeutics,~~ FoRx Therapeutics, ~~KSQ, MetaboMed, NeoMed,~~ Repare **Therapeutics** ~~, Ribon~~ , Ryvu Therapeutics, ~~Silicon~~ **Tango, Vividion, Xpose, and Eikon** Therapeutics ~~(acquired by Roivant Sciences), Tango, Vividion, Xpose and Zai Labs~~ . Development decisions and data from clinical trials of our competitors may adversely impact clinical development of our product candidates, and may additionally or alternatively have a material adverse impact on our financial condition or business prospects. Furthermore, we also face competition more broadly across the market for cost- effective and reimbursable cancer treatments. The most common methods of treating patients with cancer are surgery, radiation and drug therapy, including chemotherapy, hormone therapy and targeted drug therapy or a combination of such methods. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Insurers and other third- party payors may also encourage the use of generic products or specific branded products. We expect that if our product candidates are approved, they will be priced at a significant premium over competitive generic, including branded generic, products. As a result, obtaining market acceptance of, and a gaining significant share of the market for, any of our product candidates that we successfully introduce to the market will pose challenges. In addition, many companies are developing new therapeutics, and we cannot predict what the standard of care will be as our product candidates progress through clinical development. In some cases we may also develop diagnostics to enable relevant biomarker screening for clinical and commercial purposes in connection with our product candidates. If not already commercially available, we anticipate working in collaboration with diagnostic companies for this development, and we will face competition from other companies in establishing these collaborations. Our competitors will also compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we do. If we successfully obtain approval for any product candidate, we will face competition based on many

different factors, including the safety and effectiveness of our products, the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, coverage, reimbursement and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, less expensive or marketed and sold more effectively than any products we may develop. Competing products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan. We expect to expand our development and regulatory capabilities and potentially implement sales and distribution capabilities, and as a result, we will need to increase the size of our organization, and we may experience difficulties in managing growth. As of December 31, ~~2022~~ **2023** , we had ~~103~~ **124** employees. We will need to continue to expand our managerial, operational, finance and other resources in order to manage our operations and clinical trials, continue our development activities, submit for regulatory approval and, if approved, commercialize our product candidates or any future product candidates. Our management and personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively execute our growth strategy requires that we: • manage our preclinical studies and clinical trials effectively; • identify, recruit, retain, incentivize and integrate additional employees, including sales personnel; • manage our internal development and operational efforts effectively while carrying out our contractual obligations to third parties; and • continue to improve our operational, financial and management controls, reports systems and procedures. There is no assurance that any of these increases in scale, expansion of personnel, equipment, software and computing capacities, or process enhancements will be successfully implemented, or that we will have adequate space in our laboratory facilities to accommodate such required expansion. We currently have no sales organization. If we are unable to establish sales capabilities on our own or through third parties, we may not be able to market and sell any products effectively, if approved, or generate product revenue. We currently do not have a marketing or sales organization. In order to commercialize any product, if approved, in the United States and foreign jurisdictions, we must build our marketing, sales, distribution, managerial and other non- technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. In advance of any of our product candidates receiving regulatory approval, we expect to establish a sales organization with technical expertise and supporting distribution capabilities to commercialize each such product candidate, which will be expensive and time- consuming. We have no prior experience in the marketing, sale and distribution of pharmaceutical products, and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain, and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. Under our GSK Collaboration Agreement, GSK will be responsible for commercialization of any ~~POLQ~~ **Pol Theta** or WRN products. We may choose to collaborate with additional third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. If we are unable to enter into such arrangements on acceptable terms or at all, we may not be able to successfully commercialize our product candidates. If we are not successful in commercializing products, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would incur significant additional losses. If we fail to attract and retain senior management and key scientific personnel, our business may be materially and adversely affected. Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. We are highly dependent upon our senior management, particularly our President and Chief Executive Officer, as well as our senior scientists and other members of our senior management team. The loss of services of any of these individuals could delay or prevent the successful development of any products, initiation or completion of our planned clinical trials or the commercialization of our product candidates or any other product candidates. Competition for qualified personnel in the biotechnology and biopharmaceutical fields is intense due to the limited number of individuals who possess the skills and experience required by our industry. We will need to hire additional personnel as we expand our clinical development and if we initiate commercial activities. We may not be able to attract and retain quality personnel on acceptable terms, or at all. In addition, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output. Our employees and independent contractors, including principal investigators, consultants, collaborators, service providers and other vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have an adverse effect on our results of operations. We are exposed to the risk that our employees and independent contractors, including principal investigators, consultants, collaborators, service providers and other vendors may engage in misconduct or other illegal activity. Misconduct by these parties could include intentional, reckless and / or negligent conduct or other unauthorized activities that violate: the laws and regulations of the FDA and other similar regulatory bodies, including those laws that require the reporting of true, complete and accurate information to such regulatory bodies; manufacturing standards; U. S. federal and state healthcare fraud and abuse laws, data privacy and security laws and other similar non- U. S. laws; or laws that require the true, complete and accurate reporting of financial information or data. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, the creation of fraudulent data in our preclinical studies or clinical trials, or illegal misappropriation of product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third- parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or

regulations. In addition, we are subject to the risk that a person or government 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 and financial results, including, without limitation, the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other U. S. federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight and reporting obligations to resolve allegations of non- compliance, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could adversely affect our business, financial condition, results of operations and prospects. Our business involves the use of hazardous materials and we and our third- party manufacturers and suppliers must comply with environmental laws and regulations, which can be expensive and restrict how we do business. Our research and development activities and our third- party manufacturers' and suppliers' activities involve the controlled storage, use and disposal of hazardous materials owned by us, including the components of our product candidates and other hazardous compounds. We and any third- party manufacturers and suppliers we engage are subject to numerous federal, state and local environmental, health and safety laws, regulations and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination, which could cause an interruption of our research and development efforts, commercialization efforts and business operations, environmental damage resulting in costly clean- up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third- party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third- party facilities. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and / or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research, product development and manufacturing efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. 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 and pollution insurance to cover us for certain biological or hazardous waste exposure and contamination situations, this insurance may not provide adequate coverage against potential liabilities. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could have a material adverse effect on our business, financial condition, results of operations and prospects. We attempt to distribute our technology, biology, execution and financing risks across a range of therapeutic classes, disease states, programs and technologies. Due to the significant resources required for the development of our broad portfolio of programs, and depending on our ability to access capital, we must make certain risk assessments and prioritize development of certain product candidates. Moreover, we may expend our limited resources to pursue a particular product candidate and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success. Our organization is committed to a broad approach to precision medicine that seeks to maximize our integrated biomarker and small molecule drug discovery capabilities. Our current portfolio consists of multiple programs, extending across multiple classes of precision medicine, including direct targeting of oncogenic pathways and synthetic lethality. Together, these programs require significant capital investment. The directly targeted therapy programs are at various stages of preclinical and early clinical development, and our synthetic lethality programs are in the target identification, validation, lead optimization, and early clinical stages of development. We seek to maintain a process of prioritization and resource allocation to maintain an optimal balance between advancing and expanding our synthetic lethality and direct targeting programs. Because we have limited financial and managerial resources, we focus on specific product candidates, indications and discovery programs. As a result, we may forgo or delay pursuit of opportunities with other product candidates that could have had greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaborations, licenses and other similar arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Furthermore, as our programs progress, we or others may determine: that certain of our risk allocation decisions were incorrect or insufficient; that we made platform level technology mistakes; that individual programs or our approach to synthetic lethality or precision medicine in general has technology or biology risks that were unknown or underappreciated; that our choices on how to build our organizational infrastructure to drive our expansion will result in an inability to manufacture our products for clinical trials or otherwise impede our manufacturing capabilities; or that we have allocated resources in such a way that large investments are

not recovered and capital allocation is not subject to rapid re- direction. All of these risks may relate to our current or future precision medicine programs or companion diagnostics, and in the event material decisions in any of these areas turn out to have been incorrect or under- optimized, we may experience a material adverse impact on our business, financial condition, results of operations and prospects. **Public health outbreaks, epidemics or pandemics (such as the COVID- 19 pandemic) may materially and adversely affect our business and operations.** The COVID- 19 pandemic **previously** ~~, or any other pandemic, epidemic or outbreak of an infectious disease may materially and~~ adversely ~~affect~~ **affected** ~~our business and operations , including the pace of enrollment in current or future clinical trials. Outbreaks of epidemic, pandemic, or contagious diseases, such as the current novel coronavirus or, historically, the Ebola virus, Middle East Respiratory Syndrome, Severe Acute Respiratory Syndrome, or the H1N1 virus, could disrupt our business. For example, beginning in late 2019, the outbreak of a novel strain of virus named SARS- CoV- 2 (severe acute respiratory syndrome coronavirus 2), or coronavirus, which causes coronavirus disease 2019, or COVID- 19, has evolved into an~~ **and** ~~ongoing global pandemic. As of February 2023, the coronavirus has spread around the world and the United States continues to experience outbreaks of COVID- 19 and its variant strains. As states and localities increasingly lift COVID- 19 protocols, our offices have reopened and we have begun permitting travel and in- person events, taking into consideration government restrictions, employee safety, and health risks. Our approach may vary among geographies depending on appropriate health protocols, and may change at any time. Additionally, our efforts to reopen our offices safely may not be successful, could expose our employees to health risks, and could involve additional costs or liability. While vaccines have become widely available in certain countries, and businesses and economies have reopened, the status of global economic recovery remains uncertain and unpredictable, and will continue to be impacted by developments in the pandemic including any subsequent waves of outbreak or new variant strains of the COVID- 19 virus, which may require re- closures or other --~~ **the** ~~preventative measures. The~~ COVID- 19 pandemic ~~may also have long- term effects on the nature of the office environment, remote working and clinical trials, which may present risks for -~~ **or other actual** ~~our --~~ **or** ~~strategy~~ **threatened public health outbreaks** , ~~operational~~ **epidemics** , **or** ~~talent recruiting and retention, and workplace culture. We will continue to monitor the extent and impact of the pandemic~~ **pandemics may in** ~~and, if~~ the **future** ~~current economic conditions worsen or last for an extended period of time, we could be forced to significantly scale back our business and growth plans, which could have a material adverse~~ **adversely** ~~effect on our business, results of operations and financial condition. The COVID- 19 pandemic is affecting the United States and global economies and may~~ affect ~~our operations and those of third parties on which we rely. Some of these third parties have experienced shut- downs~~ , **among other things,** ~~supply chain and experimental study interruptions or~~ **our research** ~~slow- downs,~~ and **development efforts** ~~more third parties could experience such shut- downs , interruptions or slow- downs. Individuals at our company or at such third parties could become ill, quarantined, or otherwise unable to work and / or travel due to health reasons or governmental restrictions. The COVID- 19 pandemic could disrupt our ability to secure supplies for our facilities and to provide personal protective equipment for our employees. The safety, health and well- being of our workforce is of primary concern and we may need to enact further precautionary measures to help minimize the risk of our employees being exposed to the novel coronavirus. The evolving COVID- 19 pandemic may also, directly or indirectly, impact the pace of enrollment and impose logistical and trial management constraints in current or future clinical trials. Site initiation and patient enrollment may be delayed due to prioritization of hospital resources toward the COVID- 19 pandemic, and potential or enrolled patients may not be able or willing to comply with clinical trial protocols, whether due to quarantines impeding patient movement or interrupting healthcare services, or due to potential or enrolled patient concerns regarding interactions with medical facilities or staff. Similarly, our ability to recruit and retain principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID- 19, may be delayed or disrupted, which may adversely impact our~~ clinical trial operations **, manufacturing and supply chain operations, administrative personnel, third- party service providers, and business partners** . While the COVID- 19 pandemic did not materially adversely affect our business operations during the twelve months ended December 31, ~~2022~~ **2023** , economic and health conditions in the United States and across most of the globe continue to change rapidly and may materially affect us economically. While the potential economic impact brought by, and the duration of, **the** COVID- 19 **pandemic** may be difficult to assess or predict, a continuing widespread pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID- 19 **or a future public health outbreak** could materially affect our business and the value of our common stock ~~. The global pandemic of COVID- 19 continues to rapidly evolve~~ . The ultimate impact of the COVID- 19 pandemic or a similar **public** health ~~epidemic~~ **outbreak** is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. However, these effects could have a material ~~impact~~ **adverse effect** on our **business, results of** operations ~~,~~ and **financial condition** ~~we will continue to monitor the COVID- 19 situation closely~~ . Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain, or deploy key leadership and other personnel, or otherwise prevent products from being developed, approved, or commercialized in a timely manner or at all, which may adversely affect our business. The ability of the FDA and other government agencies to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies, including a prolonged government shutdown, or such as the European Medicines Agency following its relocation to Amsterdam and resulting staff changes, may cause significant regulatory delays and, therefore, delay our efforts to seek approvals and adversely affect our business, financial condition, results of operations, or cash flows. For example, over the last several years, the U. S.

