Risk Factors Comparison 2025-03-31 to 2024-02-08 Form: 10-K

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

You should carefully consider the risks described below in addition to the other information set forth in this Annual Report on Form 10- K, including the Management' s Discussion and Analysis of Financial Condition and Results of Operations section and the ~~consolidated~~ **Consolidated** ~~financial~~ **Financial** ~~statements~~ **Statements** and related notes. These risks, some of which have occurred and any of which may occur in the future, can have a material adverse effect on our business, financial condition, results of operations or the price of our publicly traded securities. The risks described below are not the only risks we face. Additional risks and uncertainties not currently known to us, or that we currently deem to be immaterial, may occur or become material in the future and adversely affect our business, reputation, financial condition, results of operations or the price of our publicly traded securities. Therefore, historical operating results, financial and business performance, events and trends are often not a reliable indicator of future operating results, financial and business performance, events or trends. If any of the following risks occurs, our business, financial condition, and results of operations and future growth prospects could be materially and adversely affected. RISKS RELATING TO OUR FINANCIAL RESULTS AND NEED FOR FINANCING We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. We will require substantial funds to maintain our research and development program and support operations **in the near term** . We have incurred losses and negative cash flows from operations since our inception. As of December 31, ~~2023~~ **2024** , we had $ ~~56~~ **20** . ~~3~~ **0** million in ~~existing~~ cash ~~,~~ **and** cash equivalents **. In March 2025, we completed a registered direct offering** and ~~investments~~ **concurrent private placement for net proceeds of approximately $ 9. 0 million** . We expect these available cash resources **, together with the proceeds from the March 2025 offering,** to fund our **existing** ~~operating~~ **operations** ~~expenses and capital expenditure requirements~~ into **the fourth quarter of** 2025. We have based this assessment on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. Based on our current cash ~~,~~ **and** cash equivalents ~~, and investments~~ , recurring losses and cash outflows from operations since inception, an expectation of continuing losses and cash outflows from operations for the foreseeable future and the need to raise additional capital to finance our future operations, we have concluded that we do not have sufficient cash on hand to support current operations beyond the next 12 months from the date of filing this Annual Report on Form 10- K. We will require **substantial** additional funding **in the immediate term** to fund the development of emavusertib through regulatory approval and commercialization, and to support our continued operations. We will need to seek additional funding through a number of potential avenues, including private or public equity financings, collaborations, or other strategic transactions ~~as needed~~ **. We have faced and expect to continue to face substantial difficulty in raising capital** . If ~~we~~ **sufficient funds** are **not available** ~~unable to obtain sufficient funding~~ , we will **have** ~~be forced~~ to delay, reduce ~~in~~ **the** scope **of,** or eliminate our research and development program for emavusertib, including related clinical trials and operating expenses, potentially delaying the time to market for ~~,~~ or preventing the marketing of ~~,~~ emavusertib, which ~~could~~ **would** adversely affect our business prospects and our ability to continue **our** operations, and would have a negative impact on our financial condition and ~~our~~ ability to pursue our business strategies **. In addition, we may seek to engage in one or more strategic alternatives, such as a strategic partnership with one or more parties, the licensing, sale or divestiture of some of our assets or proprietary technologies or the sale of our company, but there can be no assurance that we would be able to enter into such a transaction or transactions on a timely basis or on terms favorable to us, or at all. If we are unable to obtain sufficient capital, we would be unable to fund our operations and may be required to evaluate alternatives, which could include dissolving and liquidating our assets or seeking protection under the bankruptcy laws, and a determination to file for bankruptcy could occur at a time that is earlier than when we would otherwise exhaust our cash resources. If we decide to dissolve and liquidate our assets or to seek protection under the bankruptcy laws, it is unclear to what extent we would be able to pay our obligations, and, accordingly, it is further unclear whether and to what extent any resources would be available for distributions to stockholders** . If we are unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our audited financial statements, and it is likely that investors will lose all or a part of their investment. The report from our independent registered public accounting firm issued in connection with this Annual Report on Form 10- K contains, and future reports may contain, statements expressing substantial doubt about our ability to continue as a going concern. If we seek additional financing to fund our business activities in the future and there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide funding to us on commercially reasonable terms, if at all. We have incurred substantial losses, expect to continue to incur substantial losses for the foreseeable future and may never generate significant revenue or achieve **or maintain** profitability. We have incurred significant annual net operating losses in every year since our inception. We expect to continue to incur significant and increasing net operating losses for at least the next several years. Our net loss was $ ~~47~~ **43** . 4 million for the year ended December 31, ~~2023~~ **2024** . As of December 31, ~~2023~~ **2024** , we had an accumulated deficit of $ 1. 2 billion. As noted above, we have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. We have not completed the development of any drug candidate on our own. Other than Erivedge ®, which is being commercialized and further developed by Genentech and Roche under our collaboration agreement with Genentech, we may never have a drug candidate approved for commercialization. Since our inception, we have funded our operations primarily through private and public placements of our equity securities, license fees, contingent cash payments, research and development funding from our corporate collaborators and the monetization of certain royalty rights. We have devoted substantially all of our financial resources and efforts to research and development and general

and administrative expense to support such research and development. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. We anticipate that our expenses will increase substantially if and as we: • continue to develop and conduct clinical trials for emavusertib; • seek regulatory and marketing approvals for emavusertib, if it successfully completes clinical trials; • maintain, expand, and protect our intellectual property portfolio; • hire and retain additional personnel; • require the manufacture of larger quantities of emavusertib for clinical development and, potentially, commercialization; • establish sales, marketing, distribution and other commercial infrastructure in the future to commercialize various drugs for which we may obtain marketing approval, if any; • add equipment and physical infrastructure as may be required to support our research and development program; • seek to identify and develop additional drug candidates; and • acquire or in- license other drug candidates or technologies. Our ability to become and remain profitable depends on our ability to generate significant revenue. Our only current source of revenues comprises licensing and royalty revenues that we earn under our collaboration with Genentech related to the development and commercialization of Erivedge. A significant portion of our royalty and royalty related revenues under our collaboration with Genentech will be paid to TPC Investments I LP and TPC Investments II LP, or the Purchasers, pursuant to the royalty interest purchase agreement we and Curis Royalty entered into with the Purchasers and Lind SA LLC, or Agent, on March 22, 2019, or the Oberland Purchase Agreement. ~~In addition, in March 2023, Curis and Curis Royalty received a letter from counsel to Oberland Capital Management, LLC, the Purchasers and the Agent alleging certain defaults under the Oberland Purchase Agreement as described further below under " The alleged events of default, or any future allegations of an event of default, under the Oberland Purchase Agreement could have a material adverse effect on our business, financial condition and stock price, including our ability to continue as a going concern. " We have not received any further communication on this topic from counsel to Oberland Capital Management, LLC or the Purchasers and the Agent since the March 2023 letter. As of December 31, 2023, the estimated amount of the Put / Call Price, as defined below, is $ 56. 9 million. If Oberland elects to pursue such claims, and if Curis and Curis Royalty are unsuccessful in defending against such claims, it could have a material adverse impact on Curis and Curis Royalty, including their ability to continue as a going concern.~~ We do not expect to generate significant revenues other than those related to Erivedge unless and until we are, or any collaborator is, able to obtain marketing approval for, and successfully commercialize emauvsertib. Successful commercialization will require achievement of key milestones, including initiating and successfully completing clinical trials of emavusertib, obtaining marketing approval for emavusertib, manufacturing, marketing, and selling those drugs for which we, or any of our collaborators, may obtain marketing approval, satisfying any post marketing requirements and obtaining reimbursement for our drugs from private insurance or government payors. Because of the uncertainties and risks associated with these activities, we are unable to accurately predict the timing and amount of revenues and whether or when we might achieve profitability. We and any collaborators may never succeed in these activities and, even if we do, or any collaborators do, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of drug candidates, or continue our operations and cause a decline in the value of our common stock. We will require substantial additional capital, which may be difficult to obtain, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our drug development program or commercialization efforts **, and our ability to continue operations could be adversely affected** . We will require substantial funds to continue our research and development program for emavusertib and to fulfill our planned operating goals. Our planned operating and capital requirements currently include the support of our current and future research and development activities for emavusertib, as well as other candidates we have, and may continue to license under our collaboration with Aurigene. We will require substantial additional capital to fund the further development of emavusertib, as well as to fund our general and administrative costs and expenses. Moreover, our agreements with collaborators impose significant potential financial obligations on us. For example, under our collaboration, license and option agreement with Aurigene, we are required to make milestone and royalty fee payments, which impose significant potential financial obligations on us. **In March 2025, we completed a registered direct offering and concurrent private placement for net proceeds of approximately $ 9. 0 million.** Based upon our current operating plan, we believe that our existing cash ~~,~~ **and** cash equivalents ~~and investments~~ of $ ~~56~~ **20** . ~~3~~ **0** million as of December 31, ~~2023~~ **2024 , together with the proceeds from the March 2025 offering** , should enable us to fund our **existing** ~~operating~~ **operations** ~~expenses and capital expenditure requirements~~ into **the fourth quarter of** 2025. We have based this assessment on assumptions that may prove to be wrong, and it is possible that we will not achieve the progress that we expect with these funds because the actual costs and timing of clinical development and regulatory and commercial activities are difficult to predict and are subject to substantial risks and delays, and that we will use our capital resources sooner than we currently expect. This estimate does not reflect any additional expenditures that may result from any further strategic transactions to expand and diversify our product pipeline, including acquisitions of assets, businesses, rights to products, drug candidates or technologies or strategic alliances or collaborations that we may pursue. Our ability to raise additional funds in the future will depend on financial, economic and market conditions, many of which are outside of our control, and we may be unable to raise financing when needed, or on terms favorable to us, or at all. Furthermore, high volatility and instability in the capital markets, interest rate fluctuations, heightened inflation, and economic uncertainty have resulted in a significant disruption of the biotechnology financial markets and have had, and could continue to have, a negative impact on the price of our common stock and ability to raise capital. If the disruption persists and deepens, we could continue to experience an inability to raise additional funds, and our cost of financing or restrictions on our access to potential sources of liquidity could persist. If we are unable to obtain sufficient funding, we may be forced to delay, reduce in scope or eliminate our research and development program for emavusertib, including related clinical trials and operating expenses, potentially delaying the time to market for, or preventing

the marketing of, emavusertib. In addition, we may seek to engage in one or more strategic alternatives, such as a strategic partnership with one or more parties, the licensing, sale or divestiture of some of our assets or proprietary technologies or the sale of our company, but there can be no assurance that we would be able to enter into such a transaction or transactions on a timely basis or on terms favorable to us, or at all. Our failure to raise capital through a financing or strategic alternative as and when needed could adversely affect our business prospects and our ability to continue operations, and would have a negative impact on our financial condition and our ability to pursue our business strategy. If we are unable to raise sufficient capital we would be unable to fund our operations and may be required to evaluate alternatives, which could include dissolving and liquidating our assets or seeking protection under the bankruptcy laws, and a determination to file for bankruptcy could occur at a time that is earlier than when we would otherwise exhaust our cash resources. In ~~March~~ **February** ~~2021~~ **2024** , we entered into ~~a~~ **an amended and restated** sales agreement, or the ~~2021~~ **2024** Sales Agreement, with Cantor Fitzgerald & Co., or Cantor, and JonesTrading Institutional Services LLC, or JonesTrading, ~~pursuant~~ to **sell** ~~which,~~ from time to time ~~, we could offer and sell through Cantor and JonesTrading~~ up to $ 100. 0 million **shares** of our common stock **through an "** ~~registered under our universal shelf registration statement on Form S- 3 in one or more"~~ at- the- market ~~" offerings~~ **offering " program** ~~. To date, we have sold 229, 185 shares~~ under **which Cantor** ~~the 2021 Sales Agreement, representing gross proceeds of $ 6. 3 million. On February 8, 2024, we entered into an~~ **and** ~~amended and restated~~ **JonesTrading act as** sales **agents** ~~agreement, or the 2024 Sales Agreement, with Cantor and JonesTrading, which supersedes the 2021 Sales Agreement and pursuant to which, from time to time, we may offer and sell through Cantor and JonesTrading up to $ 100. 0 million of our common stock registered under our universal shelf registration statement on Form S- 3 in one or more" at- the- market" offerings~~ . The extent to which we utilize the 2024 Sales Agreement with Cantor and JonesTrading as a source of funding will depend on a number of factors, including the prevailing market price of our common stock, general market conditions and other restrictions and the extent to which we are able to secure funds from other sources. Accordingly, we may not be able to sell additional shares under the 2024 Sales Agreement at prices or amounts that we deem acceptable, and there can be no assurance that we will be able to sell any additional shares of common stock contemplated under the 2024 Sales Agreement **. We sold 188, 316 shares of common stock under the 2024 Sales Agreement representing gross proceeds of $ 1. 2 million during the twelve months ended December 31, 2024** . Furthermore, there are a number of factors that may affect our future capital requirements and further accelerate our need for additional working capital, many of which are outside our control, including the following: • unanticipated costs in our research and development program; • the timing and cost of obtaining regulatory approvals for emavusertib and maintaining compliance with regulatory requirements; • ~~the timing and amount of milestone payments, royalties and other payments, including~~ payments due to licensors, including Aurigene, for patent rights and technology used in our drug development ~~program~~ **programs** ~~; • unplanned costs to prepare, file, prosecute, defend, and enforce patent claims and other patent- related costs, including litigation costs and technology license fees~~ ; • the costs of commercialization activities for emavusertib if it receives marketing approval, to the extent such costs are our responsibility, including the costs and timing of establishing drug sales, marketing, distribution and manufacturing capabilities; • ~~unexpected losses in our cash investments or~~ **unplanned costs to prepare, file, prosecute, defend,** ~~an~~ **and enforce patent claims and** ~~inability to otherwise liquidate or access our cash investments due to unfavorable conditions in the~~ **other** ~~capital markets~~ **patent- related costs** , including ~~volatility~~ **litigation costs** and **technology license fees** ~~instability in the capital markets~~ ; and • **our ability to continue as a going concern. In connection with the Oberland Purchase Agreement, we transferred and encumbered certain royalty and royalty related payments on commercial sales of Erivedge; Curis Royalty granted a first priority lien and security interest in all of its assets, including its rights to the Erivedge royalty payments; and we granted the Purchasers a first priority lien and security interest in our equity interest in Curis Royalty. As a result, in the event of a default by us or Curis Royalty, Curis Royalty could lose all retained rights to certain future royalty and royalty related payments, Curis Royalty could be required to repurchase the Purchased Receivables at a price that is a multiple of the payments we have received, and our ability to enter into future arrangements may be inhibited, all of which could have a material adverse effect on our business, financial condition and stock price, including** our ability to continue as a going concern. Pursuant to the Oberland Purchase Agreement, the Purchasers acquired the rights to a portion of certain royalty and royalty related payments excluding a portion of non- U. S. royalties retained by Curis Royalty, referred to as the Purchased Receivables, owed by Genentech under our collaboration agreement with Genentech. In connection with entering into the Oberland Purchase Agreement, Curis Royalty and the Agent entered into a security agreement and Curis and the Purchasers entered into a pledge agreement. Following an event of default under the security agreement entered into between Curis Royalty and the Agent, the Agent has the right to stop all allocations of payments that would have otherwise been allocated to Curis Royalty pursuant to the Oberland Purchase Agreement and instead retain all such payments. In addition, the Oberland Purchase Agreement provides that after the occurrence of an event of default by Curis Royalty under the security agreement, as described below, the Purchasers shall have the option, for a period of 180 days, to require Curis Royalty to repurchase the Purchased Receivables at a price, referred to as the Put / Call Price, equal to 250 % of the sum of the upfront purchase price and any portion of the milestone payments paid in a lump sum by the Purchasers, if any, minus certain payments previously received by the Purchasers with respect to the Purchased Receivables. Pursuant to the security agreement, Curis Royalty granted to the Agent a first priority lien and security interest in all of its assets and all real, intangible and personal property, including all of its right, title and interest in and to the Erivedge royalty payments. The security interest secures the obligations of Curis Royalty arising under the Oberland Purchase Agreement, the security agreement or otherwise with respect to the due and prompt payment of (i) an amount equal to the Put / Call Price and (ii) all fees, costs, expenses, indemnities and other payments of Curis Royalty under or in respect of the Oberland Purchase Agreement and the security agreement. The obligations of Curis Royalty under the Oberland Purchase Agreement may be accelerated upon the occurrence of an event of default under the security agreement (subject to certain cure periods), which events of default include: • any royalty and royalty related payments to be remitted into a certain Curis Royalty designated

