Risk Factors Comparison 2024-02-27 to 2023-02-23 Form: 10-K

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We face a variety of risks and uncertainties in our business and investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this Annual Report on Form 10- K, including our consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10- K, before deciding to invest in our common stock. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also become important factors that affect our business. If any of the following risks actually occur, our business, prospects, operating results and financial condition could suffer materially. In such event, the trading price of our common stock could decline and you might lose all or part of your investment. Risks Related to Our Financial Position and Need For Additional Capital We have incurred significant losses since our inception. We expect to incur losses over at least the next several years and may never achieve or maintain profitability. Our net losses totaled $ **367. 3 million, $** 282. 5 million ~~, and~~ $ 191. 0 ~~million and $ 119. 3~~ million for the years ended December 31, **2023,** 2022, **and** 2021 ~~, and 2020~~ , respectively. As of December 31, ~~2022~~ **2023** , we had an accumulated deficit of $ ~~965~~ **1, 332** . ~~4~~ **7** million. To date, we have not generated any revenue from product sales and have financed our operations primarily through sales of our equity interests, proceeds from our collaborations, grant funding and debt financing. We are still in the early stages of development of our product candidates, and we have not completed development of any product candidates. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We anticipate that our expenses will increase substantially if and as we: • continue **our ongoing and planned** ~~a Phase 1 / 2~~ clinical ~~trial~~ **trials for vepdegestrant (** ~~of our product candidate~~ ARV- 471 **) for the** ~~, a Phase 1b clinical trial of ARV- 471 in combination with palbociclib, a Phase 1b cohort expansion in combination with a standard of care agent, and a Phase 3 trial with ARV- 471 as a second- line~~ treatment ~~, and initiate a Phase 3 trial~~ of ~~ARV- 471 in combination with palbociclib, each in~~ patients with locally advanced or metastatic ER / HER2- breast cancer **, ongoing and planned** ~~; • continue a Phase 1 / 2~~ clinical ~~trial~~ **trials for** ~~of our product candidate bavdegalutamide (~~ ARV- **766** ~~110) and a Phase 1b clinical trial of bavdegalutamide in combination with abiraterone~~ for the treatment of men with metastatic castration- resistant prostate cancer, or mCRPC, and ~~initiate one~~ **ongoing clinical trails** ~~or~~ **for** ~~more additional Phase 1b cohort expansions of~~ bavdegalutamide ~~in combination with standard of care agents and a Phase 3 clinical trial~~ , ~~in~~ **also for the treatment of** men with mCRPC; • **initiate** ~~continue a~~ Phase 1 ~~/ 2~~ clinical ~~trial~~ **trials for** ~~of our product candidate~~ ARV- ~~766 in men with mCRPC~~ **393, our PROTAC protein degrader designed to target the BCL6 protein, and ARV- 102, our PROTAC degrader designed to target the LRRK2 protein; • progress additional PROTAC protein degrader programs into IND- or CTA- enabling studies** ; • apply our PROTAC Discovery Engine to advance additional product candidates into preclinical and clinical development; • expand the capabilities of our PROTAC Discovery Engine; • seek marketing approvals for any product candidates that successfully complete clinical trials; • ultimately establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any products for which we may obtain marketing approval; • expand, maintain and protect our intellectual property portfolio; • hire additional development, including clinical and regulatory, and scientific personnel; and • add operational, financial and management information systems and personnel to support our research, product development and future commercialization efforts and support our operations as a public company. Our expenses could increase beyond our expectations if we are required by the U. S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, or other regulatory authorities to perform trials in addition to those that we currently expect or anticipate, or if there are any delays in establishing appropriate manufacturing arrangements for or in completing our clinical trials or the development of any of our current or future product candidates. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses we will incur or when, if ever, we will be able to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment. We have never generated revenue from product sales and may never be profitable. We have never generated revenue from product sales. Our ability to generate revenue from product sales and achieve profitability depends on our ability, alone or with collaboration partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, product candidates we may identify for development. We do not anticipate generating revenues from product sales for the next several years, if ever. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. To become and remain profitable, we must succeed in developing, obtaining marketing approval for and commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, establishing arrangements with third parties for the manufacture of clinical supplies of our product candidates, obtaining marketing approval for our product candidates and manufacturing, marketing and selling any products for which we may obtain marketing approval. If one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations. We will need substantial additional funding