government has shut down several times, and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. ~~Separately~~ **Additionally**, in response to the ~~global~~ COVID- 19 pandemic, the FDA postponed most inspections of domestic and foreign manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations ~~where feasible~~, ~~the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID- 19 pandemic, and~~ any resurgence of the virus or emergence of new variants may lead to further inspectional **or administrative** delays ~~. Regulatory authorities outside the United States have adopted similar restrictions or other policy measures in response to the COVID- 19 pandemic~~. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA and other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business. 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. Our corporate headquarters is located in the San Francisco Bay Area, which in the past has experienced both severe earthquakes and wildfires. We do not carry earthquake insurance. Earthquakes, wildfires 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 ~~, such as the COVID- 19 pandemic,~~ occurred that prevented us from using all or a significant portion of our headquarters or other facilities, that damaged critical infrastructure, such as our enterprise financial systems or manufacturing resource planning and enterprise quality systems, 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 currently are limited and are unlikely to prove adequate 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, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business. Furthermore, the third parties on which we depend, including suppliers, contract manufacturers and CROs are similarly vulnerable to natural disasters or other sudden, unforeseen and serious adverse events. If such an event were to affect our supply chain, manufacturing arrangements or interfere with a preclinical study or clinical trial, it could have a material adverse effect on our business. We are currently operating in a period of economic uncertainty and capital markets disruption, which has been significantly impacted by geopolitical instability due to the ongoing military conflict between Russia and Ukraine. Our business, financial condition and results of operations may be materially adversely affected by any negative impact on the global economy and capital markets resulting from the conflict in Ukraine or any other geopolitical tensions. U. S. and global markets are experiencing volatility and disruption following the escalation of geopolitical tensions and the **ongoing** ~~start of the~~ military conflict between Russia and Ukraine. In February 2022, a military invasion of Ukraine by Russian troops was reported. Following the invasion, the U. S. and global financial markets experienced volatility, which has led to disruptions to trade, commerce, pricing stability, credit availability and supply chain continuity globally. In response to the invasion, the United States, United Kingdom and European Union, along with others, imposed significant new sanctions and export controls against Russia, Russian banks and certain Russian individuals and may implement additional sanctions or take further punitive actions in the future. The full economic and social impact of the sanctions imposed on Russia (as well as possible future punitive measures that may be implemented), as well as the counter measures imposed by Russia, in addition to the ongoing military conflict between Ukraine and Russia and related sanctions, which could conceivably expand into the surrounding region, remains uncertain; however, both the conflict and related sanctions have resulted and could continue to result in disruptions to trade, commerce, pricing stability, credit availability and supply chain continuity in both Europe and globally, and has introduced significant uncertainty into global markets. Such risks and disruptions may negatively impact our supply chain, manufacturing arrangements, preclinical studies, clinical trials and our access to capital markets and ability to finance operations, which could have a materially adverse impact on our results of operations, financial condition and prospects. Risks Related to Our Dependence on Third Parties The commercial success of our partnered product candidates in our ~~POLQ~~ **Pol Theta** and WRN programs, which are part of the GSK Collaboration Agreement, will depend in large part on the development and marketing efforts of GSK. If GSK is unable to perform in accordance with the terms of the GSK Collaboration Agreement, our potential to generate future revenue from these programs would be significantly reduced and our business would be materially and adversely harmed. We will have limited influence and / or control over GSK' s approaches to development and commercialization of any ~~POLQ~~ **Pol Theta** or WRN products. While we will have the right to receive potential milestone, profit share and royalty streams payable as GSK or its sublicensees advance development of such ~~POLQ~~ **Pol Theta** or WRN products, we are likely to have limited ability to influence GSK' s development and commercialization efforts. If GSK does not perform in the manner that we expect or fulfill its responsibilities in a timely manner, or at all, the clinical development, regulatory approval and commercialization efforts related to product candidates we have licensed to GSK could be delayed or terminated. Furthermore, GSK or its licensees may elect to devote greater resources to other programs that do not relate to us or our collaboration. If we terminate the GSK Collaboration Agreement, or any program thereunder due to a material breach by GSK, we have the right to assume the responsibility at our own expense for the development of the applicable product candidates. Assumption of sole responsibility for further development will greatly increase our expenditures, and may mean we need to limit the size and scope of one or more of our programs, seek additional funding and / or choose to stop work altogether on one or more of the affected product candidates. This could result in a limited potential to generate future revenue from such product candidates, and our business could be materially and adversely affected. We rely on third parties to conduct certain of our preclinical studies and all of our clinical trials and intend to rely on third parties in the conduct of all of our future clinical trials. If these third parties do not successfully carry out their contractual duties, fail to comply with applicable regulatory requirements or meet expected deadlines, it may

delay or prevent us from seeking or obtaining regulatory approval or commercializing our current or future product candidates. We currently do not have the ability to independently conduct preclinical studies that comply with the regulatory requirements known as good laboratory practice, or GLP, requirements. We also do not currently have the ability to independently conduct any clinical trials. The FDA and regulatory authorities in other jurisdictions require us to comply with regulations and standards, commonly referred to as GCP, requirements for conducting, monitoring, recording and reporting the results of clinical trials, in order to ensure that the data and results are scientifically credible and accurate and that the clinical trial patients are adequately informed of the potential risks of participating in clinical trials. We rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct GLP- compliant preclinical studies and GCP- compliant clinical trials on our product candidates properly and on time. The third parties with whom we contract for execution of our GLP-compliant preclinical studies and our GCP- compliant clinical trials play a significant role in the conduct of these studies and trials and the subsequent collection and analysis of data. These third parties are not our employees and, except for restrictions imposed by our contracts with such third parties, we have limited ability to control the amount or timing of resources that they devote to our programs. Although we rely on these third parties to conduct our GLP- compliant preclinical studies and GCP-compliant clinical trials, we remain responsible for ensuring that each of our GLP preclinical studies and clinical trials is conducted in accordance with its investigational plan and protocol and applicable laws and regulations, and our reliance on the CROs does not relieve us of our regulatory responsibilities. Many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. Further, some of these agreements may also be terminated by such third parties on short notice, or under certain circumstances, including our insolvency. If the third parties conducting our preclinical studies or our clinical trials do not adequately perform their contractual duties or obligations, experience significant business challenges, disruptions or failures, do not meet expected deadlines, terminate their agreements with us or need to be replaced, or if the quality or accuracy of the data they obtain is compromised due to their failure to adhere to our protocols or to GCPs, or for any other reason, we may need to enter into new arrangements with alternative third parties. This could be difficult, costly or impossible, and our preclinical studies or clinical trials may need to be extended, delayed, terminated or repeated. As a result, we may not be able to obtain regulatory approval in a timely fashion, or at all, for the applicable product candidate, and our business, financial position, results of operations and prospects may be adversely affected. We rely on third parties for the manufacture of our product candidates for preclinical and clinical development and expect to continue to do so for the foreseeable future. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts. We do not own or operate manufacturing facilities and have no plans to build our own clinical or commercial scale manufacturing capabilities. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates and related raw materials for preclinical and clinical development, as well as for commercial manufacture of any future approved products. The facilities used by third- party manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, third- party manufacturers for compliance with cGMP requirements or similar applicable foreign requirements for manufacture of drug products. If these third-party manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other comparable foreign regulatory authorities, including requirements related to the manufacturing of high potency compounds, they will not be able to secure and / or maintain regulatory approval for their manufacturing facilities. These third- party manufacturers may be delayed in their manufacture or shipment of our product candidates due to **public health outbreaks** ~~the COVID- 19 pandemic~~ , heightened geopolitical conflict, increases in inflation and interest rates, or supply chain disruptions. For example, deterioration in the relationship between the United States and the PRC may impact international trade, government spending, regional stability and macroeconomic conditions. The impact of these potential developments, including any resulting sanctions, export controls or other restrictive actions that may be imposed against governmental or other entities in, for example, the PRC, may contribute to disruption of our PRC- based third- party suppliers and instability and volatility in the global markets, which in turn could adversely impact our operations and weaken our financial results. Additionally, our ability to audit these third- party manufacturers for compliance with cGMP requirements or similar foreign requirements (where applicable) and our specifications may be hindered or delayed due to **a public health outbreak or** ~~the COVID- 19 pandemic and~~ geopolitical conditions. In addition, we have no control over the ability of third-party manufacturers 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 product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. 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, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. In addition, we may be unable to establish or renew any agreements with third- party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third- party manufacturers, reliance on third-party manufacturers entails additional risks, including: • failure of third- party manufacturers to comply with regulatory requirements and maintain quality assurance; • breach of the manufacturing agreement by the third - party; • failure to manufacture our product according to our specifications; • failure to manufacture our product according to our schedule or at all; • misappropriation of our proprietary information, including our trade secrets and know- how; and • termination or nonrenewal of the agreement by the third - party at a time that is costly or inconvenient for us. Our product candidates and any products that

we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us, particularly if the COVID- 19 pandemic, geopolitical conflict and macroeconomic concerns continue or worsen. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval, and any related remedial measures may be costly or time- consuming to implement. We do not currently have arrangements in place for redundant supply or a second source for all required raw materials used in the manufacture of our product candidates. If our current third- party manufacturers cannot perform as agreed, we may be required to replace such manufacturers and we may be unable to replace them on a timely basis or at all. We rely on, and in the future may rely on, third- party databases and collaborations with third parties to inform patient selection and drug target identification for our existing product candidates and any future product candidates and for the supply of biomarker companion diagnostics. We are using bioinformatics, including data analytics, biostatistics, and computational biology, to identify new target and biomarker opportunities. As part of this approach, we interrogate public and proprietary databases comprising human tumor genetic information and specific cancer-target dependency networks. We rely on these databases and data analytics for identifying or validating some of our biomarker-target relationships and access to these databases may not continue to be available publicly or through a proprietary subscription on acceptable terms. Many of our precision medicine targeted therapeutic product candidates also rely on the availability and use of commercially available tumor diagnostics panels or data on the prevalence of our target patient population to inform the patient selection and drug target identification for our product candidates. In cases where such biomarker diagnostic is not already commercially available, we expect to establish strategic collaborations for the clinical supply and development of companion diagnostics. If these diagnostics are not able to be developed, or if commercial tumor profiling panels are not able to be updated to include additional tumor- associated genes, or if clinical oncologists do not incorporate molecular or genetic sequencing into their clinical practice, we may not be successful in developing our existing product candidates or any future product candidates. We depend on third- party suppliers for key materials required for the production of our product candidates, and the loss of these third- party suppliers or their inability to supply us with adequate materials could harm our business. We rely on third- party suppliers for certain materials, such as starting reagents, required for the production of our product candidates and / or for certain materials and assays, such as diagnostics, for clinical and commercial use of our product candidates. Our dependence on these third- party suppliers and the challenges we may face in obtaining adequate supplies of materials involve several risks, including limited control over pricing, availability, quality and delivery schedules. As a small company, our negotiation leverage is limited and we are likely to get lower priority than our competitors that are larger than we are. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Any supply interruption in limited or sole sourced raw materials could materially harm our ability to manufacture our product candidates until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business. Additionally, the facilities to manufacture our product candidates must be the subject of a satisfactory inspection before the FDA or other regulatory authorities approve an NDA or grant a marketing authorization for the product candidate manufactured at that facility. We will depend on these third- party manufacturing partners for compliance with the FDA' s requirements for the manufacture of our finished products. If our manufacturers cannot successfully manufacture material that conforms to our specifications and the FDA' s and other regulatory authorities' GMP requirements, our product candidates will not be approved or, if already approved, may be subject to recalls. Furthermore, certain of the third- party suppliers on which we rely are based in the PRC. The evolving trade dispute between the PRC and the United States has resulted in the imposition of significant tariffs on certain imports from the PRC. Any deterioration of the relationship between the United States and the PRC, or the imposition of more stringent export controls or tariffs applicable to our suppliers in the PRC, could adversely affect our ability to obtain the raw materials required for the manufacture of our product candidates, and therefore adversely affect our business, financial condition, results of operations and prospects. Reliance on third- party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including: • the possibility of a breach of the manufacturing agreements by the third parties because of factors beyond our control; • the possibility of termination or nonrenewal of the agreements by the third parties before we are able to arrange for a qualified replacement third- party manufacturer; and • the possibility that we may not be able to secure a manufacturer or manufacturing capacity in a timely manner and on satisfactory terms in order to meet our manufacturing needs. Any of these factors could cause the delay of approval or commercialization of any products, cause us to incur higher costs or prevent us from commercializing any products successfully. Furthermore, if any of our product candidates are approved and contract manufacturers fail to deliver the required commercial quantities of finished product on a timely basis and at commercially reasonable prices, and we are unable to find one or more replacement manufacturers capable of production at a substantially equivalent cost, in substantially equivalent volumes and quality and on a timely basis, we would likely be unable to meet demand for our products and could lose potential revenue. It may take several years to establish an alternative source of supply for our product candidates and to have any such new source approved by the FDA or any other relevant regulatory authority. If we fail to comply with our obligations under any of our in- license agreements, we could lose license rights that are important to our business. Our current in- license agreements or any future in- license agreements provide or may provide that we must use reasonable efforts to obtain regulatory approval for a product candidate using the licensed compound. The agreements further impose or may impose an obligation to make various milestone payments and royalty payments as well as other obligations on us. If we materially breach the terms of any in- license agreement and fail to cure such breach within the period allowed, then the licensor may terminate the license agreement. In addition, the licensor has or may have the right to