account controlled by the Agent pursuant to a control agreement, referred to as the royalty account, into which all royalty and royalty related payments must be paid by Curis or Curis Royalty are not so remitted in accordance with the Oberland Purchase Agreement; • any representation or warranty made by Curis or Curis Royalty in the Oberland Purchase Agreement or any other transaction document proves to be incorrect or misleading in any material respect when made; • a default by Curis or Curis Royalty in the performance of affirmative and negative covenants set forth in the Oberland Purchase Agreement or any other transaction document; • a default by Curis in the performance or observance of its indemnity obligations under the Oberland Purchase Agreement; • the failure by Genentech to pay material amounts owed under the Genentech collaboration agreement because of an actual breach or default by Curis under the Genentech collaboration agreement; • the failure of the security agreement to create a valid and perfected first priority security interest in any of the collateral; • a material breach or default by Curis under our agreement with Curis Royalty pursuant to which we transferred our rights to the royalty revenues under the Genentech collaboration agreement to Curis Royalty; • the voluntary or involuntary commencement of bankruptcy proceedings by either Curis or Curis Royalty and other insolvency related events; • any materially adverse effect on the binding nature of any of the Oberland Purchase Agreement, security agreement, pledge agreement or other transaction documents, the Genentech collaboration agreement or our agreement with Curis Royalty; • any person shall be designated as an independent director of Curis Royalty other than in accordance with Curis Royalty' s limited liability company operating agreement; or • Curis shall at any time cease to own, of record and beneficially, 100 % of the equity interests in Curis Royalty. Upon the occurrence and continuance of an event of default under the security agreement, the Agent may exercise its rights and remedies under the security agreement with respect to Curis Royalty and to the collateral pledged thereunder, including, among other things, acceleration of the obligations under the security agreement, the sale or other realization of the collateral and performance of Curis Royalty' s obligations under the purchase and sale agreement **that we entered into in 2012 with Curis Royalty pursuant to which we transferred to Curis Royalty rights to certain royalty and royalty- related payments owed by Genentech to us under our collaboration agreement with Genentech** . Additionally, Curis granted to the Agent a first priority lien and security interest of Curis' equity interest in Curis Royalty pursuant to a pledge agreement. Upon the occurrence and continuance of an event of default under the security agreement, the Agent may exercise its rights and remedies under the pledge agreement with respect to the equity interests, including, among other things, the rights to receive distributions and exercise voting rights with respect to the equity interests and to sell or otherwise realize upon the collateral in satisfaction of the obligations. The exercise by the Agent of the foregoing rights shall be deemed to constitute an exercise by the Purchasers of their put option under the Oberland Purchase Agreement . **If any of** ~~Although Curis and Curis Royalty dispute these -- the allegations,if Oberland elects~~ **above events of default were** to **occur** ~~pursue these claims,and if Curis and Curis Royalty are unsuccessful in defending against these claims~~ ,Curis Royalty may not have sufficient funds to pay the Put / Call Price ~~or other amounts claimed by the Purchasers~~ and the Agent could foreclose on the secured royalty and royalty related payment stream and / or our equity interests in Curis Royalty.In such an event,we could lose our right to royalty and royalty related payments not transferred to the Purchasers pursuant to the Oberland Purchase Agreement and we could lose our rights in Curis Royalty **.In addition,in the event Genentech exercises its set- off rights against royalty payments to Curis Royalty pursuant to our collaboration agreement with Genentech,Curis Royalty may be required to satisfy its royalty- sharing obligations to the Purchasers with amounts from its working capital** .The Oberland Purchase Agreement also contains exculpation and indemnification obligations of Curis and Curis Royalty on behalf of the Agent and the Purchasers ~~,and the Purchasers' claims,if successful,could result in liabilities of Curis and Curis Royalty~~ .Further,the encumbrance of all of Curis Royalty' s assets,including the right to royalties from sales of Erivedge,and our equity interests in Curis Royalty pursuant to the security agreement and pledge agreement,respectively,may inhibit us from raising additional funds or entering into other strategic arrangements. **Any of these consequences of** ~~Even if we are successful in defending against such claims,we may expend significant management time and -- an attention and funds to defend against such claims.In addition,in the~~ event ~~Genentech exercises its set-~~ **of default could have a material adverse effect on our business,financial condition and stock price,including our ability to continue as a going concern** . In March 2023, Curis and Curis Royalty received a letter from counsel to Oberland Capital Management, LLC, the Purchasers and the Agent alleging defaults under Sections 4. 04 and 6. 04 (b) of the Oberland Purchase Agreement and demanding cure of the asserted default under Section 6. 04 (b) of the Oberland Purchase Agreement ~~. The asserted basis for the alleged defaults is that Curis and Curis Royalty were required to disclose~~ , **which** ~~and failed to disclose, certain information prior to execution of the Oberland Purchase Agreement and that Curis and Curis Royalty have since failed to disclose certain information that has been requested by the Purchasers pursuant to Section 6. 04 (b) of the Oberland Purchase Agreement. The letter further alleges that these alleged defaults are events of default under the Oberland Purchase Agreement and that~~ each **such** alleged default separately entitles the Purchasers to exercise the put option, which would require Curis Royalty to repurchase the Purchased Receivables at the Put / Call Price. ~~The Purchasers have not attempted to exercise that put option but have purported to reserve their alleged right to exercise it without further notice. The Purchasers have also reserved other asserted rights in respect of the alleged defaults, including the asserted right to seek judicial remedies, including for damages and rescission, and to assert alleged claims against~~ Curis and Curis Royalty ~~for indemnification~~ **dispute these allegations. However, if Oberland elects to pursue these claims, and if Curis and Curis Royalty are unsuccessful in defending against these claims, it could have a material adverse impact** on **Curis and Curis Royalty, including** ~~the~~ **their ability to continue as a going concern** ~~basis of material breach and fraud in the inducement~~ . We have not received any further communication on this topic from counsel to Oberland Capital Management, LLC, or the Purchasers and the Agent since the March 2023 letter. As of December 31, ~~2023~~ **2024** , the estimated amount of the Put / Call Price is **approximately** $ ~~56~~ **110** . ~~9~~ **0** million . Although Curis and Curis Royalty dispute..... ability to continue as a going concern . The amount of royalty revenue Curis Royalty receives from sales of Erivedge has been adversely affected by a competing drug, and may further be affected in the future. Pursuant to the terms of our collaboration agreement with Genentech, our subsidiary

Curis Royalty is entitled to receive royalties on net sales of Erivedge that range from 5 % to 7. 5 % based upon global Erivedge sales by Roche and Genentech. The royalty rate applicable to Erivedge may be decreased in certain specified circumstances, including when a competing drug product that binds to the same molecular target as Erivedge is approved by the applicable country' s regulatory authority and is being sold in such country by a third party for use in the same indication as Erivedge, or when there is no issued intellectual property covering Erivedge in a territory in which sales are recorded. In 2015, the **U. S. Food and Drug Administration, or** FDA **,** and the **European Medicines Agency' s Committee for Medicinal Products for Human Use, or** CHMP **,** approved an additional Hedgehog signaling pathway inhibitor marketed by Sun Pharmaceutical Industries Ltd., or Sun Pharmaceutical, sonidegib (Odomzo ®), for the treatment of adults with locally advanced basal cell carcinoma, or BCC. Accordingly, Genentech reduced royalties on its net sales in the U. S. of Erivedge from 5- 7. 5 % to 3- 5. 5 %. Furthermore, Genentech has reduced by 2 % royalties on net sales of Erivedge outside of the United States on a country- by- country basis to the extent that sonidegib is approved by the applicable country' s regulatory authority and is being sold in such country. We also believe that sales of sonidegib have, and are likely to continue to, adversely affect sales of Erivedge, including those in the U. S. and ex- U. S. countries, which would adversely affect the resulting revenue we may receive from Genentech. A decrease in sales of Erivedge, or in the royalty rate that we receive for sales of Erivedge, could adversely affect our operating results. If the estimates we make and the assumptions on which we rely in preparing our financial statements prove inaccurate, our actual results may vary significantly. Our financial statements have been prepared in accordance with generally accepted accounting principles, or GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses, the amounts of charges taken by us, and disclosures related thereto. Such estimates and judgments include the value of certain liabilities. We base our estimates and judgments on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. However, these estimates and judgments, and their underlying assumptions, may change over time. Accordingly, our actual financial results may vary significantly from the estimates contained in our financial statements. RISKS RELATING TO THE DEVELOPMENT AND COMMERCIALIZATION OF OUR DRUG CANDIDATES We depend heavily on the success of emavusertib. Emavusertib is still in early clinical development. Clinical trials of emavusertib may not be successful. If we are unable to commercialize emavusertib or experience significant delays in doing so, our business will be materially harmed. Our ability to generate drug revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of emavusertib. Our success depends heavily on our ongoing and future clinical trials of emavusertib, which are in early- stage clinical development. We, and any collaborators, are not permitted to commercialize, market, promote or sell any drug candidate in the U. S. without obtaining marketing approval from the FDA. Foreign regulatory authorities, such as the **European Medicines Agency, or** EMA, impose similar requirements. We, and any collaborators, must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of emavusertib in humans before we will be able to obtain these approvals. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The clinical development of drug candidates generally, and emavusertib specifically, is susceptible to the risk of failure inherent at any stage of drug development. We, or any collaborators, may experience any of a number of possible unforeseen adverse events in connection with clinical trials of emavusertib, many of which are beyond our control and any of which could adversely affect our business, financial condition, operations and prospects and cause a decline in our stock price, including: • we, or our collaborators, may fail to demonstrate efficacy in a clinical trial or across a broad population of patients; • it is possible that even if emavusertib has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of emavusertib that is greater than the actual positive effect, if any; • adverse events or undesirable side effects caused by, or other unexpected properties of, emavusertib could cause us, any collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of emavusertib and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities; • we cannot be certain that we will not observe safety events in our clinical trials, ~~similar to that which resulted in partial clinical holds and subsequent removal of the partial clinical holds in our TakeAim Leukemia Phase 1 / 2 study and TakeAim Lymphoma Phase 1 / 2 study,~~ which may lead to future clinical holds, or necessitate additional or amended trials. • if emavusertib is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or any collaborators, may need to abandon development or limit its development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk- benefit perspective. • regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site; • we, or any collaborators, may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites; • clinical trials of emavusertib may produce unfavorable or inconclusive results, including with respect to its safety, tolerability, efficacy, or pharmacodynamic and pharmacokinetic profile; • we, or any collaborators, may decide, or regulators may require us, to conduct additional clinical trials or abandon our drug development program; • the number of patients required for clinical trials of emavusertib may be larger than we anticipate, patient 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; • our estimates of the patient populations available for study may be higher than actual patient numbers and result in our inability to sufficiently enroll our trials; • the cost of planned clinical trials of emavusertib may be greater than we anticipate; • our third party contractors, including those manufacturing emavusertib or components or ingredients thereof or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner or at all; • patients that enroll in a clinical trial may misrepresent their eligibility

to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial' s duration; • the FDA or comparable foreign regulatory authorities may disagree with our, or any collaborators', clinical trial designs or our or their interpretation of data from preclinical studies and clinical trials; • the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third party manufacturers with which we, or any collaborators, enter into agreements for clinical and commercial supplies; • the supply or quality of raw materials or manufactured emavusertib or other materials necessary to conduct clinical trials of emavusertib may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; • the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient to obtain marketing approval; • constraints on our, or any collaborators', ability to conduct or complete clinical trials for emavusertib, including slowdowns in patient enrollment, restrictions on patient monitoring at hospital clinical trial sites, closures of third party facilities, and other disruptions to clinical trial activities; and • any delay in enrolling patients or our inability to continue or complete our clinical trials of emavusertib will delay or may cause us to terminate our clinical development plans for emavusertib, may require us to incur additional clinical development costs, may slow down our drug candidate development and approval process, and could impair our ability to ultimately obtain FDA approval for emavusertib and commence product sales and generate revenue. The therapeutic efficacy of emavusertib is unproven in humans, and we may not be able to successfully develop and commercialize emavusertib. Emavusertib is a novel chemical and biologic entity and its potential benefit as a therapeutic cancer drug is unproven. For example, emavusertib may not prove to be an effective inhibitor of the molecular targets its being designed to act against, and may not demonstrate in patients any or all of the pharmacological benefits that may have been demonstrated in preclinical studies. Emavusertib may interact with human biological systems in unforeseen, ineffective or harmful ways. If the FDA determines that emavusertib is associated with significant side effects or has characteristics that are unexpected, we may need to delay or abandon its development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk benefit perspective. Moreover, we may determine after conducting clinical trials or related studies that emavusertib does not possess the anticipated therapeutic characteristics, and we may decide to abandon or discontinue any one of our clinical studies. Moreover, many drug candidates that initially showed promise in early stage testing for treating cancer have later been found to cause side effects that prevented further development of the compound or resulted in their removal from the market. As a result of these and other risks described herein that are inherent in the development and commercialization of novel therapeutic agents, we may not successfully develop or commercialize emavusertib, in which case we will not achieve profitability and the value of our stock will likely decline. If we experience delays in the enrollment of patients in our clinical trials of emavusertib, our receipt of necessary regulatory approvals could be delayed or prevented. We may not be able to initiate or continue clinical trials for emavusertib if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including: • our ability to successfully enroll ~~additional patients and to complete the monotherapy expansion phase (Phase 2a) of the TakeAim Leukemia Phase 1 / 2 study; • our ability to successfully enroll~~ patients with primary central nervous system lymphoma in the TakeAim Lymphoma Phase 1 / 2 ~~study; • our ability to initiate and enroll patients in the AML Triplet~~ study; • the size and nature of the patient population; • the severity of the disease under investigation; • the availability of approved therapeutics for the relevant disease; • the proximity of patients to clinical sites; • the eligibility criteria and design for the trial; • efforts to facilitate timely enrollment; • competing clinical trials; and • clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. In addition, many of our competitors have ongoing clinical trials for drug candidates that could be competitive with emavusertib. Patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' drug candidates or rely upon treatment with existing therapies that may preclude them from eligibility for our clinical trials. Our inability to enroll a sufficient number of patients for our clinical trials could result in significant delays or may require us to abandon one or more clinical trials altogether and may result in increased development costs for our drug candidates, which would likely cause the value of our stock price to decline. Results of preclinical studies and early clinical trials may not be predictive of results of future late stage clinical trials, and interim, " top-line, " initial, and preliminary data from our clinical trials may change as more patient data become available or as additional analyses are conducted and audit and verification procedures could result in material changes to the final data. We cannot assure you that we will be able to replicate in human clinical trials the results we observed in animal models. Moreover, the outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of clinical trials do not necessarily predict success in future clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late stage clinical trials after achieving positive results in earlier development, and we could face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a drug and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their drug candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the drug candidates. Even if we, or any collaborators, believe that the results of clinical trials for a drug candidate warrants marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of such drug candidate. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same drug candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. If we fail to receive positive results in

clinical trials of emavusertib, the development timeline and regulatory approval and commercialization prospects for emavusertib, and, correspondingly, our business and financial prospects would be negatively impacted. In addition, from time to time, we publish interim, " top- line, " initial, or preliminary data from our clinical studies. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Initial, preliminary or " top- line " data also remain subject to audit and verification procedures that may result in the final data being materially different from the data we previously published. As a result, interim, " top- line, " initial, and preliminary data should be viewed with caution until the final data are available. Material adverse changes between such data and final published data could significantly harm our business prospects. We have never obtained marketing approval for a drug candidate and we may be unable to obtain, or may be delayed in obtaining, marketing approval for emavusertib or any future drug candidates that we, or any future collaborators, may develop. We have never obtained marketing approval for a drug candidate. It is possible that the FDA may refuse to accept for substantive review any new drug applications, or NDAs, that we submit for a drug candidate such as emavusertib or may conclude after review of our data that our application is insufficient to obtain marketing approval of a drug candidate. For example, the FDA does not accept or approve our NDAs for emavusertib, it may require that we conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data before it will reconsider our application. Depending on the extent of these or any other FDA- required trials or studies, approval of such NDA may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional trials or studies, if performed and completed, may not be considered sufficient by the FDA to approve such NDAs. Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing emavusertib or any future drug candidates that we or any future collaborators may develop, or any companion diagnostics, generating revenues and achieving and sustaining profitability. If any of these outcomes occur, we may be forced to abandon our development efforts, which could significantly harm our business. Even if any drug candidates that we, or any collaborators, may develop receive marketing approval, we or others may later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, which could compromise our ability, or that of any collaborators, to market the drug. It is possible that our clinical trials, or those of any collaborator, may indicate an apparent positive effect of a drug candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a drug candidate, we, or others, discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur: • regulatory authorities may withdraw their approval of the drug or seize the drug; • we, or any future collaborators, may be required to recall the drug, change the way the drug is administered or conduct additional clinical trials; • additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular drug; • we may be subject to fines, injunctions or the imposition of civil or criminal penalties; • regulatory authorities may require the addition of labeling statements, such as a " black box " warning or a contraindication; • we, or any future collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients; • we, or any future collaborators, could be sued and held liable for harm caused to patients; • the drug may become less competitive; and • our reputation may suffer. Any of these events could harm our business and operations, and could negatively impact our stock price. Even if emavusertib receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third party payors and others in the medical community necessary for commercial success, in which case we may not generate significant revenues or become profitable. We have never commercialized a drug, and even if emavusertib is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third party payors and others in the medical community. Physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching drugs or they are required to switch therapies due to lack of reimbursement for existing therapies. Efforts to educate the medical community and third party payors on the benefits of emavusertib may require significant resources and may not be successful. If emavusertib is approved but does not achieve an adequate level of market acceptance, we may not generate significant revenues and we may not become profitable. The degree of market acceptance of emavusertib, if approved for commercial sale, will depend on a number of factors, including: • the efficacy and safety of the drug; • the potential advantages of the drug compared to competitive therapies; • the prevalence and severity of any side effects; • whether the drug is designated under physician treatment guidelines as a first-, second- or third- line therapy; • our ability, or the ability of any future collaborators, to offer the drug for sale at competitive prices; • the drug' s convenience and ease of administration compared to alternative treatments; • the willingness of the target patient population to try, and of physicians to prescribe, the drug and patient adherence to the drug' s dosing regimen once prescribed; • limitations or warnings, including distribution or use restrictions, contained in the drug' s approved labeling; • the strength of sales, marketing and distribution support; • changes in the standard of care for the targeted indications for the drug; and • availability and amount of coverage and reimbursement from government payors, managed care plans and other third party payors. We may expend our limited resources to pursue a particular drug candidate or indication and fail to capitalize on drug candidates or indications that may be more profitable or for which there is a greater likelihood of success. Because we have limited financial and managerial resources, we focus on our research and clinical development program for emavusertib as we believe it may have the best potential in certain specific indications. As a result, we have and may delay or forgo pursuit of certain opportunities with our other drug candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future proprietary research and development program for emavusertib for specific indications may not yield any commercially viable drug. If we do not accurately evaluate the commercial potential or target market for a particular drug