to continue our operations. If we are unable to raise capital when needed, we may be required to delay, limit, reduce or terminate our research or product development programs or future commercialization efforts. We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we continue our ongoing and initiate our planned clinical trials of ~~bavdegalutamide,~~ **vepdegestrant (** ARV- 471 ~~and~~ **),** ARV- 766 **, ARV- 393 and ARV- 102, in addition to our ongoing bavdegalutamide (ARV- 110) clinical trials** , advance our other oncology and neurodegenerative programs and continue research and development and initiate additional clinical trials of and potentially seek marketing approval for our lead programs and our other product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. We continue to incur significant costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on acceptable terms or not at all, we may be required to delay, limit, reduce or terminate our research, product development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. We had cash, cash equivalents, restricted cash and marketable securities of approximately $ 1. ~~2~~ **3** billion as of December 31, ~~2022~~ **2023** . We believe that our cash, cash equivalents, restricted cash and marketable securities as of December 31, ~~2022~~ **2023** will enable us to fund our planned operating expenses and capital expenditure requirements into ~~2026~~ **2027** . We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including: • the progress, costs and results of our ongoing **and planned** clinical trials for **vepdegestrant (** ARV- 471 **)** ~~,~~ ~~bavdegalutamide~~ and ARV- 766 and any future clinical development of **vepdegestrant** ~~ARV- 471, bavdegalutamide~~ and ARV- 766 **and our ongoing clinical trails for bavdegalutamide** ; • the scope, progress, costs and results of preclinical and clinical development for our other product candidates and development programs **, including ARV- 393 and ARV- 102** ; • the number of, and development requirements for, other product candidates that we pursue, including our other oncology and neurodegenerative research programs; • the success of our collaborations with Pfizer, Inc., or Pfizer; Genentech, Inc. and F. Hoffman LaRoche Ltd., collectively referred to as Genentech; and Bayer AG, or Bayer; • the costs, timing and outcome of regulatory review of our product candidates; • the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval; • the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval; • the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property- related claims; and • our ability to establish additional collaboration arrangements with other biotechnology **;** or **•** pharmaceutical companies on favorable terms, if at all, **or enter into license, marketing and royalty arrangements, and similar transactions** for the development or commercialization of our product candidates. Identifying potential product candidates and conducting preclinical testing and clinical trials is a time- consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to obtain substantial additional funds to achieve our business objectives. Adequate additional funds may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. Until such time, if ever, as we can generate substantial revenue from product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. Although we may receive potential future payments under our collaborations with Pfizer, Genentech and Bayer, we do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights as common stockholders. Debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making acquisitions or capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be acceptable or favorable to us. Our limited operating history may make it difficult for our stockholders to evaluate the success of our business to date and to assess our future viability. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, conducting discovery and research activities, filing patent applications, identifying potential product candidates, undertaking preclinical studies, establishing arrangements with third parties for the manufacture of initial quantities of our product candidates and conducting Phase 1, Phase 2 and Phase 3 clinical trials for our product candidates. However, we have not yet demonstrated our ability to successfully complete any clinical trials, obtain marketing approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions stockholders make about our future success or viability may not be as accurate as they could be if we had a longer operating history. In addition, as a ~~young~~ business with limited operating experience and no history of revenue- generating commercial activity, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition. We expect our financial condition and operating results to

continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, stockholders should not rely upon the results of any quarterly or annual periods as indications of future operating performance. Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition. Changes in tax law may adversely affect our business or financial condition. The Tax Cuts and Jobs Act of 2017, commonly referred to as the TCJA, as amended by the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, significantly revises the U. S. Internal Revenue Code of 1986, as amended, or the Code. The TCJA contains, among other things, significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35 % to a flat rate of 21 % and the limitation of the deduction for net operating losses to 80 % of current- year taxable income for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely). In addition, beginning in 2022, the TCJA eliminates the option to deduct research and development expenditures currently and requires corporations to capitalize and amortize them over five years **or 15 years (for expenditures attributable to foreign research)** . In addition to the CARES Act, as part of Congress' s response to the COVID- 19 pandemic, economic relief legislation **was** ~~has been~~ enacted in 2020 and 2021 containing tax provisions. The Inflation Reduction Act, or IRA, was also signed into law in August 2022. The IRA introduced new tax provisions, including a 1 % excise tax imposed on certain stock repurchases by publicly traded corporations. The 1 % excise tax generally applies to any acquisition by the publicly traded corporation (or certain of its affiliates) of stock of the publicly traded corporation in exchange for money or other property (other than stock of the corporation itself), subject to a de minimis exception. Thus, the excise tax could apply to certain transactions that are not traditional stock repurchases. Regulatory guidance under the TCJA, the IRA, and such additional legislation is and continues to be forthcoming, and such guidance could ultimately increase or lessen the impact of these laws on our business and financial condition. In addition, it is uncertain if and to what extent various states will conform to the TCJA, the IRA, and additional tax legislation. In the future, we might not be able to utilize a significant portion of any net operating loss carryforwards and research and development tax credit carryforwards we may have. As of December 31, ~~2022~~ **2023** , we had ~~no~~ **$ 235. 