terminate on our insolvency. If the agreement is terminated, then we will not be able to further develop or commercialize the licensed compound or any future related product candidates. Furthermore, any dispute with the licensor may result in the delay or termination of the research, development or commercialization of the licensed compound or any future related product candidates, and may result in costly litigation or arbitration that diverts management attention and resources away from our day- to- day activities, which may adversely affect our business, financial condition, results of operations and prospects. Our existing collaboration arrangements and any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our product candidates or diagnostics associated with such product candidates. In the future, we may seek to enter into additional collaboration arrangements for the development or commercialization of certain of our product candidates or diagnostics for biomarkers associated with our product candidates. To the extent that we decide to enter into additional collaboration agreements in the future, we may face significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time- consuming to negotiate, document, implement and maintain and challenging to manage. We may not be successful in our efforts to prudently manage our existing collaborations or to enter new ones should we chose to do so. The terms of new collaborations or other arrangements that we may establish may not be favorable to us. The success of our collaboration arrangements, including our GSK Collaboration Agreement, will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include risks that: • collaborators may have significant discretion in determining the efforts and resources that they will apply to collaborations; • collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus due to their acquisition of competitive products or their internal development of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities; • collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing; • collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates; • a collaborator with marketing, manufacturing and distribution rights to one or more products may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities; • we could grant exclusive rights to our collaborators that would prevent us from collaborating with others; • collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability; • disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our current or future product candidates or that results in costly litigation or arbitration that diverts management attention and resources; • collaborations may be terminated, which may result in a need for additional capital to pursue further development or commercialization of the applicable current or future product candidates; • collaborators may own or co- own intellectual property covering products that result from our collaboration with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property; • disputes may arise with respect to the ownership or inventorship of any intellectual property developed pursuant to our collaborations; and • a collaborator' s sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings. Risks Related to Commercialization of Our Product Candidates Even if we receive regulatory approval for any product candidate, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions on marketing or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved. If one of our product candidates is approved, it will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record- keeping, conduct of post- marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities. For example, the FDA or similar foreign regulatory authorities may impose significant restrictions on a product' s indicated uses or marketing or impose ongoing requirements for potentially costly and time- consuming post-approval studies, post- market surveillance or clinical trials to monitor the safety and efficacy of the product candidate. The FDA may also require a REMS as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Similar requirements may apply in foreign jurisdictions. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, the manufacturing processes, labeling, packaging, distribution, AE reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post- marketing information and reports, registration, as well as continued compliance with cGMPs or similar foreign requirements and GCP requirements for any clinical trials that we conduct post- approval. Later discovery of previously unknown problems with our product candidates, including AEs 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: • suspension or withdrawal of regulatory approval, restrictions on the marketing or manufacturing of our product candidates, withdrawal of the product from the market, or voluntary or mandatory product recalls; • restrictions on product distribution or use, or requirements to conduct post- marketing studies or additional clinical trials; • suspension of any of our ongoing clinical trials; • fines, restitutions, disgorgement of profits or revenues, warning letters, untitled letters or holds on clinical trials; • refusal by the FDA or comparable foreign regulatory authorities to approve pending applications or supplements to approved

applications filed by us or suspension or revocation of approvals; • product seizure or detention, or refusal to permit the import or export of our product candidates; and • injunctions or the imposition of civil or criminal penalties. The occurrence of any event or penalty described above may inhibit our ability to commercialize any future approved product and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity. In addition, if any of our product candidates is approved, our product labeling, advertising and promotion will be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product' s approved labeling. Similar requirements may apply in foreign jurisdictions. If we receive marketing approval for a product, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off- label uses, we may become subject to significant liability. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off- label uses, and a company that is found to have improperly promoted off- label uses may be subject to significant sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off- label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. The FDA' s and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability. The incidence and prevalence of our target patient populations are estimations. If the market opportunities for our product candidates are smaller than we estimate, our business, financial position, results of operations and prospects may be harmed. We rely on various sources, including published literature and public or proprietary databases, to ascertain an estimate of the number of patients having particular genetic alterations, such as mutations, deletions or fusions, across various tissue- type specific indications. The determinable prevalence may vary depending on the source and quality of the underlying data and in some cases, insufficient data or poorly curated data may impact our ability to accurately estimate the prevalence of our target patient populations for each indication and in the aggregate across multiple indications both in the clinical trial setting, as well as in the commercial setting, if our product is approved. If the market opportunities for our product candidates are smaller than we estimate, our business, financial position, results of operations and prospects may be harmed. In addition, upon treatment with our product candidates, patients may have or develop resistance to our product candidates, reducing the addressable patient population and the duration of treatment. Even if our product candidates or any future product candidate obtains regulatory approval, they may fail to achieve the broad degree of physician and patient adoption and use necessary for commercial success. Even if our product candidates or any future product candidate receives FDA or other regulatory approvals, the commercial success of any product will depend significantly on the broad adoption and use of the resulting product by physicians and patients for approved indications. For a variety of reasons, including among other things, competitive factors, pricing or physician preference, reimbursement by insurers, the degree and rate of physician and patient adoption of any products, if approved, will depend on a number of factors, including: • the clinical indications for which the product is approved and patient demand for approved products that treat those indications; • the safety and efficacy of our product as compared to other available therapies; • the availability of companion diagnostics for biomarkers associated with our product candidates or any other future product candidates; • the time required for manufacture and release of our products; • the availability of coverage and adequate reimbursement from managed care plans, private insurers, government payors (such as Medicare and Medicaid) and other third- party payors for any of our products that may be approved; • acceptance by physicians, operators of hospitals and clinics and patients of the product as a safe and effective treatment; • physician and patient willingness to adopt a new therapy over other available therapies for a particular indication; • proper training and administration of our product candidates by physicians and medical staff; • patient satisfaction with the results and administration of our product candidates and overall treatment experience, including, for example, the convenience of any dosing regimen; • the cost of treatment with our product candidates in relation to alternative treatments and reimbursement levels, if any, and willingness to pay for the product, if approved, on the part of insurance companies and other third- party payors, physicians and patients; • the prevalence and severity of side effects; • limitations or warnings contained in the FDA-approved labeling for our products or similar foreign requirements; • the willingness of physicians, operators of hospitals and clinics and patients to utilize or adopt our products as a solution; • any FDA requirement for a REMS or similar foreign risk mitigation measures; • the effectiveness of our sales, marketing and distribution efforts; • adverse publicity about our products or favorable publicity about competitive products; and • potential product liability claims. We cannot assure you that our current or future product candidates, if approved, will achieve broad market acceptance among physicians and patients. Any failure by our product candidates that obtain regulatory approval to achieve market acceptance or commercial success would adversely affect our business, financial condition, results of operations and prospects. The successful commercialization of any products will depend in part on the extent to which governmental authorities, private health insurers, managed care plans and other third-party payors provide coverage, adequate reimbursement levels and implement pricing policies favorable for any products. Failure to obtain or maintain coverage and adequate reimbursement for products, if approved, could limit our ability to market those products and decrease our ability to generate revenue. The availability of coverage and adequacy of reimbursement by governmental healthcare programs, such as Medicare and Medicaid, private health insurers, managed care plans and other third-party payors are essential for most patients to be able to afford medical services and pharmaceutical products such as our product candidates that receive FDA approval. Our ability to achieve acceptable levels of coverage and reimbursement by third-party payors for our products will have an effect on our ability to successfully commercialize our product candidates. No uniform policy for coverage and reimbursement for products exists among third- party payors in the United States. Therefore,

coverage and reimbursement for products can differ significantly from payor to payor. The process for determining whether a third- party payor will provide coverage for a product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. Third- party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication, or place products at certain formulary levels that result in lower reimbursement levels and higher cost- sharing obligation imposed on patients. One third- party payor' s decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service. As a result, the coverage determination process will often require us to provide scientific and clinical support for the use of our products to each payor separately and can be a time- consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. We cannot be sure that coverage will be available for any product that we may develop. A decision by a third- party payor not to cover any of our product candidates could reduce physician utilization of our products once approved and adversely affect our business, financial condition, results of operations and prospects. Assuming there is coverage for our products, if any, by a third- party payor, the resulting reimbursement payment rates may not be adequate or may require co- payments that patients find unacceptably high. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely. Third- party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third- party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third- party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our products, pricing of other third- party therapeutics may limit the amount we will be able to charge for our products. These third- party payors may deny or revoke the reimbursement status of our products, if approved, or establish prices for our products at levels that are too low to enable us to realize an appropriate return on our investment. If reimbursement is not available, is decreased or eliminated in the future, or is available only at limited levels, we may not be able to successfully commercialize our products and may not be able to obtain a satisfactory financial return on our products. Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other countries has and will continue to put pressure on the pricing and usage of our products, if any. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our products. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits. Moreover, increasing efforts by governmental and third- party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products, and, as a result, they may not cover or provide adequate payment for our products. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of any products. We face an inherent risk of product liability as a result of the planned clinical trials of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranty. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of any products. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in: • decreased demand for any products; • injury to our reputation; • withdrawal of clinical trial participants; • costs to defend the related litigation; • a diversion of management' s time and our resources; • substantial monetary awards to clinical trial participants or patients; • regulatory investigations, product recalls, withdrawals or labeling, marketing or promotional restrictions; • loss of revenue; and • the inability to commercialize any products. Our inability to obtain and maintain sufficient product liability insurance at an acceptable cost and scope of coverage to protect against potential product liability claims could prevent or inhibit the commercialization of any products. Although we have obtained and intend to maintain product liability insurance covering our clinical trials, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions and deductibles, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient funds to pay such amounts. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses. If and when we obtain approval for marketing any of our product candidates, we intend to expand our insurance coverage to include the sale of such product candidate; however, we may be unable to obtain this liability insurance on commercially reasonable terms or at all. Risks Related to Intellectual Property Our success depends on our ability to obtain and maintain protection for our intellectual property