candidate, we may relinquish valuable rights to that drug candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such drug candidate. ~~For example, in November 2022, as a result of our strategic reprioritization, while we had not yet reached the maximum tolerated dose in our Phase 1 trial of CI- 8993, we deprioritized and did not exercise our option to license this candidate~~ We currently have no sales, marketing, or distribution experience and, as such, we must build infrastructure related to product sales, marketing and distribution or make arrangements with third parties to perform these services, and any such third parties may not successfully market or sell any drugs we develop. We currently have no sales, marketing, or drug distribution experience or capabilities. If we receive required regulatory approvals to commercialize emavusertib, we may plan to rely primarily on sales, marketing and distribution arrangements with third parties, including our collaborative partners. For example, as part of our agreements with Genentech, we have granted Genentech the exclusive rights to distribute drugs resulting from such collaboration, and Genentech is currently commercializing Erivedge. We may have to enter into additional marketing and / or sales arrangements in the future and we may not be able to enter into these additional arrangements on terms that are favorable to us, if at all. In addition, we may have limited or no control over the sales, marketing, and distribution activities of these third parties, and sales through these third parties could be less profitable for us than direct sales. These third parties could sell competing drugs and may devote insufficient sales efforts or resources to our drugs. Our future revenues will be materially dependent upon the successful efforts of these third parties. We may seek to independently market and sell emavusertib. If we undertake to perform sales, marketing and distribution functions ourselves, we could face a number of additional risks, including: • we may not be able to attract and build a significant and skilled marketing staff or sales force; • the cost of establishing a marketing staff or sales force may not be justifiable in light of the revenues generated by any particular drug; and • our direct sales and marketing efforts may not be successful. We face substantial competition, and our competitors may discover, develop or commercialize drugs before or more successfully than we do. Emavusertib and Erivedge, our outlicensed program, face competition from existing and new technologies and drugs being developed by biotechnology, medical device, and pharmaceutical companies, as well as universities and other research institutions. There are several companies developing drug candidates that target the same molecular targets and signaling pathways, and in some cases the same cancer indications, ~~that~~ **which** are being pursued by us. Emavusertib. We believe our primary competitors for emavusertib are those companies pursuing oncology indications in IRAK4, R / R AML or hrMDS with a FLT3 ~~or Spliceosome~~ mutation, R / R PCNSL, and frontline AML combinations with azacitidine and venetoclax. Companies pursuing IRAK 4 inhibitors include ~~two~~ **a pre-** clinical stage ~~companies~~ **company** ~~:~~ **,** Kurome Therapeutics (IRAK1 / 4) and **a clinical stage company,** Rigel Pharmaceuticals, Inc. (R289). Astellas Pharma, Inc. (gilteritinib) has an approved FLT3 inhibitor. Other companies developing FLT3 inhibitors include: Aptose Biosciences, Inc. (tuspetinib), ~~Nerviano Medical Sciences, S. r. l. (NMS- 088),~~ HEC Pharma Co., Ltd. (HEC73543), Ellipses Pharma (EP0042), CSPC Pharmaceuticals Group Limited (SKLB1028), and **Eilean Therapeutics** ~~Kronos Bio, Inc.~~ (**lomonitnib** ~~lanraplenib in combination with gilteritinib~~). Abbvie, Inc. has an approved BTK inhibitor, ibrutinib, which is being used **pursuant to the National Comprehensive Cancer Network guidelines** as a treatment for PCNSL. Other companies pursuing R / R PCNSL are Bayer AG (copanlisib in combination with ibrutinib), Gilead Sciences, Inc. (axicabtagene ciloleucel), Ono Pharmaceuticals Co., Ltd. (tirabrutinib), and BeiGene, Ltd. (zanubrutinib in combination with rituximab and methotrexate). Additionally, there are several ~~approved compounds~~ **marketed products** that are being studied in combination as ~~a~~ **potential** ~~treatment~~ **treatments** for PCNSL (ibrutinib, rituximab and lenalidomide). Companies pursuing frontline AML in combination with **either** azacitidine and venetoclax **, or both,** include: Faron Pharmaceuticals Oy (bexmarilimab), Novartis AG (sabatolimab), OncoVerity, Inc. (cusatuzumab), Glycomimetics, Inc. (uproleselan ~~), Shattuck Labs, Inc. (SL- 17254~~), Bio- Path Holdings, Inc. (prexigebersen), Astellas Pharma, Inc. (gilteritinib), and ImmunoGen, Inc. (pivekimab sunirine). We are aware of several companies that have clinical development programs relating to compounds that modulate the Hedgehog signaling pathway and may compete with Erivedge, including PellePharm, Inc. (patidegib), and Cyclene Pharmaceuticals Inc. / Senhwa Biosciences Inc. (silmitasertib / CX- 4945). Furthermore, glasdegib (Daurismo ™) is marketed by Pfizer Inc. for the treatment of newly diagnosed adult AML patients for whom intensive chemotherapy is not an option, and sonidegib (Odomzo ™) is marketed by Sun Pharmaceutical for the treatment of adults with locally advanced BCC. Under the terms of our collaboration agreement with Genentech, our royalty on sales of Erivedge has been reduced and may be further reduced as a result of sales of sonidegib. Many of our competitors have substantially greater capital resources, research and development staff and facilities, and more extensive experience than we have. As a result, efforts by other biotechnology, medical device and pharmaceutical companies could render our programs or drugs uneconomical or result in therapies superior to those that we develop alone or with a collaborator. We face competition from companies that are more experienced in drug development and commercialization, obtaining regulatory approvals and drug manufacturing. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Other smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our program. As a result, any of these companies may be more successful in obtaining collaboration agreements or other monetary support, approval and commercialization of their drugs and / or may develop competing drugs more rapidly and / or at a lower cost. If we are not able to compete effectively, then we may not be able, either alone or with others, to advance the development and commercialization of emavusertib or Erivedge, which would adversely affect our ability to grow our business and become profitable. Even if we, or any collaborators, are able to commercialize any drug candidate that we, or they, develop, the drug may become subject to unfavorable pricing regulations, third party payor reimbursement practices or healthcare reform initiatives, any of which could harm our business. The commercial success of any drug candidate that we, or any collaborators, may develop will depend substantially, both

domestically and abroad, on the extent to which the costs of such drug candidate will be paid by third party payors, including government health care programs and private health insurers. If coverage is not available, or reimbursement is limited, we, or any collaborators, may not be able to successfully commercialize the drug candidate. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their investments. In the U. S., no uniform policy of coverage and reimbursement for drugs exists among third party payors and coverage and reimbursement levels for drugs can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our drugs to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. There is significant uncertainty related to third party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or drug licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we, or any future collaborators, might obtain marketing approval for a drug in a particular country, but then be subject to price regulations that delay commercial launch of the drug, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the drug in that country. Adverse pricing limitations may hinder our ability or the ability of any future collaborators to recoup our or their investment in one or more drug candidates, even if the drug candidate obtains marketing approval. Patients who are provided medical treatment for their conditions generally rely on third party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability, and the ability of any future collaborators, to successfully commercialize emavusertib will depend in part on the extent to which coverage and adequate reimbursement for the drug and related treatments will be available from third party payors. Third party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the U. S. and elsewhere. Government authorities and other third party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability or that of any future collaborators to sell our drug candidates profitably. These payors may not view our drug as cost-effective, and coverage and reimbursement may not be available to our customers, or those of any future collaborators, or may not be sufficient to allow our drug to be marketed on a competitive basis. Cost- control initiatives could cause us, or any future collaborators, to decrease the price we, or they, might establish for our drug, which could result in lower than anticipated drug revenues. If the prices for our drug, if any, decrease or if governmental and other third party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer. There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the drug and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services. In addition, increasingly, third party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U. S. An inability to promptly obtain coverage and adequate payment rates from both government- funded and private payors for any drug candidate for which we, or any future collaborator, obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize drugs and our overall financial condition. Product liability lawsuits against us or our collaborators could divert our resources, cause us to incur substantial liabilities and limit commercialization of any drugs that we may develop. We and our collaborators face a risk of product liability claims, which could expose us and them to significant liabilities and costs and prevent or interfere with the development or commercialization of any drug candidates or drugs that we may develop. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the drug, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we or our collaborators cannot successfully defend ourselves against product liability claims, we or our collaborators may incur substantial liabilities or be required to limit commercialization of any drug candidates or drugs that we may develop. Regardless of their merit or eventual outcome, such liability claims would require us to spend significant time, money and other resources to defend such claims, and could result in decreased demand for any drug candidates or drugs that we may develop, injury to our reputation and significant loss of revenue. Although we currently have product liability insurance for our clinical trials, this insurance is subject to deductibles and coverage limitations and may not be adequate in scope to protect us in the event of a successful product liability claim. RISKS RELATING TO OUR DEPENDENCE ON THIRD PARTIES We may not be successful in establishing additional strategic collaborations, which could adversely affect our ability to develop and commercialize emavusertib, which we have strategically determined to pursue with a collaborator. We may seek corporate collaborators or licensees for the further development and commercialization of emavusertib in one or more geographic territories, particularly in territories outside of the U. S. We face significant competition in seeking appropriate collaborators and a number of recent business combinations in the biotechnology and pharmaceutical industry may result in a reduced number of potential future collaborators. In addition, collaborations are complex and time- consuming to negotiate and document. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of emavusertib, reduce or delay its development program, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake

development or commercialization activities at our own expense. Moreover, we may not be successful in our efforts to establish a collaboration or other alternative arrangements because our research and development pipeline may be insufficient, our program may be deemed to be at too early of a stage of development for collaborative effort and / or third parties may not view emavusertib as having the requisite potential to demonstrate safety and efficacy or as sufficiently differentiated compared to existing or emerging treatments. We are also restricted under the terms of certain of our existing collaboration agreements from entering into collaborations regarding or otherwise developing drug candidates that are similar to the drug candidates that are subject to those agreements, such as developing drug candidates that inhibit the same molecular target. In addition, collaboration agreements that we enter into in the future may contain further restrictions on our ability to enter into potential collaborations or to otherwise develop emavusertib. Even if we are successful in our efforts to establish new collaborations, the terms that we agree upon may not be favorable to us and such collaboration agreements may not lead to development or commercialization of drug candidates in the most efficient manner, or at all. Moreover, if we fail to establish and maintain one or more collaborations for emavusertib: • the development of emavusertib may be terminated or delayed; • our cash expenditures related to development of emavusertib would increase significantly and we may need to seek additional financing; • we may be required to hire additional employees or otherwise develop additional expertise, such as clinical, regulatory, sales and marketing expertise, for which we have not budgeted; • we will have to bear all of the risk related to the development of emavusertib; and • our future prospects may be adversely affected and our stock price could decline. We rely in part on third parties to conduct clinical trials of emavusertib, and if such third parties perform inadequately, including failing to meet deadlines for the completion of such trials, research or testing, then we may not be able to successfully develop and commercialize emavusertib and grow our business. We rely heavily on third parties such as consultants, clinical investigators, contract research organizations and other similar entities to complete certain aspects of our preclinical testing and clinical trials and provide services in connection with such clinical trials, and expect to continue to do so for the foreseeable future. Despite having contractual remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time, skill and resources to our ongoing development program. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. These third parties may not complete activities on schedule, or at all, or may not conduct our clinical trials in accordance with the established clinical trial protocol or design. In addition, the FDA and its foreign equivalents require us to comply with certain standards, referred to as " good clinical practices, " and applicable regulatory requirements, for conducting, recording and reporting the results of clinical trials. These requirements assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Our reliance on third parties does not relieve us of these responsibilities and requirements. If any of our third party contractors do not comply with good clinical practices or other applicable regulatory requirements, we may not be able to use the data and reported results from the applicable trial. Any failure by a third party to conduct our clinical trials as planned or in accordance with regulatory requirements could delay or otherwise adversely affect our efforts to obtain regulatory approvals for and commercialize emavusertib. We depend on third parties to produce emavusertib, and if these third parties do not successfully formulate or manufacture the drug candidate, our business could be harmed. In order to continue to develop emavusertib, apply for regulatory approvals, and commercialize the drug candidate, as applicable, we or any collaborators must be able to manufacture emavusertib in adequate clinical and commercial quantities, in compliance with regulatory requirements, including those related to quality control and quality assurance, at acceptable costs and in a timely manner. The manufacture of emavusertib may be complex, may be difficult to accomplish and may be difficult to scale- up when large- scale production is required. Manufacture may be subject to delays, inefficiencies and low yields of quality drugs. The cost of manufacturing emavusertib may be prohibitively expensive. To the extent that we or any collaborators seek to enter into manufacturing arrangements with third parties, we and such collaborators will depend upon these third parties to perform their obligations in a timely and effective manner and in accordance with government regulations. We may be unable to establish any agreements with contract manufacturers or to do so on acceptable terms. Contract manufacturers may breach their manufacturing agreements because of factors beyond our and our collaborators' control, or may terminate or fail to renew a manufacturing agreement based on their own business priorities, becoming costly and / or inconvenient for us and our collaborators. Even if we are able to establish agreements with contract manufacturers, reliance on contract manufacturers entails additional risks, including: • manufacturing delays if our third party contractors give greater priority to the supply of other products over our drug candidate or otherwise do not satisfactorily perform according to the terms of the agreements between us and them, or if unforeseen events in the manufacturing process arise; • the failure of third party contractors to comply with applicable regulatory requirements; • the possible mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified; • the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and • the possible misappropriation of our proprietary information, including our trade secrets and know- how. Any manufacturing problem, the loss of a contract manufacturer or any loss of storage could be disruptive to our operations, delay our clinical trials and, if our products are approved for sale, result in lost sales. Any contract manufacturers with whom we or our collaborators enter into manufacturing arrangements will be subject to ongoing periodic, unannounced inspection by the FDA and state and foreign agencies or their designees to ensure strict compliance with current good manufacturing practices and other governmental regulations and corresponding foreign standards. Any failure by contract manufacturers, collaborators, or us to comply with applicable regulations could result in sanctions being imposed, including fines, injunctions, civil penalties, denial by regulatory authorities of marketing approval for our drug candidate, delays, suspension or withdrawal of approvals, imposition of clinical holds, seizures or recalls of our drug candidate, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business. If we or a collaborator need to change manufacturers, the FDA and corresponding foreign regulatory agencies must approve any new manufacturers in advance. This would involve testing and pre-