9 million of** federal net operating loss carryforwards, $ ~~63~~ **250** . ~~4~~ **0** million of state and local net operating loss carryforwards, ~~no~~ **$ 29. 1 million** federal ~~research and development~~ tax credit carryforwards and $ ~~1~~ **18** . ~~9~~ **7** million of state ~~research and development~~ tax credit carryforwards. ~~During the year ended December 31, 2022, we fully utilized our previously held net federal operating loss and credit carryforwards due to taxable income resulting from revenue recognition for tax purposes from our ARV- 471 Collaboration Agreement and the mandatory capitalization of qualified research and development expenses incurred on or after January 1, 2022 under the TCJA. We expect in to incur net operating losses in future periods as a result of additional product development.~~ To the extent **they expire unused, these** net operating loss and tax credit carryforwards ~~expire unused, they~~ will not be available to offset our future income tax liabilities. **Federal net operating loss carryforwards may be carried forward indefinitely, but the deductibility of such carryforwards is limited to 80 % of our taxable income in the year in which carryforwards are used.** In addition, under ~~Section~~ **Sections** 382 **and 383** of the Code, and corresponding provisions of state law, if a corporation undergoes an " ownership change, " which is 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 to offset its post- change income may be limited. We ~~believe our federal net operating losses are subject to an annual limitation as a result of changes in the Company' s ownership, as defined by Code Section 382, in July 2018 and December 2020. Notwithstanding the limitations, we expect the federal net operating losses to be fully available under Section 382, subject to any other limitations under the Code. In addition, we~~ may experience ownership changes in the future as a result of subsequent changes in our stock ownership, some of which may be outside of our control. If we determine that an ownership change has occurred and our ability to use our historical net operating loss and **research and development** tax credit carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations. 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 **and** any future net operating losses could expire or otherwise become unavailable to offset future income tax liabilities. As described above in " Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition, " the TCJA, as amended by the CARES Act, includes changes to U. S. federal tax rates and the rules governing net operating loss carryforwards that 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. Risks Related to the Discovery and Development of Our Product Candidates Our approach to the discovery and development of product candidates based on our PROTAC technology platform is unproven, which makes it difficult to predict the time, cost of development and likelihood of successfully developing any products. Our PROTAC technology platform is a relatively new technology. Our future success depends on the successful development of this novel therapeutic approach. Prior to the initiation of our Phase 1 clinical trial for bavdegalutamide in 2019, no product candidates that use a chimeric small molecule approach to protein degradation, such as our PROTAC targeted protein degraders, had been tested in humans. No product candidates of this type have been approved in the United States or Europe, and the data underlying the feasibility of developing chimeric small molecule- based therapeutic products is both preliminary and limited. We have not yet succeeded and may not succeed in demonstrating the efficacy and safety of any of our product candidates in clinical trials or in obtaining marketing approval thereafter. We have not yet completed a clinical trial of any product candidate and we have not yet completed assessment of the safety of any product candidate in humans. As such, there may be adverse effects from treatment with any of our current or future product candidates that we cannot predict at this time. As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our PROTAC Discovery Engine, or any similar or competitive protein degradation platforms, will result in the development, and