and our proprietary technologies and to avoid infringing the rights of others. Our commercial success depends in part on our ability to obtain and maintain patent, **trademark,** trade secret and other intellectual property protection for our product candidates and proprietary technologies as well as our ability to operate without infringing upon the proprietary rights of others. We and our licensors have applied, and we intend to continue applying, for patents covering important aspects of our product candidates, proprietary technologies and their uses as we deem appropriate. However, the patent prosecution process is expensive, time- consuming and complex, and we may not be able to apply for patents on certain aspects of our current or future product candidates and proprietary technologies in a timely fashion, at a reasonable cost, in all jurisdictions, or at all. If we cannot adequately obtain, maintain and enforce our intellectual property rights and proprietary technology, competitors may be able to use our technologies or the goodwill we have acquired in the marketplace and erode or negate any competitive advantage we may have and our ability to compete, which could harm our business and ability to achieve profitability and / or cause us to incur significant expenses. Failure to obtain, maintain and / or enforce intellectual property rights necessary to our business and failure to protect, monitor and control the use of our intellectual property rights could negatively impact our ability to compete and cause us to incur significant expenses. The intellectual property laws and other statutory and contractual arrangements in the United States and other jurisdictions we depend upon may not provide sufficient protection in the future to prevent the infringement, use, violation or misappropriation of our patents, trademarks, data, technology and other intellectual property rights and products by others, and may not provide an adequate remedy if our intellectual property rights are infringed, misappropriated or otherwise violated by others. Our patent applications cannot be enforced against third parties practicing the inventions claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the invention as claimed. The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our actual or potential future collaborators or licensors will be successful in protecting our product candidates and proprietary technologies by obtaining and defending patents. These risks and uncertainties include the following: • the United States Patent and Trademark Office, or USPTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other requirements during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction; • patent applications may not result in any patents being issued; • our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained or licensed patents that will limit, interfere with or eliminate our ability to make, use and sell our product candidates; • other parties may have designed or may design around our claims or developed technologies that may be related or competitive to our platform, may have filed or may file patent applications and may have received or may receive patents that overlap or conflict with our patent applications, either by claiming the same methods or devices or by claiming subject matter that could dominate our patent position; • any successful opposition to any patents owned by or licensed to us could deprive us of rights necessary for the practice of our technologies or the successful commercialization of any product candidates that we may develop; • because patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we or our licensors were the first to file any patent application related to our product candidates and proprietary technologies; • an interference proceeding can be provoked by a third **-** party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications for any application with an effective filing date before March 16, 2013; • there may be significant pressure on the U. S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and • countries other than the United States may have patent laws less favorable to patentees than those upheld by U. S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates. We rely in part on our portfolio of issued and pending patent applications in the United States and other countries to protect our intellectual property and competitive position. The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. It is possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. If we fail to timely file for patent protection in any jurisdiction, we may be precluded from doing so at a later date. And although we enter into non- disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in any of our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Moreover, should we become a licensee of a third **-** party' s patents or patent applications, depending on the terms of any future in- licenses to which we may become a party, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain or enforce the patents, covering technology in- licensed from third parties. Therefore, these patents and patent applications may not be prosecuted, maintained and / or enforced in a manner consistent with the best interests of our business. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability and it may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products or services. Accordingly, we cannot provide any assurances about which of our patent applications will issue, the breadth of any resulting patent, whether any of the issued patents will be found to be infringed, invalid or unenforceable or will be threatened or

challenged by third parties, that any of our issued patents have, or that any of our currently pending or future patent applications that mature into issued patents will include, claims with a scope sufficient to protect our products and services. The coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. We cannot offer any assurances that the breadth of our granted patents will be sufficient to stop a competitor from developing, manufacturing and commercializing a product or technologies in a non- infringing manner that would be competitive with one or more of our products or technologies, or otherwise provide us with any competitive advantage. Further, our patents or the patent rights that we license from others, may be challenged in the courts or patent offices in the United States and abroad. Once granted, patents may remain open to opposition, interference, re- examination, post- grant review, inter partes review, nullification or derivation action or similar proceedings in court or before patent offices in the United States or foreign jurisdictions for a given period after allowance or grant, during which time third parties can raise objections against such patents. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, all of which could limit our ability to stop others from using or commercializing similar or identical product candidates, or limit the duration of the patent protection of our product candidates. In addition, defending such challenges in such proceedings may be costly. Further, there can be no assurance that we will have adequate resources to enforce our patents. Thus, any patents that we may own may not provide the anticipated level of, or any, protection against competitors. Furthermore, an adverse decision may result in a third - party receiving a patent right sought by us, which in turn could affect our ability to develop, manufacture or commercialize our products or technologies. The degree of future protection for our patent rights is uncertain, and we cannot ensure that: • any of our patents, or any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect our product candidates; • any of our pending patent applications will issue as patents; • any of the patents we own or license will be found to ultimately be valid and enforceable if subject to challenge; • we were the first to make the inventions covered by each of our patents and pending applications; • we were the first to file patent applications for these inventions; • we will be able to successfully manufacture and commercialize our products on a substantial scale, if approved, before relevant patents we may have expire; • any patents issued to us or our licensors will provide a basis for an exclusive market for any commercially viable products we may develop or will provide us with any competitive advantages; • we will develop or in- license additional proprietary technologies that are patentable; • the patents of others will not have an adverse effect on our business; • others will not develop, manufacture and / or commercialize similar or alternative products or technologies that do not infringe our patents; • our competitors do not conduct research and development activities in countries where we do not have enforceable patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; and • our commercial activities or products will not infringe upon the patents of others. Our ability to enforce patent rights also depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their products and services. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor' s or potential competitor' s product or service. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful. If we initiate lawsuits to protect or enforce our patents, or litigate against third- party claims, such proceedings would be expensive and would divert the attention of our management and technical personnel. Where we obtain licenses from or collaborate with third parties, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties, or such activities, if controlled by us, may require the input of such third parties. We may also require the cooperation of our licensors and collaborators to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Moreover, if we do obtain necessary licenses, we will likely have obligations under those licenses, and any failure to satisfy those obligations could give our licensor the right to terminate the license. Termination of a necessary license, or expiration of licensed patents or patent applications, could have a material adverse impact on our competitive position, business, financial condition, results of operations and prospects. Some of our patents and patent applications may in the future be co- owned with third parties. If we are unable to obtain an exclusive license to any such third- party co- owners' interest in such patents or patent applications, such co- owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products, services and technology. In addition, we may need the cooperation of any such co- owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Furthermore, our owned and in- licensed intellectual property rights may be subject to a reservation of rights by one or more third parties. For example, the research resulting in certain of our owned and in- licensed patent rights and technology was funded in part by the U. S. government. As a result, the government may have certain rights, or march- in rights, to such patent rights and technology. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a non- exclusive license authorizing the government to use the invention for non- commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise march- in rights to use or allow third parties to use our licensed technology. The government can exercise its march- in rights if it determines that action is necessary because we fail to achieve practical application of the government- funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U. S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of such rights could harm our competitive position, business, financial condition, results of operations, and prospects. Further, we rely on a combination of contractual provisions, confidentiality procedures and patent, trademark, copyright, trade secret and other intellectual property laws to protect the proprietary aspects of our products, brands,

technologies, trade secrets, know- how and data. These legal measures afford only limited protection, and competitors or others may gain access to or use our intellectual property rights and proprietary information. Our success will depend, in part, on preserving our trade secrets, maintaining the security of our data and know- how and obtaining, maintaining and enforcing other intellectual property rights. We may not be able to obtain, maintain and / or enforce our intellectual property or other proprietary rights necessary to our business or in a form that provides us with a competitive advantage. If we fail to obtain sufficient patent or other intellectual property protection for our product candidates or proprietary technologies or if we lose any patent or other intellectual property protection for our product candidates or proprietary technologies, our business, financial condition, results of operations and prospects could be adversely affected. If we do not obtain patent term extension in the United States under the Hatch- Waxman Act and in foreign countries under similar legislation for patents covering our product candidates, our business may be materially harmed, and in any case, the terms of our patents may not be sufficient to effectively protect our product candidates and business. Patents have a limited term. In most countries, including the United States, the expiration of a patent is generally 20 years after its first effective non- provisional filing date. However, depending upon the timing, duration and specifics of FDA marketing approval of darovasertib, IDE397, our other product candidates or any future product candidates, one or more of any U. S. patents we may be issued or have licensed may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch- Waxman Amendments. The Hatch- Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. 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 may also be available in certain foreign countries upon regulatory approval of our product candidates. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration 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 will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our competitive position, business, financial condition, results of operations, and prospects could be harmed, possibly materially. If there are delays in obtaining regulatory approvals or other additional delays, the period of time during which we can market our product candidates under patent protection could be further reduced. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. Once the patent term has expired, we may be open to competition from similar or generic products. The launch of a generic version of one of our products in particular would be likely to result in an immediate and substantial reduction in the demand for that product, which could have a material adverse effect on our business, financial condition, results of operations and prospects. Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent application process to maintain patent applications and issued patents. In addition, periodic maintenance fees, renewal fees, annuity fees and various other government fees on issued patents often must be paid to the USPTO and foreign patent agencies over the lifetime of the patent and / or applications and any patent rights we may obtain in the future. While an unintentional lapse of a patent or patent application 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 with these requirements can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non- compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non- payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our products or services, we may not be able to stop a competitor from marketing products or services that are the same as or similar to our products or services, which would have a material adverse effect on our business, financial condition and results of operations. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case. Our rights to develop and commercialize our product candidates are subject in part to the terms and conditions of licenses granted to us by others, and the patent protection, prosecution and enforcement for some of our product candidates may be dependent on our licensors. We currently are reliant upon licenses of certain intellectual property rights and proprietary technology from third parties that are important or necessary to the development of our proprietary technology, including technology related to our product candidates. For example, we rely on our exclusive license agreement with Novartis for the clinical development of darovasertib and our option and license agreement with **CRT** ~~Cancer Research UK~~ for the clinical development of PARG inhibitors. These licenses, and other licenses we may enter into in the future, may not provide adequate rights to use such intellectual property rights and proprietary technology in all relevant fields of use or in all territories in which we may wish to develop or commercialize technology and product candidates in the future. Licenses to additional third- party proprietary technology or intellectual property rights that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms. In that event, we may be required to expend significant time and resources to redesign our proprietary technology or product candidates or to develop or license replacement technology, which may not be feasible on a technical or commercial basis. If we are unable to do so, we may not be able to develop and commercialize technology and product candidates in fields of use and territories for which we are not granted rights