approval inspections to ensure compliance with FDA and foreign regulations and standards. If third party manufacturers fail to perform their obligations, our competitive position and ability to generate revenue may be adversely affected in a number of ways, including: • we, and any collaborators, may not be able to initiate or continue certain preclinical and / or clinical trials of our drug candidate under development; • we, and any collaborators, may be delayed in submitting applications for regulatory approvals for our drug candidate; and • we, and any collaborators, may not be able to meet commercial demand for any approved drug products. Because we rely on a limited number of suppliers for the raw materials used in emavusertib, any delay, shortage or interruption in the supply of such raw materials or contamination in our manufacturing process could lead to delays in the manufacture and supply of emavusertib. We rely on third parties to supply certain raw materials necessary to produce emavusertib for preclinical studies and clinical trials. There are a small number of suppliers for certain raw materials that we use to manufacture our drug candidate. We purchase these materials from our suppliers on a purchase order basis and do not have long- term supply agreements in place, which exposes us to a variety of risks, including a potential inability to obtain critical materials and reduced control over production costs, delivery schedules, reliability and quality. Additionally, our suppliers are subject to risks related to cyber attacks that could cause disruptions in manufacturing. Any unanticipated disruption to our contract manufacturing caused by problems at suppliers could delay shipment of our drug candidate, increase our cost of goods sold and result in lost sales with respect to any approved products. Suppliers may extend lead times, limit supplies, or increase prices due to capacity constraints or other factors beyond our control. Any significant delay in the supply of raw materials for our drug candidate for a preclinical study or an ongoing clinical trial due to the need to replace a third party supplier could considerably delay completion of certain preclinical studies and / or clinical trials. Moreover, if we are unable to purchase sufficient raw materials after regulatory approval for our drug candidate, the commercial launch of our drug candidate could be delayed, or there could be a supply shortage, each of which would impair our ability to generate revenues from their sale. In addition, a material shortage, contamination, recall or restriction on the use of substances in the manufacture of our drug candidate, or the failure of any of our key suppliers to deliver necessary components required for the manufacture of our drug candidate, could adversely impact or disrupt the commercial manufacture or the production of clinical material, which could materially and adversely affect our development timelines and our business, financial condition, results of operations, and future prospects. We are reliant on Genentech and Roche for the successful commercialization of Erivedge. If Genentech and Roche do not successfully commercialize Erivedge for metastatic BCC and / or advanced BCC, our future revenue may be substantially harmed. Our levels of revenue in each period depend upon Genentech' s ability to successfully continue to commercialize Erivedge for patients with metastatic BCC and / or advanced BCC and to demonstrate its superiority over existing therapies and standards of care. Product sales of Erivedge could be unsuccessful if: • Erivedge becomes no longer accepted as safe, efficacious, cost- effective and preferable for the treatment of advanced BCC to current therapies in the medical community or future competing drug products and by third party payors; • Genentech and / or Roche do not continue to develop and implement effective marketing, sales and distribution strategies and operations, including a commercially viable manufacturing process that is compliant with current good manufacturing practices, for development and commercialization of Erivedge for metastatic and / or advanced BCC; • we, Genentech, or Roche encounter third party patent interference, derivation, inter partes review, post grant review, reexamination or patent infringement claims with respect to Erivedge; • Genentech and / or Roche do not comply with regulatory and legal requirements applicable to the sale of Erivedge for metastatic and / or advanced BCC; or • Genentech does not exercise its first right to maintain or defend intellectual property rights associated with Erivedge. We depend on third parties for the research and, as applicable, development and commercialization of our drug candidates. If one or more of our collaborators fails or delays in developing or, as applicable, commercializing our drug candidates based upon our technologies, our business prospects and operating results could suffer and our stock price could decline. Pursuant to our collaboration with Genentech, we have granted to Genentech exclusive rights to develop and commercialize drugs based upon our Hedgehog signaling pathway technologies. Collaborations involving our drug candidates, including our collaborations with Aurigene and Genentech, pose the following risks to us: • Our collaborators each have significant discretion in determining the efforts and resources that they will apply to their respective collaboration with us. If a collaborator fails to allocate sufficient time, attention and resources to our collaboration, the successful development and commercialization of drug candidates under such collaboration is likely to be adversely affected. • Our collaborators may develop and commercialize, either alone or with others, drugs that are similar to or competitive with the drug candidates that are the subject of our respective collaborations. For example, Genentech and Roche are involved in the commercialization of many cancer medicines and are seeking to develop several other cancer drug therapies, and Aurigene has other active cancer- focused discovery programs and has also entered into license agreements with other companies that focus on cancer therapies. • Our collaborators may change the focus of their development and commercialization efforts or pursue higher- priority programs and there can be no assurance that third parties engaged to develop or commercialize our drug candidates or products will succeed in developing or commercializing our products or devote sufficient resources to the development or commercialization of our drug candidates or products. In addition, potential competitors may have substantially greater financial and other resources and may be able to expend more funds and effort with respect to competing products than Genentech or other third parties engaged by us. • Our collaborators may enter into one or more transactions with third parties, including a merger, consolidation, reorganization, sale of substantial assets, sale of substantial stock or change of control. Any such transaction could divert the attention of our collaborative partner' s management and adversely affect its ability to retain and motivate key personnel who are important to the continued development of the program under such collaboration. In addition, an acquirer could determine to reprioritize our collaborator' s development program such that our collaborator ceases to diligently pursue the development of our program, and / or terminates our collaboration. • Our collaborators may, under specified circumstances, terminate their collaborations with us on short notice and for circumstances outside of our control, which could make it difficult for us to attract new collaborators or adversely affect how we are perceived in the scientific, biotech, pharma and financial communities. • Our collaborators may utilize our

intellectual property rights in such a way as to invite litigation that could jeopardize or invalidate our intellectual property rights, or expose us to potential liability. • Disputes may arise between collaborators and us regarding ownership of or other rights in the intellectual property generated in the course of the collaborations. • If any of our collaborators were to breach or terminate its arrangement with us, the development and commercialization of the affected drug candidate or program could be delayed, curtailed or terminated. RISKS RELATING TO EMPLOYEE MATTERS AND MANAGING GROWTH If we are not able to attract and retain key management and scientific personnel and advisors, we may not successfully develop emavusertib or achieve our other business objectives. We depend upon our senior management team. The loss of the service of any of the key members of our senior management may significantly delay or prevent the achievement of drug development and other business objectives. Our officers all serve pursuant to " at will " employment arrangements and can terminate their employment with us at any time. We do not maintain " key person " insurance for any of our executives or other employees. In the future, we may be dependent on other members of our management, scientific and development team. Our ability to compete in the biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. Our industry has experienced a high rate of turnover of management personnel in recent years. If we lose one or more of our executive officers or other key employees, our ability to successfully implement our business strategy could be seriously harmed. Furthermore, replacing executive officers or other key employees may be difficult and take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, market and commercialize drugs successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate additional key employees on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies, universities and research institutions for similarly qualified personnel. We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to develop and commercialize emavusertib will be limited. We may in the future seek to acquire complementary businesses and technologies or otherwise seek to expand our operations and grow our business, which may divert management resources and adversely affect our financial condition and operating results. We may in the future seek to expand our operations, including through internal growth and / or the acquisition of businesses and technologies that we believe are a strategic complement to our business model. We may not be able to identify suitable acquisition candidates or expansion strategies and successfully complete such acquisitions or successfully execute any such other expansion strategies. We may never realize the anticipated benefits of any efforts to expand our business. Furthermore, the expansion of our business, either through internal growth or through acquisitions, poses significant risks to our existing operations, financial condition and operating results, including: • a diversion of management attention from our existing operations; • increased operating complexity of our business, requiring greater personnel and resources; • significant additional cash expenditures to expand our operations and acquire and integrate new businesses and technologies; • unanticipated expenses and potential delays related to integration of the operations, technology and other resources of any acquired companies; • uncertainty related to the value, benefits or legitimacy of intellectual property or technologies acquired; • retaining and assimilating key personnel and the potential impairment of relationships with our employees; • incurrence of debt, other liabilities and contingent liabilities, including potentially unknown contingent liabilities; and • dilutive stock issuances. RISKS RELATING TO OUR INTELLECTUAL PROPERTY We may not be able to obtain and maintain patent protection for our technologies and drugs, our licensors may not be able to obtain and maintain patent protection for the technology or drugs that we license from them, and the patent protection we or they do obtain may not be sufficient to stop our competitors from using similar technology. The long- term success of our business depends in significant part on our ability to: • obtain patents to protect our technologies and discoveries; • protect trade secrets from disclosure to competitors; • operate without infringing upon the proprietary rights of others; and • prevent others from infringing on our proprietary rights. The patent positions of pharmaceutical and life science companies, including ours, are generally uncertain and involve complex legal, scientific and factual questions. The laws, procedures and standards that the U. S. Patent and Trademark Office and various foreign intellectual property offices use to grant and maintain patents, and the standards that courts use to interpret patents, are not always applied predictably or uniformly and have changed in significant ways and are expected to continue to change. In addition, the laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the U. S. For example, European patent law restricts the patentability of methods of treatment of the human body more than U. S. law does. Consequently, the level of protection, if any, that will be obtained and provided by our patents if we attempt to enforce them, and they are challenged, is uncertain. Patents may not issue from any of the patent applications that we own or license. If patents do issue, the type and extent of patent claims issued to us may not be sufficient to protect our technology from exploitation by our competitors. Our patents also may not afford us protection against competitors with similar technology. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. Prior to March 16, 2013, in the U. S., patent applications were subject to a " first to invent " rule of law. Applications filed on or after March 16, 2013 (with the exception of certain applications claiming priority to applications filed prior to March 16, 2013, such as continuations and divisionals) are subject to new laws including a " first to file " rule of law. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U. S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Additionally, how the U. S. Patent & Trademark Office and U. S. courts will interpret the new laws remains significantly uncertain at this time. We cannot be certain that any existing or future application will be subject to the " first to file " or " first to invent " rule of law, that we were the first to make the inventions claimed in our existing patents or pending patent applications subject to the prior laws, or that we were the first to file for patent protection of such inventions subject to the new laws. We may not have rights under patents that may cover one or

more of our drug candidates. Patents of others may overlap with our own patents regarding one or more of our drug candidates. In some cases, these patents may be owned or controlled by third party competitors and may prevent or impair our ability to exploit our technology. As a result, we or our current or potential future collaborative partners may be required to obtain licenses under third party patents to develop and commercialize some of our drug candidates. If we are unable to secure licenses to such patented technology on acceptable terms, we or our collaborative partners may not be able to develop and commercialize the affected drug candidate or candidates. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology or drugs that we license from third parties and are reliant on our licensors. If we do not control the filing, prosecution of certain patent rights, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in courts or patent offices in the U. S. and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and drugs, or limit the duration of the patent protection of our technology and drugs. Given the amount of time required for the development, testing, and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing drugs similar or identical to ours. We may become involved in expensive and unpredictable patent litigation or other contentious intellectual property proceedings, which could result in liability for damages or require us to cease our development and commercialization efforts. There are substantial threats of litigation and other adversarial opposition proceedings regarding patent and other intellectual property rights in the pharmaceutical and life science industries. We may become a party to patent litigation or other proceedings regarding intellectual property rights. Situations that may give rise to patent litigation or other disputes over the use of our intellectual property include: • initiation of litigation or other proceedings against third parties to enforce our patent rights, to seek to invalidate the patents held by third parties or to obtain a judgment that our drug candidates do not infringe such third parties' patents; • participation in interference and / or derivation proceedings to determine the priority of invention if our competitors file U. S. patent applications that claim technology also claimed by us; • initiation of opposition, reexamination, post grant review or inter partes review proceedings by third parties that seek to limit or eliminate the scope of our patent protection; • initiation of litigation by third parties claiming that our processes or drug candidates or the intended use of our drug candidates infringes their patent or other intellectual property rights; and • initiation of litigation by us or third parties seeking to enforce contract rights relating to intellectual property that may be important to our business. Any patent litigation or other proceeding, even if resolved favorably, will likely require us to incur substantial costs and be a distraction to management. Some of our competitors may be able to sustain the cost of such litigation or other proceedings more effectively than we can because of their substantially greater financial resources. In addition, our collaborators and licensors may have rights to file and prosecute claims of infringement of certain of our intellectual property, and we are reliant on them. If a patent litigation or other intellectual property proceeding is resolved unfavorably, we or any collaborative partners may be enjoined from manufacturing or selling our future drugs without a license from the other party and be held liable for significant damages. Moreover, we may not be able to obtain required licenses on commercially acceptable terms or any terms at all. In addition, we could be held liable for lost profits if we are found to have infringed a valid patent, or liable for treble damages if we are found to have willfully infringed a valid patent. Litigation results are highly unpredictable, and we or any collaborative partner may not prevail in any patent litigation or other proceeding in which we may become involved. Any changes in, or unexpected interpretations of, the patent laws may adversely affect our ability to enforce our patent position. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could damage our ability to compete in the marketplace. We face risks relating to the enforcement of our intellectual property rights in China and India that could adversely affect our business. We have conducted chemical development work through contract research agreements with contract research organizations, or CROs, in China and India. We seek to protect our intellectual property rights under this arrangement through, among other things, non- disclosure and assignment of invention covenants. Enforcement of intellectual property rights and confidentiality protections in China may not be as effective as in the U. S. or other countries. Policing unauthorized use of proprietary technology is difficult and expensive, and we might need to resort to litigation to enforce or defend patents issued to us or to determine the enforceability, scope and validity of our proprietary rights or those of others. The experience and capabilities of Chinese courts in handling intellectual property litigation vary, and outcomes are unpredictable. Further, such litigation may require significant expenditure of cash and management efforts and could harm our business, financial condition and results of operations. An adverse determination in any such litigation will impair our intellectual property rights and may harm our business, prospects and reputation. In addition, we collaborate with Aurigene, an Indian company, in the development of new therapeutic compounds. Some or all of the intellectual property arising from this collaboration may be developed by Aurigene' s employees, consultants, and third party contractors, and we have exercised our option right under the collaboration agreement to obtain exclusive licenses to Aurigene' s rights in this intellectual property. Accordingly, our rights depend in part on Aurigene' s contracts with its employees and contractors and Aurigene' s ability to protect its trade secrets and other confidential information in India, both before and after we exercise our option to obtain exclusive license rights on a program- by- program basis. Enforcement of intellectual property rights and confidentiality protections in India may not be as effective as in the U. S. or other countries. Policing unauthorized use of proprietary technology is difficult and expensive, and we or Aurigene might need to resort to litigation to protect our trade secrets and confidential information. The experience and capabilities of Indian courts in handling intellectual property litigation vary, and outcomes are unpredictable. Further, such litigation may require significant expenditure of cash and management efforts and

could harm our business, financial condition and results of operations. An adverse determination in any such litigation would impair our intellectual property rights and may harm our business, prospects and reputation. If we are unable to keep our trade secrets confidential, our technology and proprietary information may be used by competitors. We rely heavily on trade secrets, including unpatented know- how, technology and other proprietary information, to maintain our competitive position. We seek to protect this information through confidentiality and intellectual property license or assignment provisions in agreements with our employees, consultants and other third party contractors, including our contract research agreements with CROs in China and India, as well as through other security measures. Similarly, our agreements with Genentech and Aurigene require each collaborator to enter into such agreements with its employees, consultants, and other third party contractors. The confidentiality and intellectual property provisions of our agreements and security measures may be breached, and we or they may not have adequate remedies for any such breach. In addition, our trade secrets may otherwise become known or be independently developed by competitors. We have agreements under which we license rights to technology from third parties, and we could lose license rights to intellectual property that are important to our business under certain circumstances. We are party to agreements that provide us licenses of intellectual property or sharing of rights to intellectual property that is important to our business, and we may enter into additional agreements in the future that provide us licenses to valuable technology. These licenses, including our agreement with Aurigene, impose, and future licenses may impose, various commercialization, milestone and other obligations on us, including the obligation to terminate our use of licensed subject matter under certain contingencies. If a licensor becomes entitled to, and exercises, termination rights under a license, we would lose valuable rights and could lose our ability to develop our drugs. We may need to license other intellectual property to commercialize future drugs. Our business may suffer if any current or future licenses terminate, if the licensors fail to abide by the terms of the license or fail to prevent infringement by third parties, if the licensed patents or other rights are found to be invalid, or if we are unable to enter into necessary licenses on acceptable terms. We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers. As is common in the biotechnology and pharmaceutical industry, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our current and potential competitors. Although no claims against us are currently pending, we may be subject to claims that such employees, or as a result, we, have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. RISKS RELATING TO REGULATORY APPROVAL AND MARKETING OF OUR DRUG CANDIDATES AND OTHER LEGAL COMPLIANCE MATTERS Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time consuming and uncertain and may prevent us or any future collaborators from obtaining approvals for the commercialization of emavusertib. As a result, we cannot predict when or if, and in which territories, we, or any future collaborators, will obtain marketing approval to commercialize emavusertib. The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of products are subject to extensive regulation by the FDA and comparable foreign regulatory authorities. We, and any future collaborators, are not permitted to market emavusertib in the U. S. or in other countries until we, or they, receive approval of an NDA from the FDA or marketing approval from applicable regulatory authorities outside the U. S. Emavusertib is in various stages of development and is subject to the risks of failure inherent in drug development. We have not submitted an application for or received marketing approval for emavusertib in the United States or in any other jurisdiction. We have limited experience in conducting and managing the clinical trials necessary to obtain marketing approvals, including FDA approval of an NDA. The process of obtaining marketing approvals, both in the United States and abroad, is lengthy, expensive and uncertain. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the drug candidates involved. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information, including manufacturing information, to regulatory authorities for each therapeutic indication to establish the drug candidate' s safety and efficacy. The FDA or other regulatory authorities may determine that emavusertib is not safe and effective, only moderately effective or has undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use. In addition, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. For example, in December 2022, with the passage of the Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan **, or DAP,** for each Phase 3 clinical trial or any other " pivotal study " of a new drug product. These plans are meant to encourage the enrollment of more diverse patient populations in late- stage clinical trials of FDA- regulated products **. In June 2024, as mandated by FDORA, the FDA issued draft guidance outlining the general requirements for DAPs. Unlike most guidance documents issued by the FDA, the DAP guidance when finalized will have the force of law because FDORA specifically dictates that the form and manner for submission of DAPs are specified in FDA guidance** . Further, on January 31, 2022, the new Clinical Trials Regulation (EU) No 536 / 2014 became effective in the European Union and replaced the prior Clinical Trials Directive 2001 / 20 / EC. The new regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one EU Member State will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a new clinical trials portal overseen by the EMA and available to clinical trial sponsors, competent authorities of the EU Member States and the public. **Moreover, principal investigators for our future** ~~We have not previously secured authorization to conduct~~ clinical ~~studies in the EU pursuant~~ **trials may serve as scientific advisors or consultants** to **us** ~~this new regulation~~ and **receive compensation in connection with such services. Under certain circumstances** , ~~accordingly,~~ **we may be required to**