marketing approval of any products. Any development problems we experience in the future related to our PROTAC Discovery Engine or any of our research programs may cause significant delays or unanticipated costs or may prevent the development of a commercially viable product. Any of these factors may prevent us from completing our current or future preclinical studies or clinical trials or from commercializing any product candidates we may develop on a timely or profitable basis, if at all. We are early in our development efforts. If we are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed. All of our product candidates are in **clinical or preclinical** development. We are developing **vepdegestrant (** ARV- 471 **)** for the treatment of patients with locally advanced or metastatic ER / HER2- breast cancer and ~~bavdegalutamide and~~ **have been developing** ARV- 766 **and bavdegalutamide** for the treatment of men with metastatic castration- resistant prostate cancer **, and we plan to initiate clinical development for ARV- 393 and ARV- 102 in the first half of 2024** . Additional product candidates are still in preclinical development. Our ability to generate revenue from product sales, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of one or more of our product candidates. The success of our product candidates will depend on several factors, including the following: • successfully completing preclinical studies and clinical trials; • receipt and related terms of marketing approvals from applicable regulatory authorities; • obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates; • making arrangements with third- party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of our product candidates; • establishing sales, marketing **, market access** and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others; • acceptance of our products, if and when approved, by patients, the medical community and third- party payors; • obtaining and maintaining third- party coverage and adequate reimbursement; • maintaining a continued acceptable safety profile of the products following approval; and • effectively competing with other therapies. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. Drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur unexpected costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates. We have product candidates in clinical development and preclinical development. The risk of failure for each of our product candidates is high. We are unable to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support our planned INDs in the United States or similar applications in other jurisdictions. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the FDA or similar regulatory authorities outside the United States will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of our programs. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to the outcome. A failure of one or more clinical trials can occur at any stage of testing. We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including: • regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site; • we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites; • clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs; • the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate; • our third- party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all; • we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks; • regulators or institutional review boards may require that we or our investigators suspend or terminate clinical trials for various reasons, including noncompliance with regulatory requirements; • our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials; • unforeseen global instability, including political instability or instability from an outbreak of pandemic or contagious disease, such as the **recent** COVID- 19 pandemic, in or around the countries in which we conduct our clinical trials, could delay the commencement or timing of completion of our clinical trials; • the cost of clinical trials of our product candidates may be greater than we anticipate and could be exacerbated by macroeconomic conditions such as inflation; and • the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate, or their cost could increase dramatically making them financially infeasible. If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may: • be delayed in obtaining marketing approval for our product candidates; • not obtain marketing approval at all; • obtain approval for indications or patient populations that are not as broad as intended or desired; • obtain approval with labeling that includes significant use or distribution restrictions or safety warnings; • be subject to additional post- marketing testing requirements; or • have the product removed from the market after obtaining marketing approval. Our product development costs will also increase if we experience delays in preclinical studies or clinical trials or in obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical study

or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. Further, cancer therapies are sometimes characterized as first- line, second- line, or third- line, and the FDA often approves new therapies initially only for third- line use. When cancer is detected early enough, first- line therapy, usually hormone therapy, surgery, radiation therapy or a combination of these, is sometimes adequate to cure the cancer or prolong life without a cure. Second- and third- line therapies are administered to patients when prior therapy is not effective. Our current clinical trials for ~~bavdegalutamide,~~ **vepdegestrant (** ARV- 471 ~~and~~ **),** ARV- 766 **and bavdegalutamide** are in ~~patients who have received prior treatments~~ **both first- and second- line settings** . Subsequently, for those products that prove to be sufficiently beneficial, if any, we would expect to seek approval potentially as a first- line therapy, but any product candidates we develop, even if approved, may not be approved for first- line therapy, and, prior to any such approvals, we may have to conduct additional clinical trials. If serious adverse events, undesirable side effects, or unexpected characteristics are identified during the development of any product candidates we may develop, we may need to abandon or limit our further clinical development of those product candidates. If any product candidates we develop are associated with serious adverse events, or undesirable side effects, or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the adverse events, undesirable side effects or other characteristics are less prevalent, less severe, or more acceptable from a risk- benefit perspective, any of which would have a material adverse effect on our business, financial condition, results of operations, and prospects. Many product candidates that initially showed promise in early- stage testing for treating cancer or other diseases have later been found to cause side