pursuant to such licenses, which could harm our business, financial condition, results of operations and prospects significantly. Third- party patents may exist which might be enforced against our current or future product candidates, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and / or other forms of compensation to third parties. In some circumstances, we may not have the right to control the preparation, filing, prosecution and enforcement of patent applications, or to maintain the patents, covering technology that we license from third parties. In addition, some of our agreements with our licensors require us to obtain consent from the licensor before we can enforce patent rights, and our licensor may withhold such consent or may not provide it on a timely basis. Therefore, we cannot be certain that our licensors or collaborators will prosecute, maintain, enforce and defend such intellectual property rights in a manner consistent with the best interests of our business, including by taking reasonable measures to protect the confidentiality of know-how and trade secrets, or by paying all applicable prosecution and maintenance fees related to intellectual property registrations for any of our product candidates. We also cannot be certain that our licensors have drafted or prosecuted the patents and patent applications licensed to us in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such applications. This could cause us to lose rights in any applicable intellectual property that we in- license, and as a result our ability to develop and commercialize product candidates may be adversely affected and we may be unable to prevent competitors from making, using and selling competing products. Our current licenses impose, and our future licenses likely will impose, various royalty payments, milestones, and other obligations on us. If we fail to comply with any of these obligations, we may be subject to liability, including the payment of damages, and the licensor may have the right to terminate the license. Termination by the licensor would cause us to lose valuable rights, and could prevent us from developing and commercializing our product candidates and proprietary technologies. Furthermore, if any current or future licenses terminate, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties may gain the freedom to seek regulatory approval of, and to market, products similar or identical to our planned products. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor' s rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in product candidates that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize product candidates, we may be unable to achieve or maintain profitability. In addition, we may seek to obtain additional licenses from our licensors and, in connection with obtaining such licenses, we may agree to amend our existing licenses in a manner that may be more favorable to the licensors, including by agreeing to terms that could enable third parties (potentially including our competitors) to receive licenses to a portion of the intellectual property rights that are subject to our existing licenses. Any of these events could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects. We may fail to comply with any of our obligations under existing or future agreements pursuant to which we license or have otherwise acquired intellectual property rights or technology, which could result in the loss of rights or technology that are material to our business. We are party to various agreements that we depend on to operate our business, including intellectual property rights relating to darovasertib, in particular, our agreement with Novartis. Our rights to use currently licensed intellectual property, or intellectual property to be licensed in the future, are or will be subject to the continuation of and our compliance with the terms of these agreements. These agreements are complex, and certain provisions in such agreements may be susceptible to multiple interpretations which could lead to disputes, including but not limited to those regarding: • the scope of rights granted under the license agreement; • the extent to which our proprietary technology and product candidates infringe on intellectual property of the licensor that is not subject to the licensing agreement; • the sublicensing of patent and other rights; • diligence obligations under the license agreement and what activities satisfy those diligence obligations; • the ownership of inventions and know-how resulting from the creation or use of intellectual property by us or our counterparties, alone or jointly; • the scope and duration of our payment obligations; • the priority of invention of patented technology; • rights upon termination of such agreement; and • the scope and duration of exclusivity obligations of each party to the agreement. The resolution of any contractual interpretation dispute that may arise, if unfavorable to us, could have a material adverse effect on our business, financial condition, results of operations and prospects. Such resolution could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, increase what we believe to be our financial or other obligations under the relevant agreement or decrease the third - party' s financial or other obligations under the relevant agreement. Furthermore, if disputes over intellectual property rights that we have licensed or acquired from third parties prevent or impair our ability to maintain our current license agreements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. If we fail to comply with our obligations under current or future license agreements, these agreements may be terminated or the scope of our rights under them may be reduced and we might be unable to develop, manufacture or market any product that is licensed under these agreements. We are generally also subject to all of the same risks with respect to protection of intellectual property that we may license as we are for intellectual property that we own, which are described herein. If we or any of our current or future licensors fail to adequately protect this intellectual property, our ability to commercialize product candidates could suffer. We may become subject to third- party claims alleging infringement, misappropriation or violation of such third - party' s patents or other intellectual property rights and / or third - party claims seeking to invalidate our patents, which could require us to spend significant time and money and, if successfully asserted against us, could delay or prevent us from developing, manufacturing and selling our products. Our commercial success depends significantly on our ability to develop, manufacture or commercialize our products and product candidates without infringing, misappropriating or otherwise violating the intellectual property rights of third parties. However, our research, development and commercialization activities may nonetheless be subject to claims that we infringe or otherwise violate patents or other

intellectual property rights owned or controlled by third parties. Claims by third parties that we infringe their intellectual property rights may result in liability for damages or prevent or delay our developmental and commercialization efforts. We cannot assure you that our operations do not, or will not in the future, be found to infringe existing or future patents. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our product candidates or impair our competitive position. As the biotechnology industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell our product candidates. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, reexaminations, inter partes review proceedings and post- grant review proceedings before the USPTO and / or corresponding foreign patent offices, and companies in the industry have used these proceedings to gain a competitive advantage. Numerous third- party U. S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. There may be third- party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. For example, we are aware of an international patent application published as PCT WO 2017 / 096165 A1. If a patent issues from such patent application with claims similar to those published, our ability to commercialize a product candidate for our MAT2A program may be adversely affected if we do not obtain a license under such patent. Furthermore, the scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent' s prosecution history and can involve other factors such as expert opinion. Our analysis of these issues, including interpreting the relevance or the scope of claims in a patent or a pending application, determining applicability of such claims to our proprietary technologies or product candidates, predicting whether a third - party' s pending patent application will issue with claims of relevant scope, and determining the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. We do not always conduct independent reviews of pending patent applications of and patents issued to third parties. Additionally, patent applications in the United States and elsewhere are typically published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Certain U. S. applications that will not be filed outside the United States can remain confidential until patents issue. In addition, patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived. Furthermore, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our product candidates or the use of our product candidates. These applications may later result in issued patents, or the revival of previously abandoned patents, that will prevent, limit or otherwise interfere with our ability to make, use or sell our products. As a result, we may be unaware of third- party patents that may be infringed by commercialization of darovasertib, IDE397 or our other product candidates, and cannot be certain that we were the first to file a patent application related to a product candidate or proprietary technology. In addition, identification of third- party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. Moreover, we may face patent infringement claims from non- practicing entities that have no relevant product revenue and against whom our own patent portfolio may thus have no deterrent effect. We may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of our product candidates. Further, we may be required to indemnify future collaboration partners against claims of infringement, misappropriation, or other violations of intellectual property rights. We are not aware of any threatened or pending claims related to these matters, but in the future litigation may be necessary to defend against such claims. If a patent infringement suit were brought against us, we could be forced, including by court order to stop or delay development, manufacturing and / or sales of the product or product candidate that is the subject of the suit. As a result of patent infringement claims, or in order to avoid potential claims, we may choose to seek, or be required to seek, a license from the third - party and would most likely be required to pay license fees or royalties or both. These licenses may not be available on commercially reasonable terms, or at all, in which event our business would be materially and adversely affected. Even if we were able to obtain a license, we may be unable to maintain such licenses and the rights may be nonexclusive, which could give our competitors access to the same intellectual property. Although no third - party has asserted a claim of patent infringement against us as of December 31, ~~2022~~ **2023** , others may hold proprietary rights that could prevent darovasertib, IDE397, our other product candidates or any future product candidates from being marketed. Any patent- related legal action against us claiming damages and seeking to enjoin commercial activities relating to our product candidates or proprietary technologies could subject us to potential liability for damages, including treble damages if we were determined to willfully infringe or attorney' s fees and costs of litigation to the party whose intellectual property rights we may be found to be infringing, and require us to obtain a license to manufacture or market darovasertib, IDE397, our other product candidates or any future product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be time- consuming and a substantial diversion of management and employee resources from our business. Even if we believe such claims are without merit, we cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Even if such licenses are available, we could incur substantial costs related to royalty payments for licenses obtained from third parties, which could negatively affect our gross margins, and the rights may be non- exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. In addition, we cannot be certain that we could redesign our product candidates or proprietary

technologies to avoid infringement, if necessary, or on a cost- effective basis. If we were to challenge the validity of any such third - party U. S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U. S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U. S. patent. We will have similar burdens to overcome in foreign courts in order to successfully challenge a third - party claim of patent infringement. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing darovasertib, our other product candidates or any future product candidates, until the asserted patent expires or is held finally invalid or not infringed in a court of law. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity or the disclosure of confidential information, and the perceived value of our product candidates or intellectual property could be diminished correspondingly. Additionally, our collaborators or any third parties with which we collaborate in the future, may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation or potential liability. Further, collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability. Also, we may be obligated under our agreements with our collaborators, licensors, suppliers and others to indemnify and hold them harmless for damages arising from intellectual property infringement by us. Any of the foregoing could harm our competitive position, business, financial condition, results of operations, and prospects. We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time- consuming, and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged. Third parties, including our competitors may currently, or in the future, infringe, misappropriate or otherwise violate our issued patents or other intellectual property rights or those of our licensors. To prevent infringement or unauthorized use, we may be required to file lawsuits or initiate other proceedings to protect or enforce our patents or other intellectual property rights, which can be expensive, time- consuming and unsuccessful. However, the steps we have taken, and are taking, to protect our proprietary rights may not be adequate to enforce our rights as against such infringement, misappropriation or violation of our intellectual property rights. In certain circumstances it may not be practicable or cost-effective for us to enforce our intellectual property rights fully, particularly in certain developing countries or where the initiation of a claim might harm our business relationships. We may also be hindered or prevented from enforcing our rights with respect to a government entity or instrumentality because of the doctrine of sovereign immunity. Our ability to enforce our patent or other intellectual property rights depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their products or technologies. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor' s or potential competitor' s product or technologies. Thus, we may not be able to detect unauthorized use of, or take appropriate steps to enforce, our intellectual property rights. Any inability to meaningfully enforce our intellectual property rights could harm our ability to compete and reduce demand for our products and product candidates. In addition, in a patent infringement proceeding, a court or administrative tribunal may decide that a patent we own or in- license is not valid, is unenforceable and / or is not infringed. If we or any of our collaborators or potential future collaborators, were to initiate legal proceedings against a third - party to enforce a patent directed at one of our product candidates, the defendant could counterclaim that our patent is invalid and / or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and / or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non- enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. Similar mechanisms for challenging the validity and enforceability of a patent exist in foreign patent agencies. The outcome following legal assertions of invalidity and unenforceability is unpredictable, and could result in the revocation, cancellation, or amendment of our patents or those of our licensors. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. A court may decide that a patent or other intellectual property right of ours is invalid or unenforceable, in whole or in part, construe the patent' s claims or other intellectual property narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents or other intellectual property do not cover the technology in question. If a defendant were to prevail on a legal assertion of invalidity and / or unenforceability, we could lose at least part, and perhaps all, of the patent protection on an affected product candidate. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations and prospects. Additionally, interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO, or equivalent actions brought in foreign jurisdictions, may be necessary to determine the priority of invention with respect to our patents or patent applications or those of our licensors. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. An unfavorable outcome could require us to cease using the covered technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non- exclusive license is offered and our competitors gain access to the same technology. These and other uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our product candidates to market. Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or

investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. 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 conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. Any of the foregoing could harm our business, financial condition, results of operations and prospects. Even if our patents or other intellectual property rights are found to be valid and infringed, a court may refuse to grant injunctive relief against the infringer and instead grant us monetary damages and / or ongoing royalties. Such monetary compensation may be insufficient to adequately offset the damage to our business caused by the infringer' s competition in the market. An adverse result in any litigation or administrative proceeding could put one or more of our patents or other intellectual property rights at risk of being invalidated or interpreted narrowly, which could adversely affect our competitive business position, financial condition and results of operations. We may be subject to claims that we or our employees, consultants, advisors or other third parties have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers. We may be subject to claims that our employees or consultants have wrongfully used for our benefit or disclosed to us confidential information of third parties. As is common in the biotechnology and biopharmaceutical industries, in addition to our employees, we engage the services of consultants, advisors and other third parties to assist us in the development of our product candidates. Many of these individuals, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other biotechnology or biopharmaceutical companies including our competitors or potential competitors. Some of these employees, consultants and contractors, may have executed proprietary rights, non- disclosure and non- competition agreements in connection with such previous employment or engagement. Although we try to ensure that individuals working for or collaborating with us do not use the intellectual property rights, proprietary information or know- how of others in their work for us, and do not perform work for us that is in conflict with their obligations to another employer or any other entity, we may become subject to claims that we, our employees, consultants, advisors or other third parties have, inadvertently or otherwise, misappropriated the intellectual property, including know- how, trade secrets or other information proprietary to their former or current employers or clients. We may also be subject to claims that patents and applications we have filed to protect inventions of our employees, consultants, advisors or other third parties, even those related to one or more of our product candidates, are rightfully owned by their former or concurrent employer. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, which could adversely affect our competitive position, business, financial condition, results of operations, and prospects. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team. We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property rights. We may also be subject to claims that our former employees, contractors or collaborators, or other third parties have an ownership interest in our current or future patents, patent applications, or other intellectual property rights, including as an inventor or co- inventor. We may be subject to ownership or inventorship disputes in the future arising, for example, from conflicting obligations of employees, consultants or others who were or are involved in developing our products or product candidates. Although it is our policy to require our employees and our personnel who may be involved in the development of intellectual property to execute agreements assigning such inventions, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. The assignment of intellectual property may not be self- executing and despite such agreement, such inventions may become assigned to third parties. In the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information. We may be subject to claims that former employees, consultants, advisors or other third parties have an ownership interest in our patents or other intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property rights, and other owners may be able to license their rights to other third parties, including our competitors. Such an outcome could have a material adverse effect on our business. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel. In addition, we may face claims by third parties challenging ownership interest in or inventorship of intellectual property rights we regard as our own, based on claims that our agreements with employees, consultants, advisors or other third parties obligating them to assign intellectual property to us are ineffective or in conflict with prior or competing contractual obligations of assignment, which could result in ownership disputes regarding intellectual property we have developed or will develop and interfere with our ability to capture the commercial value of such intellectual property. We are not aware of any threatened or pending claims related to these matters, but in the future litigation may be necessary to defend against these and other claims challenging inventorship or ownership and it may be necessary or we may desire to obtain a license to such third - party' s intellectual property rights to settle any such claim; however, there can be no assurance that we would be able to obtain such license on commercially reasonable terms, if at all. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. A court could prohibit us from using technologies, features or other intellectual property rights that are essential to our products or technologies, if such

technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of another person or entity, including another or former employers. An inability to incorporate technologies, features or other intellectual property rights that are important or essential to our products or product candidates could have a material adverse effect on our business, financial condition, results of operations, and competitive position, and may prevent us from developing, manufacturing and / or commercializing our products or technologies. In addition, we may lose valuable intellectual property rights or personnel. Such an outcome could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects. Even if we are successful in defending against such claims, litigation could result in substantial costs and distraction to management and other employees. Any 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 develop, manufacture and / or commercialize our products or services, which could materially and adversely affect our business, financial condition and results of operations. If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. In addition to patent protection, we also rely on other intellectual property rights, including protection of copyright, trade secrets, know- how, technology and / or other proprietary information that is not patentable or that we elect not to patent. Trade secrets can be difficult to protect, and some courts are less willing or unwilling to protect trade secrets. To maintain the confidentiality of our trade secrets and proprietary information, we rely heavily on confidentiality agreements with third parties, and confidential information and invention assignment agreements with employees, consultants, advisors and appropriate third parties. However, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes and we may not enter into such agreements with all employees, consultants and third parties who have been involved in the development of our intellectual property rights. Although we generally require all of our employees, consultants, advisors and any third parties who have access to our proprietary know- how, information, or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using commonly accepted physical and technological security measures. Despite these efforts, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. In addition, such security measures may not provide adequate protection for our proprietary information, for example, in the case of misappropriation of a trade secret by an employee, consultant, customer or third - party with authorized access. Our security measures may not prevent an employee, consultant, advisor or other third - party from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. 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. Therefore, we may not be able to prevent the unauthorized disclosure or use of our technical knowledge or other trade secrets by such employees, consultants, advisors or third parties, despite the existence generally of these confidentiality restrictions. These agreements may not provide meaningful protection against the unauthorized use or disclosure of our trade secrets, know- how or other proprietary information in the event the unwanted use is outside the scope of the provisions of the contracts or in the event of any unauthorized use, misappropriation, or disclosure of such trade secrets, know- how, or other proprietary information. There can be no assurances that such employees, consultants, advisors or third parties will not breach their agreements with us, that we will have adequate remedies for any breach, or that our trade secrets will not otherwise become known or independently developed by third parties, including our competitors. Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our products that we consider proprietary. We may not be able to obtain adequate remedies in the event of such unauthorized use. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time- consuming, and the outcome is unpredictable. Further, we may not be able to obtain adequate remedies for any breach. Even though we use commonly accepted security measures, trade secret violations are often a matter of state law in the United States, and the criteria for protection of trade secrets can vary among different jurisdictions. If the steps we have taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time- consuming, and the outcome is unpredictable. Because from time to time we expect to rely on third parties in the development, manufacture, and distribution of our products and provision of our services, we must, at times, share trade secrets with them. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Trade secrets will over time be disseminated within the industry through independent development, the publication of journal articles and the movement of personnel skilled in the art from company to company or academic to industry scientific positions. Though our agreements with third parties typically restrict the ability of our advisors, employees, collaborators, licensors, suppliers, third- party contractors and consultants to publish data potentially relating to our trade secrets, our agreements may contain certain limited publication rights. In addition, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Despite employing the contractual and other security precautions described above, the need to share trade secrets increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position, business, financial condition, results of operations, and prospects would be harmed. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed. The exposure of our trade secrets and other proprietary information would impair our competitive advantages and could have a material adverse effect on our

business, financial condition and results of operations. In particular, a failure to protect our proprietary rights may allow competitors to copy our technology, which could adversely affect our pricing and market share. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized. Intellectual property rights do not necessarily address all potential threats to our competitive advantage. The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. For example: • others may be able to make precision medicines that are similar to ours but that are not covered by the claims of the patents that we own or have exclusively licensed; • we or our licensors or future collaborators might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or have exclusively licensed; • we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions; • others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights; • it is possible that our pending patent applications or those that we may own in the future will not lead to issued patents; • issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors; • the patents of others may harm our business; • we may choose not to seek patent protection for some of our proprietary technology to maintain certain trade secrets or know- how, and a third - party may subsequently file a patent covering such trade secrets or know- how; • our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; and • we may not develop additional proprietary technologies that are patentable; Should any of these events occur, they could significantly harm our business, financial condition, results of operations and prospects. Risks Related to Government Regulation Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set. In the United States, the EU and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U. S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private payors. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following: • an annual, non- deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs; • an increase to the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and an extension the rebate program to individuals enrolled in Medicaid managed care organizations; • a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; • expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133 % of the federal poverty level, thereby potentially increasing a manufacturer' s Medicaid rebate liability; • a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70 % point- of- sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer' s outpatient drugs to be covered under Medicare Part D; • a new Patient- Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and • establishment of a Center for Medicare and Medicaid Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Since its enactment, there have been judicial, executive and congressional challenges to certain aspects of the ACA. On June 17, 2021, the U. S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the U. S. Supreme Court' s decision, President Biden issued an executive order initiating a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare. In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, led to aggregate reductions of Medicare payments to providers. These reductions went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional action is taken by Congress. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. The American Rescue Plan Act of 2021 was also signed into law, which eliminates the statutory Medicaid drug rebate cap, ~~currently set~~ **beginning January 1, 2024. The rebate was previously capped** at 100 % of a drug' s average manufacturer price ~~, beginning January 1, 2024~~ . Moreover, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law, which among other things, includes prescription drug provisions that have significant implications for the pharmaceutical industry and beneficiaries, including extending enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025, allowing the federal government to negotiate a maximum fair price for certain high- priced single source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price

negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out- of- pocket prescription drug costs for beneficiaries **. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations, although the drug price negotiation program is currently subject to legal challenges. For that and other reasons, it is currently unclear how the IRA will be effectuated** . The implementation of cost containment measures, including the prescription drug provisions under the IRA, as well as other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved. Complying with any new legislation and regulatory changes could be time- intensive and expensive, resulting in a material adverse effect on our business. Individual states in the United States have also 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. Legally- mandated price controls on payment amounts by third- party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. Furthermore, there has been increased interest by third **-** party payors and governmental authorities in reference pricing systems and publication of discounts and list prices. These reforms could reduce the ultimate demand for our product candidates or put pressure on our product pricing. In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than **EU** ~~European Union~~ , law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most **EU** ~~European Union~~ member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever- increasing **EU** ~~European Union~~ and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post- approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the United States and European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States, the EU or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability. Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third- party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties. Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third- party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. Such laws include: • the U. S. federal Anti- Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under any U. S. federal healthcare program, such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation; • the U. S. federal civil and criminal false claims and civil monetary penalties laws, including the civil False Claims Act, which prohibit, among other things, including through civil whistleblower or qui tam actions, individuals or entities from knowingly presenting, or causing to be presented, to the U. S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U. S. federal government. Pharmaceutical manufacturers can cause false claims to be presented to the U. S. federal government by engaging in impermissible marketing practices, such as the off- label promotion of a product for an indication for which it has not received FDA approval. In addition, the government may assert that a claim including items and services resulting from a violation of the U. S. federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act; • the Health Insurance Portability and Accountability Act, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U. S. federal Anti- Kickback Statute, a person or entity does not need to have actual knowledge of the healthcare fraud statute implemented under HIPAA or specific intent to violate it in order to have committed a violation; • the Federal Food Drug or Cosmetic Act, or FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices; • the U.

S. Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children' s Health Insurance Program, with specific exceptions, to report annually to the government information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non- physician practitioners (nurse practitioners, certified nurse anesthetists, physician assistants, clinical nurse specialists, anesthesiology assistants and certified nurse midwives), and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members; • federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; • analogous U. S. state laws and regulations, including: state anti- kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third- party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry' s voluntary compliance guidelines and the relevant compliance guidance promulgated by the U. S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; and state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; state and local laws requiring the registration of pharmaceutical sales representatives; • the U. S. Foreign Corrupt Practices Act of 1977, as amended, which prohibits, among other things, U. S. companies and their employees and agents from authorizing, promising, offering, or providing, directly or indirectly, corrupt or improper payments or anything else of value to foreign government officials, employees of public international organizations and foreign government owned or affiliated entities, candidates for foreign political office, and foreign political parties or officials thereof; and • similar healthcare laws and regulations in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government- funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non- compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits 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 are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time- consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition. The regulatory environment surrounding information security, data collection and privacy is increasingly demanding. We are subject to numerous U. S. federal and state laws and non- U. S. regulations governing the protection of personal and confidential information of our clinical patients, clinical investigators, employees and vendors / business contacts, including in relation to medical records, credit card data and financial information. Outside the United States, an increasing number of laws, regulations, and industry standards apply to data privacy and security. For example, in Europe, European Union General Data Protection Regulation, or GDPR, went into effect in May 2018, implementing more stringent requirements in relation to our use of personal data. The GDPR applies to any company established in the European Economic Area, or EEA, as well as to those outside the EEA if they collect and use personal data in connection with the offering of goods or services to individuals in the EEA or the monitoring of their behavior. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to € 20 million or 4 % of the annual global revenues of the noncompliant company, whichever is greater. Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the U. S., and the efficacy and longevity of current transfer mechanisms between the EU and the U. S. remains uncertain ~~. For example~~ , ~~in 2016, the EU~~ and **the efficacy and longevity of current** ~~U. S. agreed to a~~ transfer ~~framework for data transferred~~ **mechanisms between the EEA, and the United States remains uncertain. Case law** from ~~the EU to the U. S., called the Privacy Shield, but in July 2020,~~ the Court of Justice of the European Union, or CJEU, **states that reliance** ~~invalidated the Privacy Shield for purposes of international transfers and imposed further restrictions~~ on the ~~use of~~ standard contractual clauses ~~,~~ ~~or SCCs~~ **- a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism- alone may not necessarily be sufficient in all circumstances and that transfers must be assessed on a case- by- case basis** . ~~In March~~ **On October 7,** 2022, ~~the US~~ **President Biden signed** ~~and~~ **an** ~~EU announced a~~ **Executive Order on ' Enhancing Safeguards for United States Intelligence Activities' which introduced** new ~~regulatory regime intended~~ **redress mechanisms and binding safeguards** to ~~replace~~ **address** the ~~invalidated~~ **concerns raised by the CJEU in** ~~regulations~~ ~~---~~ **relation** ~~; however, this~~ **to data transfers from the EEA to the United States and which formed the basis of the** new EU- US Data Privacy Framework **, or DPF,** ~~has~~ **as released** ~~not been implemented beyond an executive order signed by President Biden~~ on ~~October 7~~ **December 13** , 2022 **. The European Commission adopted its Adequacy Decision in relation to the DPF** on ~~Enhancing Safeguards~~ **July 10, 2023, rendering the DPF effective as a GDPR transfer mechanism to U. S. entities**