report some of ~~there~~ **these** ~~is~~ **relationships to the FDA or comparable foreign regulatory authorities. The FDA or** a ~~risk~~ **comparable foreign regulatory authority may conclude** that ~~we~~ **a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself** may be **jeopardized. This could result in a** ~~delayed~~ -- **delay** in ~~commencing such studies~~ **approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates** . Regulatory authorities have substantial discretion in the approval process and varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a drug candidate. The FDA or other regulatory authorities may determine that (i) our drug candidate is not safe and effective, only moderately effective or has undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use; (ii) the dose used in a clinical trial has not been optimized and require us to conduct additional dose optimization studies; or (iii) the comparator arm in a trial is no longer the appropriate comparator due to the evolution of the competitive landscape or subsequent data of the comparator product, even if the FDA or other regulatory authority had previously approved the trial design, and we may be required to amend the trial or we may not receive approval of the indication. Any marketing approval we, or any future collaborators, ultimately obtain may be limited or subject to restrictions or post approval commitments that render the approved product not commercially viable. ~~Finally~~ **Further, the FDA may determine that we must provide additional evidence and data before approving a NDA for our candidate products. For example, the FDA reviews an application to determine whether there is " substantial evidence " to support a finding of effectiveness for the proposed product for its intended use (s), The FDA has interpreted this evidentiary standard to generally require at least two adequate and well- controlled clinical trials to establish effectiveness of a new product. Under certain circumstances, however, the FDA has indicated that a single trial with certain characteristics and additional confirmatory evidence may satisfy this standard. The FDA issued draft guidance in September 2023 that outlines considerations for relying on confirmatory evidence in lieu of a second clinical trial to demonstrate effectiveness. In the event that we submit an NDA on the basis of one clinical trial and confirmatory evidence, the FDA could determine that such information is not sufficient to support approval of the application and the agency could require us to conduct an additional trial in support of the NDA. In addition, we could be adversely affected by several significant administrative law cases decided by the U. S. Supreme Court in 2024. In Loper Bright Enterprises v. Raimondo, for example, the court overruled Chevron U. S. A., Inc. v. Natural Resources Defense Council, Inc., which for 40 years required federal courts to defer to permissible agency interpretations of statutes that are silent or ambiguous on a particular topic. The U. S. Supreme Court stripped federal agencies of this presumptive deference and held that courts must exercise their independent judgment when deciding whether an agency such as the FDA acted within its statutory authority under the Administrative Procedure Act, or the APA. Additionally, in Corner Post, Inc. v. Board of Governors of the Federal Reserve System, the court held that actions to challenge a federal regulation under the APA can be initiated within six years of the date of injury to the plaintiff, rather than the date the rule is finalized. The decision appears to give prospective plaintiffs a personal statute of limitations to challenge longstanding agency regulations. Another decision, Securities and Exchange Commission v. Jarkesy, overturned regulatory agencies' ability to impose civil penalties in administrative proceedings. These decisions could introduce additional uncertainty into the regulatory process and may result in additional legal challenges to actions taken by federal regulatory agencies, including the FDA and Centers for Medicare & Medicaid Services, or CMS, that we rely on. In addition to potential changes to regulations as a result of legal challenges, these decisions may result in increased regulatory uncertainty and delays and other impacts, any of which could adversely impact our business and operations. Further** , our ability to develop and market new drug products may be ~~threatened~~ **impacted** by ~~ongoing~~ litigation challenging the FDA' s approval of ~~mifepristone~~ **another company' s drug product** . **In** ~~Specifically, on~~ April ~~7,~~ 2023, the U. S. District Court for the Northern District of Texas invalidated the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various measures adopted under a REMS. **The Court of Appeals for the Fifth Circuit declined to order the removal of mifepristone from the market but did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone, which the FDA authorized in 2016 and 2021, were arbitrary and capricious.** In ~~reaching~~ **June 2024, the Supreme Court reversed** that decision **after unanimously finding that the plaintiffs (anti- abortion doctors and organizations) did not have standing to bring this legal action against the FDA. On October 11** , **2024, the Attorneys General of three states (Missouri, Idaho and Kansas) filed an amended complaint in** the district court ~~made a number of findings that numerous representatives of the pharmaceutical and biotechnology industry believe will chill the development, approval and distribution of new drug products~~ in **Texas** ~~the United States. Among other determinations, the district court substituted its scientific judgement for that of the FDA and it held that FDA must provide a special justification for any differences between an approved drug' s labeling and the conditions that existed in the drug' s clinical trials. Further, the district court read the jurisdictional requirements governing litigation in federal court so as to potentially allow virtually any party to bring a lawsuit against the FDA in connection with its decision to approve an NDA or establish requirements under a REMS. On April 13, 2023, the district court decision was stayed, in part, by the U. S. Court of Appeals for the Fifth Circuit. Thereafter, on April 21, 2023, the U. S. Supreme Court entered a stay pending disposition of the appeal of the district court decision in the Court of Appeals for the Fifth Circuit or the Supreme Court. The Court of Appeals for the Fifth Circuit held oral arguments in the case on May 17, 2023 and, on August 16, 2023, issued its decision. The court declined to order the removal of mifepristone from the market, finding that a challenge~~ **challenging** ~~to the~~ FDA' s **actions** ~~initial approval in 2000 is barred by the statute of limitations. But the Court of Appeals did hold that changes allowing for expanded access of mifepristone that FDA~~

~~authorized in 2016 and 2021 were arbitrary and capricious in violation of federal law .~~ On ~~September 8~~ **January 16** , ~~2023~~ **2025** , the **district** ~~Justice Department and a manufacturer of mifepristone asked the Supreme Court~~ **court agreed** to ~~review~~ **allow** ~~the~~ **these states to file an amended complaint and continue to pursue this challenge** ~~Court of Appeals' decision. On December 12, 2023, the Supreme Court announced that it will review the Court of Appeals' decision .~~ Depending on the outcome of this litigation ~~and the regulatory uncertainty it has engendered~~ , our ability to develop new drug **product** candidates and to maintain approval of existing ~~drug products and measures adopted under a REMS is at risk and our efforts to develop and market new~~ drug products could be delayed, undermined or subject to protracted litigation. Any delay in obtaining or failure to obtain required approvals could negatively affect our ability or that of any future collaborators to generate revenue from emavusertib, which likely would result in significant harm to our financial position and adversely impact our stock price. Failure to obtain marketing approval in foreign jurisdictions would prevent emavusertib from being marketed abroad. Any approval we may be granted for emavusertib in the U. S. would not assure approval of emavusertib in foreign jurisdictions and if emavusertib is approved for marketing in a foreign jurisdiction, it will be subject to risk associated with foreign operations. In order to market and sell our products in the European Union and other foreign jurisdictions, we, and any future collaborators, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, a product must be approved for reimbursement before the product can be approved for sale in that country. We, and any future collaborators, may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the U. S. does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may file for marketing approvals but not receive the necessary approvals to commercialize our products in any market. In many countries outside the United States, a drug candidate must also be approved for reimbursement before it can be sold in that country. In some cases, the price that we intend to charge for our product, if approved, is also subject to approval. Obtaining non- U. S. regulatory approvals and compliance with non- U. S. regulatory requirements could result in significant delays, difficulties and costs for us and any future collaborators and could delay or prevent the introduction of our drug candidate in certain countries. In addition, if we or any future collaborators fail to obtain the non- U. S. approvals required to market our drug candidate outside the United States or if we or any future collaborators fail to comply with applicable non- U. S. regulatory requirements, our target market will be reduced and our ability to realize the full market potential of our drug candidate will be harmed and our business, financial condition, results of operations and prospects may be adversely affected. ~~The~~ **Additionally, we could face heightened risks with respect to obtaining marketing authorization in the** United Kingdom ~~left~~ **, or UK, as a result of the withdrawal of the UK from** the EU ~~on January 31, 2020~~ , commonly referred to as Brexit. The **UK** ~~United Kingdom~~ is no longer part of the European Single Market and **EU** ~~European Union~~ Customs Union ~~as~~ **. As** of January 1, ~~2021~~ **2025** . ~~A trade and cooperation agreement that outlines the future trading relationship between the United Kingdom and the EU was agreed to in December 2020 and entered into force on May 1, 2021. As of January 1, 2021~~ , the Medicines and Healthcare ~~products~~ **Products** Regulatory Agency, or ~~the~~ MHRA, ~~became~~ **is** responsible for **approving all** ~~supervising medicines and medical~~ **medicinal** ~~devices in~~ **products destined for the UK market (i. e.,** Great Britain ~~, comprising England, Scotland~~ and ~~Wales under domestic law, whereas~~ Northern Ireland ~~will continue to be subject to EU rules under the Northern Ireland Protocol (as amended by the so- called Windsor Framework relating to Northern Ireland agreed to in February 2023~~). **At** ~~The MHRA relies on~~ the **same time** ~~Human Medicines Regulations 2012 (SI 2012 / 1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law of the body of EU law instruments governing medicinal products that pre- existed prior to the United Kingdom' s withdrawal from the EU. Since a significant proportion of the regulatory framework for pharmaceutical products in the United Kingdom covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit may have a material impact upon the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our drug candidates in the United Kingdom. For example, the United Kingdom is no longer covered by the centralized procedures for obtaining EU- wide marketing authorization from the EMA, and a separate marketing authorization will be required to market our drug candidates in the United Kingdom. Until December 31, 2023, it was possible for the MHRA to rely on a decision taken by the European Commission on the approval of a new marketing authorization via the centralized procedure. From January 1, 2024 on~~ , a new international recognition procedure, or IRP, ~~applies~~ **will apply,** which intends to facilitate approval of pharmaceutical products in the **UK** ~~United Kingdom~~ . The IRP is open to applicants that have already received an authorization for the same product from one of **the** MHRA' s specified Reference Regulators, or RRs. The RRs notably include EMA and regulators in the **EU / European Economic Area, or** EEA **,** member states for approvals in the **EU** ~~E. U.~~ centralized procedure and ~~the Mutual~~ **mutual** ~~Recognition~~ **recognition** ~~/ Decentralised Reliance, or MRDC,~~ procedure as well as the FDA (for product approvals granted in the U. S.). However, the concrete functioning of the IRP is currently unclear. Any delay in obtaining, or an inability to obtain, any marketing approvals ~~, as a result of Brexit or otherwise,~~ may force us **or our collaborators** to restrict or delay efforts to seek regulatory approval in the **UK** ~~United Kingdom~~ for our ~~drug~~ **product** candidates, which could significantly and materially harm our business **. In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission' s proposal for revision of several legislative instruments related to medicinal products, which may reduce the duration of regulatory data protection and exclusivity periods for orphan drugs, and revise the eligibility for**

expedited pathways in addition to other changes, was published on April 26, 2023. On April 10, 2024 the European Parliament adopted a position on the proposal requesting several amendments to the package. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may, however, have a significant impact on the pharmaceutical industry and our business in the long term . We expect that we will be subject to additional risks in commercializing emavusertib if it receives marketing approval outside the United States, including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States. We, or any future collaborators, may not be able to obtain orphan drug designation or orphan drug exclusivity for emavusertib and, even if we do, that exclusivity may not prevent the FDA or the EMA from approving competing products. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is a product intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200, 000 individuals annually in the United States. Generally, a product with orphan drug designation only becomes entitled to orphan drug exclusivity if it receives the first marketing approval for the indication for which it has such designation, in which case the FDA or the EMA will be precluded from approving another marketing application for the same product for that indication for the applicable exclusivity period. The applicable exclusivity period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. We or any future collaborators may seek orphan drug designations for emavusertib and may be unable to obtain such designations. Even if we do secure such designations and orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. Further, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, to be more effective or to make a major contribution to patient care. Finally, orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. The FDA and Congress may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a **September 2021** decision from the Court of Appeals for the 11th Circuit ~~in September 2021 finding~~ **. In Catalyst Pharms, Inc. v. Becerra, or Catalyst, held** that, for the purpose of determining the scope of **orphan drug** exclusivity, the term " same disease or condition " **in the statute** means the designated " rare disease or condition " and could not be interpreted by the ~~agency~~ **FDA** to mean the " indication or use. " Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the **approved** " indication or use. " Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, **the** FDA announced that, in matters beyond the scope of the **Catalyst** court ~~' s~~ order, **the** FDA will continue to apply its existing regulations tying orphan- drug exclusivity to the uses or indications for which the orphan drug ~~was~~ **is** approved **. More recently however, on February 14, 2025, a federal district court in Washington, DC fully embraced the reasoning of the Catalyst decision in another decision challenging the scope of orphan drug exclusivity. The implications of this decision, and its impact on the FDA' s implementation of the Orphan Drug Act, are unclear at this point** . We do not know if, when, or how the FDA or Congress may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted. **In addition, to obtain orphan drug designation in the EU, we would need to demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the medicinal product will be of significant benefit to those affected by that condition. There is no assurance that we would be able to meet that standard for any of our product candidates. Further, if we do obtain orphan drug designation for a candidate product in the EU, we will not be able to maintain that designation if we are not able to show, to the satisfaction of the EU regulatory authorities, that the candidate product is of significant benefit to patients over available commercial products for the indication in the EU and any additional products that are ahead of our product candidate in clinical development for the indication.** If we, or our collaborators, obtain marketing approval for emavusertib, it will be subject to ongoing regulation and could be subject to restrictions or withdrawal from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements, when and if emavusertib is approved. If we, or our collaborators, obtain marketing approval for emauvsertib, it will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post- marketing information and reports, registration and listing requirements, **current Good Manufacturing Practices, or similar foreign standards, which we refer to as** ~~cGMP~~ **cGMPs** ~~requirements~~ **,** relating to quality control and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. In addition, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post- marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a risk evaluation and mitigation strategy. Accordingly, if we receive marketing approval for emavusertib, we will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we fail to comply with these requirements, we could have the marketing approvals for our product withdrawn by regulatory authorities and our ability to