self- certified under the DPF. The DPF also introduced a new redress mechanism for **EU citizens which addresses a key concern in** ~~United States Signals Intelligence Activities. European court and regulatory decisions subsequent to~~ the **previous** CJEU **judgments and may mean** ~~decision of July 16, 2020 have taken a restrictive approach to international data~~ transfers **under standard contractual clauses are less likely to be challenged in future** . **We currently rely** ~~As supervisory authorities issue further guidance~~ on ~~personal data export mechanisms, including circumstances where~~ the **EU standard contractual clauses** ~~SCCs cannot be used,~~ and ~~/ or start taking enforcement action~~ **the UK Addendum to the EU standard contractual clauses** , **as relevant** ~~we could suffer additional costs~~ , ~~complaints and / or regulatory investigations or fines, and / or if we are otherwise unable~~ to transfer personal data ~~between~~ **outside the EEA** and **the UK** ~~among countries and regions in which we operate~~ , ~~it could affect~~ **including to the United States, with respect to both intragroup and third party transfers. We expect the existing legal complexity and uncertainty regarding international personal data transfers to continue. In particular, we expect the DPF Adequacy Decision to be challenged and international transfers to the United States and to the other** ~~manner in which we provide our services~~ **jurisdictions more generally to continue to be subject to enhanced scrutiny by regulators. As a result** , **we may have to make certain operational changes and we will have to implement revised standard contractual clauses and** ~~the~~ **other** ~~geographical location or segregation of our~~ relevant **documentation for existing data transfers within required time frames** ~~systems and operations, and could adversely affect our financial results~~ . Further, from January 1, 2021, companies have had to comply with the GDPR and also the **UK** ~~UKdata~~ -- **data** protection regime, which imposes separate but similar obligations to those under the GDPR. The UK GDPR mirrors the fines under the GDPR ~~,~~ **(** e. g. **,** fines up to the greater of € 20 million (£ 17. 5 million) or 4 % of global turnover **)** . ~~The relationship between~~ **On October 12, 2023,** the **UK Extension** ~~United Kingdom and the EU in relation~~ to ~~certain aspects of~~ **the DPF came into effect (as approved by the UK Government), as a UK GDPR** data ~~protection~~ **transfer mechanism to U. S. entities self- certified under the UK Extension to the DPF. As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional** ~~law~~ **laws** ~~remains unclear,~~ and ~~it is unclear~~ **regulations that may affect** how **we conduct business** ~~United Kingdom data protection laws and regulations will develop in the medium to longer term, and how data transfers to and from the United Kingdom will be regulated in the long term. The European Commission has adopted an adequacy decision in favor of the United Kingdom, enabling data transfers from EU member states to the United Kingdom without additional safeguards. However, the UK adequacy decision will automatically expire in June 2025 unless the European Commission re- assesses and renews / extends that decision~~ . In the United States, HIPAA imposes privacy, security and breach reporting obligations with respect to individually identifiable health information upon " covered entities " (health plans, health care clearinghouses and certain health care providers), and their respective business associates, individuals or entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. While we do not believe that we are currently acting as a covered entity or business associate under HIPAA and thus are not directly regulated under HIPAA, any person may be prosecuted under HIPAA' s criminal provisions either directly or under aiding- and- abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA- covered healthcare provider or research institution that has not satisfied HIPAA' s requirements for disclosure of individually identifiable health information. In addition, certain states govern the privacy and security of health- related and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. By way of example, the California Consumer Privacy Act, or CCPA, went into effect on January 1, 2020, and imposes increased privacy and security obligations on entities handling certain personal information of consumers or households, and gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that has increased the likelihood of, and risks associated with data breach litigation. The CCPA may increase our compliance costs and potential liability. Further, **the** ~~theCalifornia~~ -- **California** Privacy Rights Act, or CPRA, generally went into effect on January 1, 2023, and significantly amends the CCPA. It imposes additional data protection obligations on covered companies doing business in California, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also ~~creates~~ **created** a new California data protection agency specifically tasked to enforce the law, which would likely result in increased regulatory scrutiny of California businesses in the areas of data protection and security. Additional compliance investment and potential business process changes may also be required. Similar laws have passed in ~~Virginia, Colorado, Connecticut and Utah, and have been proposed in~~ other states and **are continuing to be proposed** at the **state and** federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition. If any person, including any of our employees, clinical trial collaborators or those with whom we share such information, negligently disregards or intentionally breaches our established controls with respect to clinical subject, clinical investigator or employee data, or otherwise mismanages or misappropriates that data, we could be subject to significant monetary damages, regulatory enforcement actions, fines and / or criminal prosecution in one or more jurisdictions. In addition, a data breach could result in negative publicity which could damage our reputation and have an adverse effect on our business, financial condition or results of operations. Risks Related to Our Common Stock Our stock price may be volatile and you may not be able to resell shares of our common stock at or above the price you paid. The trading price of our common stock could be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. These factors include those discussed in this " Risk Factors " section of this Annual Report on Form 10- K and others such as: • results from, and any delays

in, our clinical trials for **darovasertib (IDE196),** IDE397 ~~, darovasertib~~ , IDE161, or any other future clinical development programs, including public misperception of the results of our clinical trials; • announcements by academic or other third parties challenging the fundamental premises underlying our approach to treating cancer and / or biopharmaceutical product development; • announcements of regulatory approval or disapproval of our current or any future product candidates; • failure or discontinuation of any of our research and development programs; • manufacturing setbacks or delays of or issues with the supply of the materials for our product candidates; • announcements relating to, or results from, our GSK Collaboration Agreement; • announcements relating to future licensing, collaboration or development agreements; • delays in the commercialization of our current or any future product candidates; • public misperception regarding the use of our therapies; • acquisitions and sales of new products, technologies or businesses; • quarterly variations in our results of operations or those of our future competitors; • changes in earnings estimates or recommendations by securities analysts; • announcements by us or our competitors of new products, significant contracts, commercial relationships, acquisitions or capital commitments; • developments with respect to intellectual property rights; • our commencement of, or involvement in, litigation; • changes in financial estimates or guidance, including our ability to meet our future revenue and operating profit or loss estimates or guidance; • major changes in our board of directors or management; • new legislation in the United States relating to the sale or pricing of pharmaceuticals; • FDA or other U. S. or comparable foreign regulatory actions affecting us or our industry; • product liability claims or other litigation or public concern about the safety of our product candidates; • market conditions in the biopharmaceutical and biotechnology sectors, particularly as a result of the volatility in the market caused by the COVID- 19 pandemic, as well as adverse geopolitical and macroeconomic developments, such as the ongoing Ukraine- Russia conflict **, the Israel- Hamas conflict,** and related sanctions **, instability in the global banking system** , actual and anticipated changes in interest rates, economic inflation and the responses by central banking authorities to control such inflation; and • general economic and geo- political conditions in the United States and abroad. In addition, the stock markets in general, and the markets for biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility. In particular, the market prices of securities of smaller biotechnology have experienced dramatic fluctuations that often have been unrelated or disproportionate to the operating results of these companies. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. Furthermore, the trading price of our common stock may be adversely affected by third- parties trying to drive down the market price. Short sellers and others, some of whom post anonymously on social media, may be positioned to profit if our stock declines and their activities can negatively affect our stock price. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our management would be diverted from the operation of our business. An active, liquid and orderly market for our common stock may not be maintained, and you may not be able to resell your common stock. Prior to our initial public offering, or IPO, in May 2019, there was no public market for shares of our common stock. Our stock **currently trades** ~~recently began trading~~ on the Nasdaq Global Select Market, but we can provide no assurance that we will be able to maintain an active trading market on the Nasdaq Global Select Market or any other exchange in the future. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. An inactive market may also impair our ability to raise capital by selling shares and may impair our ability to acquire other businesses, applications, or technologies using our shares as consideration. Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall. If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. As of December 31, ~~2022~~ **2023** , we have outstanding a total of ~~48~~ **65** . ~~2~~ **0** million shares of common stock, of which the holders of approximately 2. 3 million shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock. In addition, as of December 31, ~~2022~~ **2023** , approximately ~~6~~ **11** . ~~7~~ **4** million shares of common stock that are either subject to outstanding options or reserved for future issuance under our existing equity incentive plan will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline. General Risks Our information technology systems, or those of our collaborators, CROs or other contractors or consultants, may fail or suffer security breaches, which could adversely affect our business. Security breaches, loss of data or financial assets, and other disruptions could compromise sensitive information related to our business or prevent us from accessing critical information and expose us to liability. We collect and maintain information in digital form that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information **, preclinical and clinical trial data, health- related information** and personal information **, or collectively, Confidential Information** . It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such ~~confidential~~ **Confidential** ~~information~~ **Information** , including both our own and that of third parties. We have established physical, electronic and organizational measures to safeguard and secure our systems to prevent a data compromise, and rely on commercially available systems, software, tools, and monitoring to provide security for our information technology systems and the processing, transmission and storage of digital information. We have also outsourced elements of our information technology infrastructure, and as a result a number of third- party vendors may or could have access to our ~~confidential~~ **Confidential** ~~information~~ **Information** . Our internal information technology systems and infrastructure, and those of our current and any future collaborators, contractors and consultants and other third parties on which we rely, are vulnerable

to attack, damage and interruption from computer viruses, malware (e. g. ransomware), malicious code **, misconfigurations, " bugs " or other vulnerabilities** , natural disasters, terrorism, war, telecommunication and electrical failures, hacking, cyberattacks or intrusions over the Internet, phishing attacks and other social engineering schemes, attachments to emails, human error, fraud, denial or degradation of service attacks, sophisticated nation- state and nation- state- supported actors, employee theft or misuse, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption or data loss, particularly through **cyberattacks** ~~cyber- attacks~~ or cyber- intrusion, including by computer hackers, foreign governments and cyber- terrorists, has generally increased as the number, level of persistence, intensity and sophistication of attempted attacks and intrusions from around the world have increased. Emerging and evolving cybersecurity threats such as the attack on SolarWinds and the Log4j vulnerability reported in December 2021 pose unique challenges and involve sophisticated threat actors. In addition, the pervasive use of mobile devices that access ~~confidential~~ **Confidential** ~~information~~ **Information** increases the risk of data security breaches, which could lead to the loss of ~~confidential~~ **Confidential** ~~information~~ **Information** ~~or other intellectual property~~ , including both our own and that of third parties. As a result of the ~~COVID- 19 pandemic, and~~ continuing hybrid working environment, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities ~~. Furthermore, as a result of the ongoing conflict between Russia and the Ukraine, in February 2022 the U. S. Cybersecurity and Infrastructure Security Agency issued a" Shields Up" alert for American organizations noting the potential for Russia' s cyberattacks on Ukrainian government and critical infrastructure organizations to impact organizations both within and beyond the United States, particularly in the wake of sanctions imposed by the United States and its allies~~ . We rely on industry- accepted security measures and technology to securely maintain all confidential and proprietary information on our information systems. We have devoted and will continue to devote significant resources to the security of our ~~computer~~ **information technology** systems, but they may still be vulnerable to these threats. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. The costs to us to mitigate network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position. **There can also be no assurance that our programs, and our future collaborators', contractors' and consultants' cybersecurity risk management programs and processes, including policies, controls or procedures, will be fully implemented, complied with or effective in protecting our systems, networks and Confidential Information.** We and certain of our service providers are from time to time subject to cyberattacks and security incidents. While we do not believe that we have experienced any significant system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs. For example, the loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Moreover, if a computer security breach affects our systems or results in the unauthorized release of personally identifiable information, our reputation could be materially damaged. In addition, such a breach may require notification to governmental agencies, the media or individuals pursuant to applicable privacy and security laws. We would also be exposed to a risk of loss, including financial assets ~~or ,~~ litigation and potential liability **and significant incident response** , **system restoration or remediation and future compliance costs, all of** which could materially adversely affect our business, financial condition, results of operations and prospects. We maintain cyber liability insurance; however, this insurance may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems. If we engage in future acquisitions or strategic collaborations, it may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and subject us to other risks. We may evaluate various acquisitions and strategic collaborations, including licensing or acquiring complementary products, intellectual property rights, technologies, or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including: • increased operating expenses and cash requirements; • the assumption or incurrence of additional indebtedness or contingent liabilities; • the issuance of our equity securities; • assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel; • the diversion of our management' s attention from our existing product programs and initiatives in pursuing such a strategic merger or acquisition; • loss of key personnel, and uncertainties in our ability to maintain key business relationships; • uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and • our inability to generate revenue from acquired technology and / or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs. In addition, if we undertake acquisitions, we may incur large one- time expenses and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business. We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in- licenses. Our programs may require the use of intellectual property rights held by third parties to which we do not have rights. In such a case, the growth of our business will depend in part on our ability to acquire, in- license or use these rights. However, we may be unable to acquire or in- license any compositions, methods of use, processes or other third- party intellectual property rights from third parties that we identify as necessary for our product candidates on reasonable terms and conditions or at all. The acquisition or licensing of intellectual property rights for pharmaceutical products is very competitive. If we seek to acquire or license additional