market any products could be limited, which could adversely affect our ability to achieve or sustain profitability. If we obtain marketing approval for emavusertib, we and our collaborators must also comply with requirements concerning advertising and promotion for emavusertib. Promotional communications with respect to prescription products are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product' s approved labeling. Thus, we will not be able to promote emavusertib for indications or uses for which it is not approved. The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post- approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. **We will also need to carefully navigate the FDA' s various regulations, guidance and policies, along with recently enacted legislation, to ensure compliance with restrictions governing promotion of our products.** In September 2021, the FDA published final regulations which describe the types of evidence that the ~~agency~~ **Agency** will consider in determining the intended use of a drug **or biologic** . Moreover, with passage of the ~~PIE~~ **Pre- Approval Information Exchange** Act in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. In addition, in ~~October~~ **January** ~~2023~~ **2025** , the FDA published ~~draft~~ **final** guidance outlining **its** ~~the agency' s non- binding~~ policies governing the distribution of scientific information ~~on~~ **to healthcare providers about** unapproved uses ~~to healthcare providers of approved products~~ . ~~This draft~~ **The final** guidance calls for such communications to be truthful, non- misleading ~~, factual,~~ and ~~unbiased~~ **scientifically sound** and **to** include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use **of the approved product. If a company engages in such communications consistent with the guidance' s recommendations, the FDA indicated that it will not treat such communications as evidence of unlawful promotion of a new intended use for the approved product** . Violations of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws. Failure to comply with regulatory requirements, may yield various results, including: • restrictions on such products, manufacturers or manufacturing processes; • restrictions on the labeling or marketing of a product; • restrictions on distribution or use of a product; • requirements to conduct post- marketing studies or clinical trials; • warning letters or untitled letters; • withdrawal of the products from the market; • refusal to approve pending applications or supplements to approved applications that we submit; • recall of products; • damage to relationships with collaborators; • unfavorable press coverage and damage to our reputation; • fines, restitution or disgorgement of profits or revenues; • suspension or withdrawal of marketing approvals; • refusal to permit the import or export of our products; • product seizure; • injunctions or the imposition of civil or criminal penalties; and • litigation involving patients using our products. Non- compliance with EU requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the EU' s requirements regarding the protection of personal information can also lead to significant penalties and sanctions. Further, the marketing and promotion of authorized drugs, including industry- sponsored continuing medical education and advertising directed toward the prescribers of drugs and / or the general public, are strictly regulated in the EU notably under Directive 2001 / 83EC, as amended, and are also subject to EU Member State laws. Direct- to-consumer advertising of prescription medicines is prohibited across the EU. Accordingly, assuming we, or our collaborators, receive marketing approval for emavusertib, we, and our collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we, and our collaborators, are not able to comply with post- approval regulatory requirements, our or our collaborators' ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post- approval regulations may have a negative effect on our operating results and financial condition **. We may seek approval from the FDA or comparable foreign regulatory authorities to use accelerated development pathways for our drug product candidates. If we are not able to use such pathways, we may be required to conduct additional clinical trials beyond those that are contemplated, which would increase the expense of obtaining, and delay the receipt of, necessary marketing approvals, if we receive them at all. In addition, even if an accelerated approval pathway is available to us, it may not lead to expedited approval of our drug product candidates, or approval at all. Under the Federal Food, Drug and Cosmetic Act, or the FDCA, and implementing regulations, the FDA may grant accelerated approval to a product candidate to treat a serious or life- threatening condition that provides meaningful therapeutic benefit over available therapies, upon a determination that the product 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 measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug. 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. Prior to seeking such accelerated approval, we will continue to seek feedback from the FDA or comparable foreign regulatory agencies and otherwise evaluate our ability to seek and receive such accelerated approval. There can be no assurance that the FDA or foreign regulatory agencies will agree with our surrogate endpoints or intermediate clinical endpoints in any of our clinical trials, or that we will decide**

to pursue or submit any additional applications for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that, after feedback from the FDA or comparable foreign regulatory agencies, we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval. Furthermore, for any submission of an application for accelerated approval or application under another expedited regulatory designation, there can be no assurance that such submission or application will be accepted for filing or that any expedited development, review or approval will be granted on a timely basis, or at all. Finally, there can be no assurance that we will satisfy all FDA requirements, including new provisions that govern accelerated approval. For example, with passage of the FDORA in December 2022, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized the FDA to require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded and to submit progress reports on its post- approval studies to FDA every six months until the study is completed. Moreover, FDORA established expedited procedures authorizing FDA to withdraw an accelerated approval if certain conditions are met, including where a required confirmatory study fails to verify and describe the predicted clinical benefit or where evidence demonstrates the product is not shown to be safe or effective under the conditions of use. The FDA may also use such procedures to withdraw an accelerated approval if a sponsor fails to conduct any required post- approval study of the product with due diligence, including with respect to " conditions specified by the Secretary. " The new procedures include the provision of due notice and an explanation for a proposed withdrawal, and opportunities for a meeting with the Commissioner or the Commissioner' s designee and a written appeal, among other things. We will need to fully comply with these and other requirements in connection with the development and approval of any product candidate that qualifies for accelerated approval. In March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The FDA indicated that the accelerated approval pathway is commonly used for approval of oncology drugs due to the serious and life- threatening nature of cancer. Although single- arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. To that end, the FDA outlined considerations for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology therapeutics. Subsequently, in December 2024 and January 2025, the FDA issued additional draft guidances relating to accelerated approval. These guidances describe FDA' s views on what it means to conduct a confirmatory trial with due diligence and how the agency plans to interpret whether such a study needs to be underway at the time of approval. While these guidances are currently only in draft form and will ultimately not be legally binding even when finalized, sponsors typically observe the FDA' s guidance closely to ensure that their investigational products qualify for accelerated approval. In the EU, a conditional marketing authorization may be granted in cases where all the required safety and efficacy data are not yet available. A conditional marketing authorization is subject to conditions to be fulfilled for generating missing data or ensuring increased safety measures. A conditional marketing authorization is valid for one year and has to be renewed annually until fulfillment of all relevant conditions. Once the applicable pending studies are provided, a conditional marketing authorization can become a " standard " marketing authorization. However, if the conditions are not fulfilled within the timeframe set by the EMA, the marketing authorization will cease to be renewed. Accordingly, a failure to obtain and maintain accelerated approval or any other form of expedited development, review or approval for our product candidates, or withdrawal of a product candidate, would result in a longer time period until commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace . We may seek certain designations for emavusertib, including Breakthrough Therapy and Fast Track designations, in the U. S., and PRIME Designation in the EU, but we might not receive such designations, and even if we do, such designations may not lead to a faster development or regulatory review or approval process. We may seek certain designations for emavusertib that could expedite review and approval by the FDA. A Breakthrough Therapy product is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drug 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. Products designated as Breakthrough Therapies by the FDA may also be eligible for priority review if supported by clinical data at the time the NDA is submitted to the FDA. The FDA may also designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life - threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product' s application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. Designation as a Breakthrough Therapy or Fast Track is within the discretion of the FDA. Accordingly, even if we believe that emavusertib meets the criteria for these designations, the FDA may disagree and instead determine not to make such designation. Further, even if we receive Breakthrough Therapy or Fast Track designation, the receipt of such designation for a drug candidate may not result in a faster development or regulatory review or approval process compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if emavusertib qualifies for one of these designations, the FDA may later decide that it no longer meets the

conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Project Optimus is an initiative of the Oncology Center of Excellence at the FDA. This project focuses on dose optimization and dose selection in oncology drug development, and whether the current paradigm based on cytotoxic chemotherapeutics leads to doses and schedules of molecularly targeted therapies that provide more toxicity without additional efficacy, among other things. There is no assurance, however, that this initiative will lead to early discussions with the FDA or expedited studies leading to optimization of dose selection for emavusertib, and could subject us to incur additional costs and extend the testing of our drug candidate to further evaluate dose optimization and dose selection, which could further delay our ability to obtain regulatory approvals, if at all. In the EU, we may seek PRIME designation for emavusertib in the future. PRIME is a voluntary program aimed at enhancing the EMA' s role to reinforce scientific and regulatory support in order to optimize development and enable accelerated assessment of new medicines that are of major public health interest with the potential to address unmet medical needs. The program focuses on medicines that target conditions for which there exists no satisfactory method of treatment in the EU or even if such a method exists, it may offer a major therapeutic advantage over existing treatments. PRIME is limited to medicines under development and not authorized in the EU and for which the sponsor intends to apply for an initial marketing authorization application through the centralized procedure. To be accepted for PRIME, a drug candidate must meet the eligibility criteria in respect of its major public health interest and therapeutic innovation based on information that is capable of substantiating the claims. The benefits of a PRIME designation include the appointment of a CHMP rapporteur to provide continued support and help to build knowledge ahead of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review, meaning reduction in the review time for an opinion on approvability to be issued earlier in the application process. PRIME enables a sponsor to request parallel EMA scientific advice and health technology assessment advice to facilitate timely market access. Even if we receive PRIME designation for emavusertib, the designation may not result in a materially faster development process, review or approval compared to conventional EMA procedures. Further, obtaining PRIME designation does not assure or increase the likelihood of EMA' s grant of a marketing authorization. If we are required by the FDA to obtain clearance or approval of a companion diagnostic in connection with approval of a candidate therapeutic product, and we do not obtain or there are delays in obtaining FDA clearance or approval of a diagnostic device, we will not be able to commercialize the drug candidate and our ability to generate revenue will be materially impaired. In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and in vitro companion diagnostics. According to the guidance, if the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic is not also approved or cleared for that indication. Under the Federal Food, Drug, and Cosmetic Act, or FDCA, companion diagnostics are regulated as medical devices and the FDA has generally required companion diagnostics intended to select the patients who will respond to cancer treatment to obtain premarket approval, or a PMA. Consequently, we anticipate that certain of our companion diagnostics may require us or our collaborators to obtain a PMA. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device' s safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA approval is not guaranteed and may take considerable time, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time- consuming to generate and that can substantially delay approval. As a result, if we or our collaborators are required by the FDA to obtain approval of a companion diagnostic for a candidate therapeutic product, and we or our collaborators do not obtain or there are delays in obtaining FDA approval of a diagnostic device, we will not be able to commercialize the drug candidate and our ability to generate revenue will be materially impaired. **It is possible that an in vitro companion diagnostic device could be subject to FDA enforcement discretion from compliance with the FDCA if it meets the definition of a Laboratory Developed Test, or LDT. However, FDA issued a final rule in April 2024 to end enforcement discretion for LDTs and actively regulate such products as medical devices. Under this final rule, LDTs are required to come into compliance with FDA' s medical device regulatory requirements in a staged approach over the course of four years. The implementation of this LDT final rule could potentially be affected by the Executive Order, Regulatory Freeze Pending Review, issued by President Trump on January 20, 2025 and / or the anticipated change in leadership at FDA under the new administration. Further, while the final regulation is set to take effect on May 6, 2025, a number of parties have challenged the legality of the LDT regulation in a federal district court. That court held a hearing on this matter on February 19, 2025, and is expected to issue a ruling soon.** In its August 2014 guidance, the FDA also indicated that companion diagnostics used to make treatment decisions in clinical trials of a therapeutic product generally will be considered investigational devices. When a companion diagnostic is used to make critical treatment decisions, such as patient selection, the FDA stated that the diagnostic will be considered a significant risk device requiring an investigational device exemption. The FDA may find that a companion diagnostic that we, alone or with a third party, plan to develop does not comply with those requirements and, if this were to occur, we would not be able to proceed with our planned trial of the applicable drug candidate in these patient populations. Given our limited experience in developing and commercializing diagnostics, we do not plan to develop companion diagnostics internally and thus will be dependent on the sustained cooperation and effort of third party collaborators in developing and obtaining approval for these companion diagnostics. We may not be able to enter into arrangements with a provider to develop a companion diagnostic for use in connection with a registrational trial for our drug candidates or for commercialization of our drug candidates, or do so on commercially reasonable terms, which could adversely affect and / or delay the development or commercialization of our drug candidates. We and our future collaborators may encounter difficulties in developing and obtaining approval for the companion

diagnostics, including issues relating to selectivity / specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by our collaborators to develop or obtain regulatory approval of the companion diagnostics could delay or prevent approval of our drug candidates. In addition, we, our collaborators or third parties may encounter production difficulties that could constrain the supply of the companion diagnostics, and both they and we may have difficulties gaining acceptance of the use of the companion diagnostics by physicians. We believe that adoption of screening and treatment into clinical practice guidelines is important for payer access, reimbursement, utilization in medical practice and commercial success, but both our collaborators and we may have difficulty gaining acceptance of the companion diagnostic into clinical practice guidelines. If such companion diagnostics fail to gain market acceptance, it would have an adverse effect on our ability to derive revenues from sales, if any, of any of our drug candidates that are approved for commercial sale. In addition, any companion diagnostic collaborator or third party with whom we contract may decide not to commercialize or to discontinue selling or manufacturing the companion diagnostic that we anticipate using in connection with development and commercialization of our drug candidate, or our relationship with such collaborator or third party may otherwise terminate. We may not be able to enter into arrangements with another provider to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our drug candidates or do so on commercially reasonable terms, which could adversely affect and / or delay the development or commercialization of our drug candidate. **Disruptions at** ~~Inadequate funding for~~ the FDA, the SEC and other government agencies, including from government shutdowns, **funding shortages, global health concerns, personnel losses, regulatory reform** or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business. The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new drug candidates to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable. **Further, while the FDA' s review of NDAs and other applications is funded through the user fee program established under PDUFA, the Trump Administration has indicated that it will be reviewing that program and its implementation.** Disruptions at the FDA and other agencies may also slow the time necessary for new drug candidates to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U. S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations **. In addition, disruptions may result from events similar to the COVID- 19 pandemic. During the COVID- 19 pandemic, a number of companies announced receipt of complete response letters due to the FDA' s inability to complete required inspections for their applications. In the event of a similar public health emergency in the future, the FDA may not be able to continue its current pace and review timelines could be extended. Regulatory authorities outside the United States facing similar circumstances may adopt similar restrictions or other policy measures in response to a similar public health emergency and may also experience delays in their regulatory activities. There is also substantial uncertainty as to how measures being implemented by the new Trump Administration across the government will impact the FDA, CMS and other federal agencies with jurisdiction over our activities. For example, since taking office, President Trump has issued a number of executive orders, which could have a significant impact on the manner in which the FDA conducts its operations and engages in regulatory and oversight activities. These include E. O. 14192, " Unleashing Prosperity Through Deregulation, " January 31, 2025; E. O. 14212, " Establishing the President' s Make America Healthy Again Commission, " February 13, 2025; and E. O. 14219, Ensuring Lawful Governance and Implementing the President' s ' Department of Government Efficiency " Deregulatory Initiative, " February 21, 2025. If these or other orders or executive actions impose constraints on FDA' s ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. In addition, the loss of FDA personnel could lead to further disruptions and delays in FDA review and oversight of our product candidates. Similarly, efforts by the new administration to substantially reduce or delay research funding by the National Institutes of Health of medical research could have substantial direct or indirect impacts on our research activities** . If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets. If the FDA, EMA or other comparable foreign regulatory authorities approve generic versions of any of our small molecule investigational products that receive marketing approval, or such authorities do not grant our products appropriate periods of exclusivity before approving generic versions of those products, the sales of our products, if approved, could be adversely affected. Once an NDA is approved, the product covered thereby becomes a " reference listed drug " in the FDA' s publication, " Approved Drug Products with Therapeutic Equivalence Evaluations, " commonly known as the Orange Book. Manufacturers may seek approval of generic versions of reference listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a

generic manufacturer need not conduct clinical trials to assess safety and efficacy. Rather, the sponsor generally must show that its product has the same active ingredient (s), dosage form, strength, route of administration and conditions of use or labelling as the reference listed drug and that the generic version is bioequivalent to the reference listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference listed drug is typically lost to the generic product. The FDA may not approve an ANDA for a generic product until any applicable period of **regulatory** ~~non- patent~~ exclusivity for the reference listed drug has expired. The FDCA provides a period of five years of **regulatory** ~~non- patent~~ exclusivity for a new drug containing a new chemical entity. Specifically, in cases where such exclusivity has been granted, an ANDA may not be submitted to the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference listed drug is either invalid or will not be infringed by the generic product, in which case the sponsor may submit its application four years following approval of the reference listed drug. Generic drug manufacturers may seek to launch generic products following the expiration of any applicable **regulatory** exclusivity period we obtain if our products are approved, even if we still have patent protection for such products. Competition that our product could face from generic versions of our product could materially and adversely affect our future revenue, profitability, and cash flows and substantially limit our ability to obtain a return on the investments we have made in the drug candidate. Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain reimbursement for any drug candidate that does receive marketing approval and our ability to generate revenue will be materially impaired. In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our drug candidates, restrict or regulate post- approval activities and affect our ability to profitably sell any drug candidates for which we obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any collaborators, may receive for any approved products. In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, or PPACA, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $ 1. 2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation' s automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2 % per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 under the CARES Act ~~. Pursuant to subsequent legislation, however, these Medicare sequester reductions were and reduced in 2021 and 2022 but, as of July 1, 2022, the full 2 % cut resumed. Under current legislation, the actual reductions in Medicare payments may vary up to 4 %~~. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Further, with the passage of the Inflation Reduction Act, or the IRA, in August 2022, Congress extended the expansion of PPACA premium tax credits through 2025. These and other laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our products or drug candidates for which we may obtain regulatory approval or the frequency with which any such product is prescribed or used. For example, the Consolidated Appropriations Act, which was signed into law by President Biden in December 2022, made several changes to sequestration of the Medicare program. Section 1001 of the Act delays the 4 % Statutory Pay- As- You- Go Act of 2010 (PAYGO) sequester for two years, through the end of calendar year 2024. Triggered by enactment of the American Rescue Plan Act of 2021, the 4 % cut to the Medicare program would have taken effect in January 2023. The Act' s health care offset title includes Section 4163, which extends the 2 % Budget Control Act of 2011 Medicare sequester for six months into fiscal year 2032 and lowers the payment reduction percentages in fiscal years 2030 and 2031. Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the " individual mandate. " The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019 ~~.~~ Further, ~~on December 14, 2018, a U. S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. The U. S. Supreme Court heard this case on November 10, 2020 and~~ on June 17, 2021, **the U. S. Supreme Court** dismissed ~~this~~ **an** action **challenging the PPACA** after finding that the plaintiffs ~~do~~ **did** not have standing to challenge the constitutionality of the ~~ACA~~ **law**. Litigation and legislation over the ~~ACA~~ **PPACA** are likely to continue, with unpredictable and uncertain results. ~~The~~ **During the first** Trump Administration ~~also took~~ **, the Congress and administration sought to overturn the ACA and related measures. Shortly after taking office in January 2025, President Trump revoked numerous** executive **orders issued by** ~~actions related to the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however,~~ President Biden ~~issued a new~~ **, including at least two** ~~Executive~~ **executive** ~~Order which directs federal agencies to reconsider rules~~ **orders (e. g., EO 14009, Strengthening Medicaid** and ~~other~~ -- **the** ~~policies that limit~~ **Affordable Care Act, and EO 14070, Continuing to Strengthen** Americans' ~~access~~ **Access** to **Affordable, Quality** ~~health~~ **Health Coverage) where were designed** ~~care, and consider actions that will protect and strengthen that access. Under~~