intellectual property rights, we may face substantial competition from a number of more established companies, some of which have acknowledged strategies to license or acquire products, and many of which have more institutional experience and greater financial and other resources than we have. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities, as may other emerging companies taking similar or different approaches to product licenses and / or acquisitions. In addition, a number of established research-based pharmaceutical and biotechnology companies may acquire products in late stages of development to augment their internal product lines, which may provide those companies with an even greater competitive advantage. Furthermore, companies that perceive us to be a competitor may be unwilling to assign or license rights to us or may interfere with our acquisition or licensing of rights from others. We also may be unable to license or acquire third- party intellectual property rights on terms that would allow us to make an appropriate return on our investment. We have collaborated with U. S. academic institutions and may in the future collaborate with U. S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. These institutions may provide us with an option to negotiate a license to any of the institution' s rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to successfully obtain rights to required third- party intellectual property rights or maintain the existing intellectual property rights we have on reasonable terms, we may have to abandon development of that program and our competitive position, business, financial condition, results of operations, and prospects could suffer. If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential collaborators or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations and prospects. Changes in patent law in the United States or in other countries could diminish the value of patents in general, thereby impairing our ability to protect our product candidates. Our patent rights may be affected by developments or uncertainty in the United States' or other jurisdictions' patent statutes, patent case law, USPTO rules and regulations or the rules and regulations of other jurisdictions' patent offices. There are a number of recent changes to U. S. patent laws that may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, on September 16, 2011, the Leahy- Smith America Invents Act, or Leahy- Smith Act, was signed into law. The Leahy- Smith Act includes a number of significant changes to U. S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy- Smith Act, the United States transitioned in March 2013 to a " first to file " system in which the first inventor to file a patent application is typically entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and may become involved in post- grant proceedings including opposition, derivation, reexamination, inter partes review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. In addition, the U. S. congress may pass additional patent reform legislation that is unfavorable to us. The 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 to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on decisions by the U. S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future. Similarly, statutory or judicial changes to the patent laws of other countries may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. We may not be able to protect our intellectual property rights throughout the world. Filing, prosecuting and defending all current and future patents in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. The legal systems of many foreign countries do not favor the enforcement of patents and other intellectual property

protection, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights. For example, some foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, some countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected. **Further, on June 1, 2023, the European Union Patent Package (EU Patent Package) regulations were implemented with the goal of providing a single pan- European Unitary Patent and a new European Unified Patent Court (UPC) for litigation involving European patents. As a result, all European patents, including those issued prior to ratification of the EU Patent Package, now by default automatically fall under the jurisdiction of the UPC. It is uncertain how the UPC will impact granted European patents in the biotechnology and pharmaceutical industries. Our European patent applications, if issued, could be challenged in the UPC. During the first seven years of the UPC' s existence, the UPC legislation allows a patent owner to opt its European patents out of the jurisdiction of the UPC. We may decide to opt out our future European patents from the UPC, but doing so may preclude us from realizing the benefits of the UPC. Moreover, if we do not meet all of the formalities and requirements for opt- out under the UPC, our future European patent applications and patents could remain under the jurisdiction of the UPC. The UPC will provide our competitors with a new forum to centrally revoke our European patents, and allow for the possibility of a competitor to obtain pan- European injunction. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize our technology and product candidates and, resultantly, on our business, financial condition, prospects and results of operations.** 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 provisions during the patent process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and / or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and / or applications. We employ reputable professionals and rely on such third parties to help us comply with these requirements and effect payment of these fees with respect to the patents and patent applications that we own, and if we license intellectual property we may have to rely upon our licensors to comply with these requirements and effect payment of these fees with respect to any patents and patent applications that we license. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case. If securities or industry analysts do not continue to publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline. The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline. We incur significant costs as a result of operating as a public company, and our management devotes substantial time to new compliance initiatives. We may fail to comply with the rules that apply to public companies, including Section 404 of the Sarbanes- Oxley Act of 2002, which could result in sanctions or other penalties that would harm our business. We incur significant legal, accounting and other expenses as a public company, including costs resulting from public company reporting obligations under the Exchange Act and regulations regarding corporate governance practices. The listing requirements of the Nasdaq Global **Select** Market and the rules of the Securities and Exchange Commission, or SEC, require that we satisfy certain corporate governance requirements relating to director independence, filing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel devote a substantial amount of time to ensure that we comply with all of these requirements. Moreover, the reporting requirements, rules and regulations will increase our legal and financial compliance costs and make some activities more time- consuming and costly. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as executive officers, or to obtain certain types of insurance, including D & O insurance, on acceptable terms. As a public company, we are subject to Section 404 of the Sarbanes- Oxley Act of 2002, or Section 404, and the related rules of the SEC, which generally require our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. **This assessment** ~~Beginning with the second annual report that we~~ will **need** ~~be required~~ to **include disclosure of** ~~file with the~~

~~SEC, Section 404 requires an~~ **any** ~~annual~~ **material weaknesses identified by our** management **in** ~~assessment of the effectiveness of~~ our internal control over financial reporting. ~~However~~ **Additionally** , ~~for so long~~ as ~~we remain~~ **a result of our ceasing to be** an emerging growth company **and being deemed a large accelerated filer** as ~~defined in the Jumpstart Our Business Startups Act~~ of **January 1,** ~~2012~~ **2024** , **commencing** ~~or JOBS Act, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not emerging growth companies, including, but not limited to, not being required to comply~~ with **this Annual Report on Form 10- K** ~~the auditor attestation requirements of Section 404. Once we are no longer an emerging growth company or~~ **for** , ~~if prior to such date, we opt to no longer take advantage of~~ the ~~applicable exemption~~ **year ending December 31** , **2023,** ~~we will be required to include an opinion from~~ our independent registered public accounting firm **is required to issue an opinion** on the effectiveness of our internal control over financial reporting. We **expect to incur significant expenses and devote substantial management effort toward ensuring compliance with the auditor attestation requirements of Section 404. Furthermore, we** will ~~remain~~ **also have to file a more expansive proxy statement** ~~an~~ **and be subject to shorter filing deadlines** ~~emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of our IPO~~ , ~~(b) in~~ which **will require additional time and expense as well** ~~we have total annual gross revenue of at least $ 1~~ . ~~235 billion~~ **It may require significant resources and management oversight to maintain and** , **if necessary, improve** ~~or~~ **our** ~~(c) in~~ **disclosure controls and procedures and internal control over financial reporting to meet this standard. As a result, management' s attention may be diverted from other business concerns,** which **could adversely affect our business and operating results. To comply with these requirements,** we ~~are deemed~~ **may need** to ~~be a large accelerated filer~~ **hire more employees in the future or engage outside consultants** , which **would increase** ~~means the market value of~~ our **costs** ~~common stock that is held by non- affiliates exceeds $ 700. 0 million as of the prior June 30th,~~ and **expenses** ~~(2) the date on which we have issued more than $ 1. 0 billion in non- convertible debt during the prior three- year period~~ . In order to provide the reports required by these rules, we must conduct reviews and testing of our internal controls. During the course of our review and testing, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal control over financial reporting, we may not detect errors on a timely basis and our audited financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we are required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. In order to report our results of operations and financial statements on an accurate and timely basis, we will depend on CROs and contract manufacturing organizations, or CMOs, to provide timely and accurate notice of their costs to us and on GSK to provide timely and accurate reports of cost sharing under the GSK Collaboration Agreement. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from the Nasdaq Global **Select** Market or other adverse consequences that would materially harm to our business. If we are unable to maintain effective internal controls, our business, financial position, results of operations and prospects could be adversely affected. As a public company, we are subject to reporting and other obligations under the Exchange Act, including Section 404, which require annual management assessments of the effectiveness of our internal control over financial reporting. ~~However~~ **As a result of our ceasing to be an emerging growth company and being deemed a " large accelerated filer " as of January 1, 2024, commencing with this Annual Report on Form 10- K for the year ending December 31, 2023** , our independent registered public accounting firm will ~~not~~ be required to formally attest to the effectiveness of our internal control over financial reporting pursuant to Section 404 ~~until we are no longer an emerging growth company if we continue to take advantage of the exemptions available to us through the JOBS Act~~ . The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes- Oxley Act of 2002. These reporting and other obligations place significant demands on our management and administrative and operational resources, including accounting resources **, which we expect to further increase in 2024 when we are no longer be an emerging growth company and are deemed a large accelerated filer** . Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States. Any failure to maintain effective internal controls could have an adverse effect on our business, financial position, and results of operations. ~~We are an " emerging growth company, " and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors. We are an " emerging growth company, " as defined in the JOBS Act. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor' s report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a non- binding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. As a result, the information we provide stockholders will be different than the information that is available with respect to other public companies. We cannot predict whether investors will find our common stock less attractive because we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our~~

~~common stock, and our stock price may be more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards, and, therefore, we are subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.~~ If we sell shares of our common stock in future financings, stockholders may experience immediate dilution and, as a result, our stock price may decline. We may from time to time issue additional shares of common stock at a discount from the current trading price of our common stock. As a result, our stockholders would experience immediate dilution upon the purchase of any shares of our common stock sold at such discount. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, preferred stock or common stock. If we issue common stock or securities convertible into common stock, our common stockholders would experience additional dilution and, as a result, our stock price may decline. Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited. We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an " ownership change, " generally defined as a greater than 50 percentage point change (by value) in its ~~equity~~ **stock** ownership by certain stockholders over a three- year period, the corporation' s ability to use its pre- change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research and development tax credits) to offset its post- change taxable income ~~or tax liability~~ may be limited. As a result of such ownership changes, our ability to utilize certain NOLs and other tax attributes may be permanently limited if such attributes will expire unused. ~~If finalized, Treasury Regulations currently proposed under Section 382 of the Code may further limit our ability to utilize our pre- change NOLs or credits if we undergo a future ownership change.~~ We have experienced ownership changes in the past, and we may experience ownership changes in the future due to subsequent shifts in our stock ownership (some of which may be outside our control). As a result, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes **to offset** ~~, which could potentially result in increased~~ future **taxable income** ~~tax liability to us~~. Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management. Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent changes in control or changes in our management without the consent of our board of directors. These provisions include the following: • a classified board of directors with three- year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors; • no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates; • the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors; • the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquiror; • the ability of our board of directors to alter our amended and restated bylaws without obtaining stockholder approval; • the required approval of at least 66 2 / 3 % of the shares entitled to vote at an election of directors to adopt, amend or repeal our amended and restated bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors; • a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders; • the requirement that a special meeting of stockholders may be called only by our chief executive officer or president or by the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and • advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror' s own slate of directors or otherwise attempting to obtain control of us. We are also subject to the anti- takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15 % or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction. Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us. Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law. In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that: • we will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person' s conduct was unlawful; • we may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law; • we are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification; • we will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to

indemnification; • the rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons; and • we may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents. If the costs of maintaining adequate D & O insurance coverage increase significantly in the future, our operating results could be materially adversely affected. Likewise, if any of our current D & O insurance coverage should become unavailable to us or become economically impractical, we may need to decrease our coverage limits or increase our self- insured retention or we may be unable to renew such insurance at all. If we incur liabilities that exceed our coverage or incur liabilities not covered by our insurance, we would have to self- fund any indemnification amounts owed to our directors and officers and employees in which case our results of operations and financial condition could be materially adversely affected. Additionally, a lack of 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. Our amended and restated certificate of incorporation provides for an exclusive forum in the Court of Chancery of the State of Delaware and in the U. S. federal district courts for certain disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees. Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for any state law derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, any action to interpret, apply, enforce, or determine the validity of our amended and restated certificate of incorporation or amended and restated bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine. The choice of forum provision may limit a stockholder' s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees and result in increased costs for investors to bring a claim. We do not intend to pay dividends on our common stock, and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock. We do not intend to pay any cash dividends on our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, you are not likely to receive any dividends on your common stock for the foreseeable future. Since we do not intend to pay dividends, your ability to receive a return on your investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.