~~this Order, federal agencies are directed~~ to **further implement** ~~re- examine: policies that undermine protections for people with pre- existing conditions, including complications related to COVID- 19; demonstrations and waivers under Medicaid and~~ the ACA **. We anticipate similar efforts** ~~that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult~~ to **change** ~~enroll in Medicaid and~~ the ACA ~~;~~ **,** and **the accompanying uncertainty,** ~~policies that reduce affordability of coverage or~~ **for the foreseeable future** ~~financial assistance, including for dependents~~ . We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and / or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from a drug candidate that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize the drug candidate. The prices of prescription pharmaceuticals in the United States and foreign jurisdictions are subject to considerable legislative and executive actions and could impact the prices we obtain for our products, if and when licensed. The prices of prescription pharmaceuticals have been the subject of considerable discussion in the United States. There have been ~~several recent~~ U. S. Congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid ~~. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician- administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, the Centers for Medicare & Medicaid Services, or CMS, issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence- based care~~ . In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America, or PhRMA, but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. ~~Nine~~ **Seven** states ~~(Colorado, Florida, Maine, New Hampshire, New Mexico, North Dakota, Texas, Vermont and Wisconsin)~~ have passed laws allowing for the importation of drugs from Canada. **Two** ~~Certain of these~~ states have **passed legislation establishing workgroups to examine the impact of a state importation program. As of May 2024, five states had** submitted Section 804 Importation Program proposals **to the** ~~and are awaiting~~ FDA ~~approval. On~~ **and, on** January 5, ~~2023~~ **2024** , the FDA approved Florida' s plan for Canadian drug importation. **That state now has authority to import certain drugs from Canada for a period of two years once certain conditions are met. Florida will first need to submit a pre- import request for each drug selected for importation, which must be approved by the FDA. The state will also need to relabel the drugs and perform quality testing of the products to meet FDA standards.** Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The final rule would also eliminate the current safe harbor for Medicare drug rebates and create new safe harbors for beneficiary point- of- sale discounts and pharmacy benefit manager service fees. It was originally set to go into effect on January 1, 2022, but with passage of the IRA has been delayed by Congress to January 1, 2032 ~~. In September 2021, acting pursuant to an executive order signed by President Biden, the HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (a) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (b) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments~~ . On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap ~~; imposes rebates under Medicare Part B~~ and **it** ~~Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and~~ replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025) **. In addition, the IRA established inflation rebate programs under Medicare Part B and Part D. These programs require manufacturers to pay rebates to Medicare if they raise their prices for certain Part B and Part D drugs faster than the rate of inflation. On December 9, 2024, with issuance of its 2025 Physician Fee Schedule final regulation, CMS finalized its rules governing the IRA inflation rebate programs** . The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single- source drug products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices

for ten high- cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years ~~, but it does not apply to drugs that have been approved for a single rare disease or condition~~ . Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would be fully at risk of government action if our products are the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years **. The first cycle of negotiations for the Medicare Drug Price Negotiation Program commenced in the summer of 2023. On August 15, 2024, the HHS published the results of the first Medicare drug price negotiations for ten selected drugs that treat a range of conditions, including diabetes, chronic kidney disease, and rheumatoid arthritis. The prices of these ten drugs will become effective January 1, 2026. On January 17, 2025, CMS announced its selection of 15 additional drugs covered by Part D for the second cycle of negotiations. Thereafter, following the change in administrations, CMS issued a public statement on January 29, 2025, declaring that lowering the cost of prescription drugs is a top priority of the new administration and CMS is committed to considering opportunities to bring greater transparency in the negotiation program. The second cycle of negotiations with participating drug companies will occur during 2025, and any negotiated prices for this second set of drugs will be effective starting January 1, 2027. In addition, we will need to carefully navigate the IRA and its provisions governing orphan drugs. Specifically, the IRA includes a provision, known as the orphan drug exclusion, that excludes from price negotiations those orphan drugs that have been designated for only one rare disease or condition and for which the only approved indication (or indications) is for such disease or condition. Thus, as CMS stated in final guidance in July 2023, a drug or biologic that is designated for more than one rare disease or condition will not qualify for the orphan drug exclusion, even if the drug or biologic is not approved for any indications for the additional diseases or conditions. While there is Congressional support for expanding the orphan drug exclusion to include orphan drugs with more than one approved indication, no legislation has been enacted. Accordingly, if one of our product candidates is designated and approved as an orphan drug for one disease or condition, and we subsequently receive approval of that product for a different disease or condition, the product will no longer be excluded from the IRA price negotiation provision under the orphan drug exclusion and that could impact our revenues and business** . Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated " maximum fair price " under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out- of- pocket drug costs at an estimated $ 4, 000 a year in 2024 and, thereafter beginning in 2025, at $ 2, 000 a year. In addition, the IRA potentially raises legal risks with respect to individuals participating in a Medicare Part D prescription drug plan who may experience a gap in coverage if they required coverage above their initial annual coverage limit before they reached the higher threshold, or " catastrophic period " of the plan. Individuals requiring services exceeding the initial annual coverage limit and below the catastrophic period, must pay 100 % of the cost of their prescriptions until they reach the catastrophic period. Among other things, the IRA contains many provisions aimed at reducing this financial burden on individuals by reducing the co- insurance and co- payment costs, expanding eligibility for lower income subsidy plans, and price caps on annual out- of- pocket expenses, each of which could have potential pricing and reporting implications. On June 6, 2023, Merck & Co. filed a lawsuit against the HHS and CMS asserting that, among other things, the IRA' s Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U. S. Chamber of Commerce, Bristol Myers Squibb Company, PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against the HHS and CMS **. HHS has generally won the substantive disputes in these cases, and various federal district court judges have expressed skepticism regarding the merits of the legal arguments being pursued by the pharmaceutical industry. Certain of these cases are now on appeal and, on October 30, 2024, the Court of Appeals for the Third Circuit heard oral argument in three of these cases.** We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results. Accordingly, while it is currently unclear how the IRA will be effectuated, we cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition. At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare organizations 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. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our drug candidates or additional pricing pressures **. This may be increasingly true with respect to products approved pursuant to the accelerated approval pathway. State Medicaid programs and other payers are developing strategies and implementing significant coverage barriers, or refusing to cover these products outright, arguing that accelerated approval drugs have insufficient or limited evidence despite meeting the FDA' s standards for accelerated approval** . In the European Union, similar political, economic and regulatory

developments may affect our ability to profitably commercialize our drug candidates, if approved. In markets outside of the United States and the European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. In many countries, including those of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or our collaborators may be required to conduct a clinical trial that compares the cost- effectiveness of our product to other available therapies. If reimbursement of our product is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed. We may be subject to certain healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations, and diminished profits and future earnings. Healthcare providers, third party payors and others will play a primary role in the recommendation and prescription of any product for which we obtain marketing approval. Our future arrangements with healthcare providers and third party payors will expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any product for which we obtain marketing approval. Potentially applicable U. S. federal and state healthcare laws and regulations include the following: Anti- Kickback Statute. The federal Anti- Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid; False Claims Laws. The federal false claims laws, including the civil False Claims Act, impose criminal and civil penalties, including those from civil whistleblower or qui tam actions against individuals or entities for knowingly presenting, or causing to be presented to the federal government claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government; HIPAA. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing or attempting to execute a scheme to defraud any healthcare benefit program; False Statements Statute. The federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; Transparency Requirements. The federal Physician Payments Sunshine Act requires certain manufacturers of drugs for which payment is available under Medicare, Medicaid, or the Children' s Health Insurance Program, with specific exceptions, to report annually to the HHS information related to healthcare provider payments and other transfers of value and healthcare provider ownership and investment interests; and Analogous State and Foreign Laws. Analogous state laws and regulations, such as state anti- kickback and false claims laws, and transparency laws, may apply to sales or marketing arrangements, and claims involving healthcare items or services reimbursed by non- governmental third party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry' s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures. Efforts to ensure that our business arrangements with third parties, and our business generally, will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, and reputational harm, any of which could substantially disrupt our operations. If any of the physicians or other providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. We are subject to stringent privacy laws, information security laws, regulations, policies, and contractual obligations and failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations. We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally- identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information, including comprehensive regulatory systems in the U. S., EU and United Kingdom. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. Failure to comply with any of these laws and regulations could result in enforcement action against us, including fines, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects. There are numerous U. S. federal and state laws and regulations related to the privacy and security of personal information. In particular, regulations promulgated pursuant to HIPAA establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Determining whether protected health information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation. These obligations may be applicable to some or all of our business activities now or in the future. If we are unable to properly protect the privacy and security of protected health information, we could be found

to have breached our contracts. Further, if we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems. In addition to federal privacy requirements there also are state law requirements that may impact our business operations. In 2018, California passed into law the California Consumer Privacy Act, or the CCPA, which took effect on January 1, 2020, and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA' s requirements are similar to those found in the General Data Protection Regulation, or the GDPR, including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt out of " sales " of their personal information. The CCPA contains significant penalties for companies that violate its requirements. In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act, or the CPRA, which went into effect on January 1, 2023, and significantly expand the CCPA to incorporate additional GDPR- like provisions including requiring that the use, retention and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities. In addition to California, ~~eleven~~ **at least 18** other states have ~~already~~ passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of " sensitive " data ~~,~~**(** which includes health data in some cases **)** . Some of the provisions of these laws may apply to our business activities. There are also states that are ~~strongly~~ considering or have already passed comprehensive privacy laws during the ~~2024~~ **2023** legislative sessions that will go into effect in ~~2025~~ **2024** and beyond ~~, including New Hampshire and New Jersey~~ . **There are also states that are** ~~In addition, the State of Washington passed the My Health My Data Act in 2023 which~~ specifically ~~regulated~~ **regulating** health information that **may affect our business** ~~is not otherwise regulated by the HIPAA rules~~ . ~~Connecticut and Nevada have also~~ **For example, Washington state recently** passed **a** ~~similar laws regulating consumer~~ health ~~data, and more states (such as Vermont) are considering such legislation in 2024. In addition, Congress has also been debating passing a federal~~ privacy law **that will regulate the collection and sharing of health information, and the law also has a private right of action, which further increases the relevant compliance risk** . These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products **. Plaintiffs' lawyers are also increasingly using privacy- related statutes at both the state and federal level to bring lawsuits against companies for their data- related practices. In particular, there have been a significant number of cases filed against companies for their use of pixels and other web trackers. These cases often allege violations of the California Invasion of Privacy Act and other state laws regulating wiretapping, as well as the federal Video Privacy Protection Act. The rise in these types of lawsuits creates potential risk for our business** . Similar to the laws in the U. S., there are significant privacy and data security laws that apply in Europe and other countries. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in the European Economic Area, or the EEA, and the processing of personal data that takes place in the EEA, is regulated by the GDPR, which went into effect in May 2018 and which imposes obligations on companies that operate in our industry with respect to the processing of personal data and the cross- border transfer of such data. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and policies. If our or our partners' or service providers' privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and / or fines of up to 20 million Euros or up to 4 % of the total worldwide annual turnover of the group of companies of the preceding financial year, whichever is higher, as well as compensation claims by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill. The GDPR places restrictions on the cross- border transfer of personal data from the EU to countries that have not been found by the EC to offer adequate data protection legislation. There are ongoing concerns about the ability of companies to transfer personal data from the EU to other countries. In July 2020, the Court of Justice of the EU, or the CJEU, invalidated the EU- U. S. Privacy Shield, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the U. S. The CJEU decision also drew into question the long- term viability of an alternative means of data transfer, the standard contractual clauses, for international transfers of personal data from the EEA. This CJEU decision resulted in increased scrutiny on data transfers and increased our costs of compliance with data privacy legislation as well as our costs of negotiating appropriate privacy and security agreements with our vendors and business partners. In October 2022, President Biden signed an executive order to implement the EU- U. S. Data Privacy Framework, which serves as a replacement to the EU- U. S. Privacy Shield. The EC adopted the adequacy decision on July 10, 2023. The adequacy decision permits U. S. companies who self- certify to the EU- U. S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the EU to the U. S. However, some privacy advocacy groups have already suggested that they will be challenging the EU- U. S. Data Privacy Framework. If these challenges are successful, they may not only impact

the EU- U. S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue has the potential to impact our business. Following the withdrawal of the UK from the EU, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the UK and includes parallel obligations to those set forth by GDPR. In relation to data transfers, both the UK and the EU have determined, through separate " adequacy " decisions, that data transfers between the two jurisdictions are in compliance with the UK Data Protection Act and the GDPR, respectively. The UK and the U. S. have also agreed to a U. S.- UK " Data Bridge ", which functions similarly to the EU- U. S. Data Privacy Framework and provides an additional legal mechanism for companies to transfer data from the UK to the U. S. In addition to the UK, Switzerland is also in the process of approving an adequacy decision in relation to the Swiss- U. S. Data Privacy Framework (which would function similarly to the EU- U. S. Data Privacy Framework and the U. S.- UK Data Bridge in relation to data transfers from Switzerland to the U. S.). Any changes or updates to these developments have the potential to impact our business. Beyond GDPR, there are privacy and data security laws in a growing number of countries around the world. While many loosely follow GDPR as a model, other laws contain different or conflicting provisions. These laws will impact our ability to conduct our business activities, including both our clinical trials and the sale and distribution of commercial products, through increased compliance costs, costs associated with contracting and potential enforcement actions. While we continue to address the implications of the recent changes to data privacy regulations, data privacy remains an evolving landscape at both the domestic and international level, with new regulations coming into effect and continued legal challenges, and our efforts to comply with the evolving data protection rules may be unsuccessful. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. We must devote significant resources to understanding and complying with this changing landscape. Failure to comply with laws regarding data protection would expose us to risk of enforcement actions taken by data protection authorities in the EEA and elsewhere and carries with it the potential for significant penalties if we are found to be non- compliant. Similarly, failure to comply with federal and state laws in the U. S. regarding privacy and security of personal information could expose us to penalties under such laws. Any such failure to comply with data protection and privacy laws could result in government- imposed fines or orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects. Accordingly, any breach of privacy laws or data security laws, particularly any breach resulting in a significant security incident or breach involving the misappropriation, loss or other unauthorized use or disclosure of sensitive or confidential patient or consumer information, could have a material adverse effect on our business, reputation and financial condition. As a data controller, we will be accountable for any third- party service providers we engage to process personal data on our behalf, including our CROs. There is no assurance that privacy and security- related safeguards we implement will protect us from all risks associated with the third- party processing, storage and transmission of such information. In certain situations, both in the United States and in other countries, we also may be obligated as a result of a security breach to notify individuals and / or government entities about these breaches. Given the breadth and depth of changes in data protection obligations, preparing for and complying with such requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations. We are subject to U. S. and foreign anti- corruption and anti- money laundering laws with respect to our operations and non- compliance with such laws can subject us to criminal and / or civil liability and harm our business. We are subject to the U. S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U. S. domestic bribery statute contained in 18 U. S. C. § 201, the U. S. Travel Act, the USA PATRIOT Act, and other state and national anti- bribery and anti- money laundering laws in countries in which we conduct activities. Anti- corruption laws are interpreted broadly and prohibit companies and their employees, agents, third party intermediaries, joint venture partners and collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We may have direct or indirect interactions with officials and employees of government agencies or government- affiliated hospitals, universities, and other organizations. In addition, we may engage third party intermediaries to promote our clinical research activities abroad and / or to obtain necessary permits, licenses, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of these third party intermediaries, our employees, representatives, contractors, partners, and agents, even if we do not explicitly authorize or have actual knowledge of such activities. We have adopted a code of business conduct and ethics that mandates compliance with the FCPA and other anti- corruption laws applicable to our business throughout the world. We cannot assure you, however, that our employees and third party intermediaries will comply with this code or such anti- corruption laws. Noncompliance with anti- corruption and anti- money laundering laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and / or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage, and other collateral consequences. If any subpoenas, investigations, or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially

harmed. In addition, responding to any action will likely result in a materially significant diversion of management' s attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens. We are subject to governmental export and import controls that could impair our ability to compete in international markets due to licensing requirements and subject us to liability if we are not in compliance with applicable laws. Our products and solutions are subject to export control and import laws and regulations, including the U. S. Export Administration Regulations, U. S. Customs regulations, and various economic and trade sanctions regulations administered by the U. S. Treasury Department' s Office of Foreign Assets Controls. Exports of our products and solutions outside of the United States must be made in compliance with these laws and regulations. If we fail to comply with these laws and regulations, we and certain of our employees could be subject to substantial civil or criminal penalties, including the possible loss of export or import privileges, fines, which may be imposed on us and responsible employees or managers, and, in extreme cases, the incarceration of responsible employees or managers. In addition, changes in our products or solutions or changes in applicable export or import laws and regulations may create delays in the introduction, provision, or sale of our products and solutions in international markets, prevent customers from using our products and solutions or, in some cases, prevent the export or import of our drugs and solutions to certain countries, governments or persons altogether. Any limitation on our ability to export, provide, or sell our products and solutions could adversely affect our business, financial condition and results of operations. **Changes in U. S. and international trade policies, particularly with respect to China and Canada, may adversely impact our business and operating results. We rely on third party contract manufacturing organizations, or CMOs, to produce our product candidate. One of our CMOs has a Chinese subcontractor that produces regulatory starting materials. Another CMO operates in Canada and produces our drug product. The U. S. government has recently made statements and taken certain actions that may lead to potential changes to U. S. and international trade policies, including imposing several rounds of tariffs and export control restrictions. Recently both China and Canada have each imposed tariffs indicating the potential for further trade barriers. It is unknown whether and to what extent new tariffs, export controls, or other new laws or regulations will be adopted, or the effect that any such actions would have on us or our industry. Sustained uncertainty about, or the further escalation of, trade and political tensions could result in a disadvantageous manufacturing environment in China and Canada. Any unfavorable government policies on international trade, such as capital controls or tariffs, or export controls, may increase the cost of manufacturing of our product candidate, and may affect the import of raw materials and drug product used in our preclinical and clinical studies from China, Canada, or other countries.** If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business. We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations. 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, however this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions. Our employees may engage in misconduct or other improper activities, including non- compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation. We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions. Our internal computer systems, or those of any collaborators or contractors or consultants, may fail or suffer security breaches **or other cyber incidents** , which could result in a material disruption of our product development program. Despite the implementation of security measures and certain data recovery measures, our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage or other impacts from cyber- attacks, computer viruses, unauthorized access, sabotage, natural disasters, terrorism, war and telecommunication and electrical failures. We may experience security breaches of our information technology systems. Any system failure, accident or security breach that causes interruptions in our operations, for us or those third parties with

which we contract, could result in a material disruption of our product development program and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from an ongoing, completed or future clinical trial could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we may incur liabilities, our competitive position could be harmed and the further development and commercialization of emavusertib may be delayed. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events. We **are** ~~could be~~ subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company, including personal information of our employees. In addition, outside parties have ~~attempted~~ **in the past penetrated** , and may in the future ~~attempt, to~~ penetrate **,** our systems or those of our vendors or fraudulently induce our employees or employees of our vendors to disclose sensitive information to **an unintended recipient or to** gain access to our data. Like other companies, we **have experienced, and** may **in the future** experience **,** threats to our data and systems, including malicious codes and viruses **, phishing** , and other cyber-attacks. The number and complexity of these threats continue to increase over time. If a material breach of our security or that of our vendors occurs, the market perception of the effectiveness of our security measures could be harmed, we could lose business and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely. RISKS RELATING TO OUR COMMON STOCK If we fail to meet the requirements for continued listing on the Nasdaq Capital Market, our common stock could be delisted from trading, which would decrease the liquidity of our common stock and our ability to raise additional capital. Our common stock is currently listed on the Nasdaq Capital Market. We are required to meet specified requirements to maintain our listing on the Nasdaq Capital Market, including a minimum bid price of $ 1. 00 per share for our common stock and standards relative to minimum stockholders' equity, minimum market value of publicly held shares and various additional requirements. In the past we have, from time to time, received deficiency letters from Nasdaq as a consequence of our failure to satisfy such **requirements. On February 21, 2025, we received a deficiency letter from Listing Qualifications Department of Nasdaq notifying us that the market value of our listed securities had closed for the last 30 consecutive business days below the minimum $ 35, 000, 000 requirement for continued listing on the Nasdaq Capital Market pursuant to Nasdaq Listing Rule 5550 (b) (2), or Minimum MVLS Requirement. We have 180 calendar days, or until August 20, 2025, or Compliance Period, to regain compliance with the Minimum MVLS Requirement. In order to regain compliance, the market value of our listed securities must close at $ 35, 000, 000 or more for a minimum of ten consecutive business days. If we do not regain compliance within the Compliance Period, we will receive written notification that our securities are subject to delisting from the Nasdaq Capital Market. There can be no assurance that we can regain, or maintain in the future, compliance with the Nasdaq continued listing** requirements. If we fail to satisfy the Nasdaq Capital Market' s continued listing requirements and we are delisted from Nasdaq, we may transfer to and commence trading on the OTC Markets or another quotation medium. As a result, an investor would likely find it more difficult to trade or obtain accurate price quotations for our shares. Delisting would likely also reduce the visibility, liquidity, and value of our common stock, reduce institutional investor interest in our company, and may increase the volatility of our common stock. Delisting could also cause a loss of confidence of potential industry partners, lenders, and employees, which could further harm our business and our future prospects. Some or all of these material adverse consequences may contribute to a further decline in our stock price. Our stock price has and may continue to fluctuate significantly and the market price of our common stock could drop below the price paid by our investors. The trading price of our common stock has been volatile and is likely to continue to be volatile in the future. The stock market, particularly in recent years, has experienced significant volatility with respect to pharmaceutical and biotechnology company stocks. Prices for our stock will be determined in the marketplace and may be influenced by many factors, including: • the timing and result of clinical trials of emavusertib; • regulatory actions with respect to emavusertib or our competitors' products and drug candidates; • market conditions in the biotechnology and pharmaceutical sectors; • actual or anticipated changes to our research and development plans; • the success of, and announcements regarding, existing and new technologies and / or drug candidates by us or our competitors; • rumors relating to us or our collaborators or competitors; • commencement or termination of collaborations; • litigation or public concern about the safety of emavusertib; • deviations in our operating results from the estimates of securities analysts or the failure by one or more securities analysts to continue to cover our stock; • entering into new collaboration agreements or termination of existing collaboration agreements; • adverse results or delays in clinical trials being conducted by us or any collaborators; • any intellectual property disputes or other lawsuits involving us; • third party sales of large blocks of our common stock; • sales of our common stock by our executive officers, directors or significant stockholders; • sales by us of our common stock to fund our operations; • the loss of any of our key scientific or management personnel; • limited trading volume in our common stock; • actual or anticipated variations in our quarterly operating results and any subsequent restatement of such results; • general economic and market conditions, including adverse changes in the domestic and international financial markets; and • the other factors described in this " Risk Factors " section. While we cannot predict the individual effect that these factors may have on the price of our common stock, these factors, either individually or in the aggregate, could result in significant variations in price during any given period of time. In the past, securities class action litigation has often been instituted against companies following periods of volatility in their stock price. This type of litigation

could result in substantial costs and divert our management' s attention and resources ~~. The liquidity of our common stock may be adversely affected by our September 2023 reverse stock split. On September 28, 2023, we effected a 1- for- 20 reverse stock split of our common stock, or the Reverse Stock Split. The liquidity of our common stock may be adversely affected by the Reverse Stock Split given the reduced number of shares that are outstanding following the Reverse Stock Split, which may lead to reduced trading and a smaller number of market makers for our common stock. In addition, the Reverse Stock Split may have increased the number of stockholders who own " odd lots " of less than 100 shares of our common stock. Odd lot shares may be more difficult to sell, and brokerage commissions and other costs of transactions in odd lots may be higher than the costs of transactions in " round lots " of even multiples of 100 shares. Despite the Reverse Stock Split, the resulting per- share trading price of our common stock may nevertheless fail to attract institutional investors and may not satisfy the investing guidelines of such investors and, consequently, the trading liquidity of our common stock may be adversely affected. Accordingly, the Reverse Stock Split may not achieve the desired results of increasing marketability of our common stock~~ . Fluctuations in our quarterly and annual operating results could adversely affect the price of our common stock which could result in substantial losses for purchasers of our common stock. Our quarterly and annual operating results may fluctuate significantly. Some of the factors that may cause our operating results to fluctuate on a period- to- period basis include: • payments we may be required to make to collaborators to exercise license rights and satisfy milestones and royalty obligations; • the status of, and level of expenses incurred in connection with, our program for emavusertib; • any intellectual property infringement lawsuit or other litigation in which we may become involved; • the implementation of restructuring and cost- savings strategies; • the occurrence of an event of default under the Oberland Purchase Agreement; • the implementation or termination of collaboration, licensing, manufacturing or other material agreements with third- parties, and non- recurring revenue or expenses under any such agreement; • compliance with regulatory requirements; • fluctuations in sales of Erivedge and related royalty and milestone payments; and • general conditions in the global economy and financial markets. If any of the foregoing matters were to occur, or if our operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially, which could result in substantial losses for purchasers of our common stock. In addition, we currently have no drug revenues and depend entirely on funds raised through other sources, such as funding through equity offerings. Our ability to raise funds in this manner depends upon, among other things, our stock price. We and our collaborators may not achieve projected research, development, commercialization and marketing goals in the time frames that we or they announce, which could have an adverse impact on our business and could cause our stock price to decline. We set goals for, and make public statements regarding, the timing of certain accomplishments, such as the commencement and completion of preclinical studies, and clinical trials, and other developments and milestones relating to our business and our collaboration agreements. Our collaborators may also make public statements regarding their goals and expectations for their collaborations with us. The actual timing of any such events can vary dramatically due to a number of factors including delays or failures in our and our current and potential future collaborators' preclinical studies or clinical trials, the amount of time, effort and resources committed to our program by all parties, and the inherent uncertainties in the regulatory approval and commercialization process. As a result: • our or our collaborators' preclinical studies and clinical trials may not advance or be completed in the time frames we or they announce or expect; • we or our collaborators may not make regulatory submissions, receive regulatory approvals or commercialize approved drugs as predicted; and • we or our collaborators may not be able to adhere to our or their current schedule for the achievement of key milestones under any program. If we or any collaborators fail to achieve research, development and commercialization goals as planned, our business could be materially adversely affected and the price of our common stock could decline. Future sales of shares of our common stock, including by us, employees and large stockholders, including pursuant to our **2024** ~~amended and restated sales~~ **Sales** ~~agreement~~ **Agreement** with Cantor and JonesTrading could result in dilution to our stockholders and negatively affect our stock price. Most of our outstanding common stock can be traded without restriction at any time. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell such shares, could reduce the market price of our common stock. We have a significant number of shares that are subject to outstanding options and in the future, we may issue additional options, warrants or other derivative securities convertible into our common stock. The exercise of any such options, warrants or other derivative securities, and the subsequent sale of the underlying common stock, could cause a further decline in our stock price and could dilute our stockholders. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. In addition, we may offer and sell up to $ 100. 0 million shares of common stock registered under our universal shelf registration statement on Form S- 3 pursuant to our 2024 Sales Agreement with Cantor and JonesTrading, in one or more " at- the- market " offerings. We have sold ~~229~~ **188** , ~~185~~ **316** shares under our ~~previous 2021~~ **2024** Sales Agreement, representing gross proceeds of $ ~~6~~ **1** . ~~3~~ **2** million **during the year ended December 31, 2024** . The extent to which we **continue to** utilize the 2024 Sales Agreement with Cantor and JonesTrading as a source of funding will depend on a number of factors, including the prevailing market price of our common stock, general market conditions and other restrictions and the extent to which we are able to secure funds from other sources. In addition, sales of substantial amounts of shares of our common stock or other securities by us or our employees and other stockholders could dilute our stockholders, lower the market price of our common stock and impair our ability to raise capital through the sale of equity or equity- related securities. We do not intend to pay dividends on our common stock, and any return to investors will come, if at all, only from potential increases in the price of our common stock. We have never declared nor paid cash dividends on our common stock. We currently plan to retain all of our future earnings, if any, to finance the operation, development and growth of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. We have anti- takeover defenses that could delay or prevent an acquisition that our stockholders may consider favorable, or prevent attempts by our stockholders to replace or remove current management, which could result in a decline in the price of our common stock. Provisions of our certificate of incorporation, our bylaws, and

Delaware law may deter unsolicited takeovers or delay or prevent changes in control of our management, including transactions in which our stockholders might otherwise receive a premium for their shares over then- current market prices. In addition, these provisions may limit the ability of stockholders to approve transactions that they may deem to be in their best interest. For example, we have divided our board of directors into three classes that serve staggered three- year terms, we may issue shares of our authorized " blank check " preferred stock, and our stockholders are limited in their ability to call special stockholder meetings. In addition, we are subject to the anti- takeover provisions of Section 203 of the Delaware General Corporation Law, which prohibits an " interested stockholder, " which is either a person who owns at least 15 % of our outstanding voting stock or an affiliate or associate of ours who owned at least 15 % of our outstanding voting stock at any time within the prior three years, from engaging in a business combination with us for a period of three years after the date of the transaction in which the person became an " interested stockholder " unless the business combination is approved in a prescribed manner. These provisions could discourage, delay or prevent a change in control. GENERAL RISK FACTORS If we are not able to maintain effective internal controls under Section 404 of the Sarbanes- Oxley Act, our business and stock price could be adversely affected. Section 404 of the Sarbanes- Oxley Act of 2002 requires us, on an annual basis, to review and evaluate our internal controls. Any failure by us to maintain the effectiveness of our internal controls in accordance with the requirements of Section 404 of the Sarbanes- Oxley Act, as such requirements exist today or may be modified, supplemented or amended in the future, could have a material adverse effect on our business, operating results and stock price. Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited. Under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, if a company undergoes an " ownership change, " generally defined as a greater than 50 % change (by value) in its equity ownership by certain stockholders over a three- year period, the corporation' s ability to use its pre- change net operating loss carryforwards and other pre- change tax attributes (such as research tax credits) to offset its post change taxable income or taxes may be limited. Changes in our stock ownership, some such changes being out of our control, may have resulted or could in the future result in an ownership change. If such an ownership change occurred or occurs in the future, utilization of a portion of our net operating loss and tax credit carryforwards could be limited in future periods and a portion of the carryforwards could expire before being available to reduce future income tax liabilities. There is also a risk that due to regulatory changes, such as suspensions on the use of net operating losses, or other unforeseen reasons, our existing net operating losses could expire or otherwise become unavailable to offset future income tax liabilities. In addition, under current law, net operating loss carryforwards arising after December 31, 2017 may only be used to offset 80 % of taxable income in a year (although such losses may be carried forward indefinitely), which may significantly impact our ability to utilize our net operating losses to offset taxable income in the future. In addition, state net operating losses generated in one state cannot be used to offset income generated in another state. For these reasons, even if we attain profitability, we may be unable to use a material portion of our net operating losses and other tax attributes. We are subject to risks associated with public health crises and epidemics / pandemics, such as the COVID- 19 pandemic. Public health outbreaks, epidemics, and pandemics of contagious or infectious diseases, such as COVID- 19, may significantly disrupt our business. Such outbreaks pose the risk that we or our employees, contractors, suppliers, or other partners may be prevented from conducting business activities for an indefinite period of time due to spread of the disease, or due to shutdowns that may be requested or mandated by federal, state and local governmental authorities. Business disruptions could include disruptions or restrictions on our ability to travel, as well as temporary closures of our facilities or the facilities of our contractors, suppliers, and other partners. Outbreaks could also impact the global supply chain, primarily through constraints on raw materials. Constraints on raw materials could also impact companies outside of our direct industry, which could result in a competitive supply environment causing higher costs. Additionally, the risk of cyber- attacks or other privacy or data security incidents may be heightened as a result of our moving increasingly towards a remote working environment as a result of public health outbreaks, which may be less secure and more susceptible to hacking attacks.