effects that prevented further clinical development of the product candidates or limited their competitiveness in the market. It is impossible to predict when or if any product candidates we may develop will prove safe in humans. There can be no assurance that our PROTAC technology will not cause undesirable side effects. A potential risk in any protein degradation product is that healthy proteins or proteins not targeted for degradation will be degraded or that the degradation of the targeted protein in itself could cause adverse events, undesirable side effects, or unexpected characteristics. It is possible that healthy proteins or proteins not targeted for degradation could be degraded using our PROTAC technology in any of our ongoing, planned or future clinical studies. There is also the potential risk of delayed adverse events following treatment using our PROTAC technology. Positive data from preclinical or early clinical studies of our product candidates are not necessarily predictive of the results of later clinical studies and any future clinical trials of our product candidates. If we cannot replicate the positive data from our preclinical or early clinical studies of our product candidates in our future clinical trials, we will be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates. The results of preclinical studies may not be predictive of the results of clinical trials, and the results of early- stage clinical trials may not be predictive of the results of the later- stage clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. In particular, the small number of patients in our ongoing early clinical trials may make the results of these trials less predictive of the outcome of later clinical trials. For example, even if successful, the results of the **ongoing and planned** clinical trials of **vepdegestrant (** ARV- 471 **)** , ~~bavdegalutamide and~~ and ARV- 766 **, ARV- 303, the ongoing clinical trials of bavdegalutamide, and the planned clinical trials of ARV- 102,** may not be predictive of the results of ~~further~~ **any future** clinical trials of these product candidates or any of our other product candidates. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Our current or future **preclinical studies and** clinical trials may not ultimately be successful or support further clinical development of any of our product candidates. There is a high failure rate for product candidates proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving encouraging results in earlier studies. Any such setbacks in our clinical development could materially harm our business and results of operations. Interim top- line and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data. From time to time, we have published and may in the future publish interim top- line or preliminary data from our clinical trials. Interim data from clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. For example, the initial safety, tolerability, pharmacokinetic and efficacy data that we have disclosed in connection with our ongoing ~~Phase 1 / 2~~ clinical trials of **vepdegestrant (** ARV- 471 **), ARV- 766** and bavdegalutamide (ARV- 110) may not be indicative of the full results of those trials obtained upon completion. 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 preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our reputation and business prospects. If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary marketing approvals could be delayed or prevented. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside of the United States. In particular, we are conducting several clinical trials **of vepdegestrant (** ~~, including a Phase 1 / 2 clinical trial and Phase 3 clinical trial with~~ ARV- 471 ~~as a second~~ **), ARV** - **766** ~~line treatment~~ , ~~of~~ **bavdegalutamide (ARV- 110) and planning clinical trials for** ARV- 471 ~~for patients with locally advanced or metastatic ER / HER2- breast cancer~~ , ~~a Phase 1 / 2 clinical trial of bavdegalutamide for men with mCRPC, and a Phase 1 / 2 clinical trial of~~ ARV- 766 ~~for men with mCRPC~~ **, ARV- 393 and ARV- 102** . We cannot predict how difficult it will be to enroll patients for trials in these indications. Therefore, our ability to identify and enroll eligible patients for **our** ~~ARV- 471, bavdegalutamide, and ARV- 766~~ clinical trials may be limited or may

result in slower enrollment than we anticipate. In addition, some of our competitors have ongoing clinical trials for product candidates that treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. Patient enrollment is affected by other factors including: • the **prevalence and** severity of the disease under investigation; • the eligibility criteria for the trial in question **; • the requirements of the trial protocols** ; • the perceived risks and benefits of the product candidates under study; • the efforts to facilitate timely enrollment in clinical trials; • the availability of competing therapies; • the patient referral practices of physicians; • the burden on patients due to inconvenient procedures; • the ability to monitor patients adequately during and after treatment; and • the proximity and availability of clinical trial sites for prospective patients. ~~In~~ **For example, in** April 2020, we announced that, as a result of the COVID- 19 pandemic, two trial sites for our ongoing Phase 1 / 2 clinical trial of bavdegalutamide had publicly announced pauses in patient enrollment for clinical trials, including our trials. In addition, one trial site for our ongoing Phase 1 / 2 clinical trial of ARV- 471 had a pause in patient enrollment for clinical trials, including our trial. **We also** ~~While the pauses at each of the trial sites have been lifted, we may nonetheless face difficulties recruiting or retaining patients in our ongoing and planned clinical trials if patients are affected by the virus or are fearful of traveling to, or are unable to travel to, our clinical trial sites because of the outbreak. For example, we~~ experienced a short delay in the enrollment for one cohort of **one of** our **vepdegestrant (** ARV- 471 **)** ~~trial~~ **trials** as a result of screening slowdowns attributable to COVID- 19. In addition, we may engage in conversations with regulators regarding clinical trial protocols, which could result in delays to our anticipated timing to enroll patients in our studies. Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success. Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. **For example, in 2023, we announced that we plan to prioritize the initiation of a Phase 3 clinical trial with ARV- 766 in mCRPC instead of the previously planned Phase 3 clinical trial for bavdegalutamide.** Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing **, marketing** or other royalty arrangements **or similar transactions** in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. We are developing and ~~may~~ **plan to** continue to develop our product candidates in combination with other drugs. If the FDA or similar regulatory authorities outside of the United States do not approve these other drugs, or revoke their approval of such drugs, or if safety, efficacy, manufacturing or supply issues arise with the drugs we choose to evaluate in combination with our product candidates, we may be unable to obtain approval of or market our products. We are currently conducting clinical trials of **vepdegestrant (** ARV- 471 **)** , ~~bavdegalutamide and~~ ARV- 766 **, and bavdegalutamide (ARV- 110)** and intend to conduct other clinical trials for each of **vepdegestrant (** ARV- 471 **)** ~~,~~ ~~bavdegalutamide~~ and ARV- 766 and potentially other product candidates, in combination with other therapies. We did not develop or obtain marketing approval for, nor do we manufacture or sell, any of the currently approved drugs that we are or may study in combination with **vepdegestrant (** ARV- 471 **)** , ~~bavdegalutamide or~~ ARV- 766 **or bavdegalutamide (ARV- 110)** . If the FDA or similar regulatory authorities outside of the United States revoke their approval of the drug or drugs in combination with which we determine to develop **vepdegestrant (** ARV- 471 **)** ~~, bavdegalutamide~~ or ARV- 766 we will not be able to market **vepdegestrant (** ARV- 471 **)** ~~, bavdegalutamide~~ or ARV- 766 in combination with such revoked drugs. If safety or efficacy issues arise with any of these drugs, we could experience significant regulatory delays, and the FDA or similar regulatory authorities outside of the United States may require us to redesign or terminate the applicable clinical trials. If the drugs we use are replaced as the standard of care for the indications we choose for ~~bavdegalutamide or~~ **vepdegestrant (** ARV- 471 **) or ARV- 766** , the FDA or similar regulatory authorities outside of the United States may require us to conduct additional clinical trials. In addition, if manufacturing or other issues result in a shortage of supply of the drugs with which we determine to combine with ~~bavdegalutamide or~~ **vepdegestrant (** ARV- 471 **) or ARV- 766** , we may not be able to complete clinical development of ~~bavdegalutamide or~~ **vepdegestrant (** ARV- 471 **) or ARV- 766** on our current timeline or at all. Even if ~~bavdegalutamide or~~ **vepdegestrant (** ARV- 471 **) or ARV- 766** were to receive marketing approval or be commercialized for use in combination with other existing drugs, we would continue to be subject to the risks that the FDA or similar regulatory authorities outside of the United States could revoke approval of the drug used in combination with ~~bavdegalutamide or~~ **vepdegestrant (** ARV- 471 **) or ARV- 766** or that safety, efficacy, manufacturing or supply issues could arise with these existing drugs. Combination therapies are commonly used for the treatment of cancer, and we would be subject to similar risks if we develop any of our other product candidates for use in combination with other drugs or for indications other than cancer. This could result in our own products being removed from the market or being less successful commercially. We plan to conduct clinical trials for our product candidates at sites outside the United States, and the FDA may not accept data from trials conducted in such locations. We plan to conduct clinical trials of our product candidates outside the United States, including our planned ~~global~~ Phase 3 trial for **ARV- 766 in** ~~bavdegalutamide for the treatment of men with~~ mCRPC ~~with~~ **and planned Phase 1 trial for** ~~AR~~ **ARV - 102** ~~T878 / H875 tumor mutations~~ . Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and be performed by qualified investigators in accordance with ethical principles. The

trial population must also adequately represent the U. S. population, and the data must be applicable to the U. S. population and U. S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will depend on its determination that the trials also complied with all applicable U. S. laws and regulations. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time- consuming and could delay or permanently halt our development of the applicable product candidates. In addition, there are risks inherent in conducting clinical trials in multiple jurisdictions, inside and outside of the United States, such as: • regulatory and administrative requirements of the jurisdiction where the trial is conducted that could burden or limit our ability to conduct our clinical trials; • foreign exchange rate fluctuations; • manufacturing, customs, shipment and storage requirements; • cultural differences in medical practice and clinical research; and • the risk that the patient populations in such trials are not considered representative as compared to the patient population in the target markets where approval is being sought. We may not be successful in our efforts to identify or discover additional potential product candidates. A key element of our strategy is to apply our PROTAC Discovery Engine to address a broad array of targets and new therapeutic areas. The therapeutic discovery activities that we are conducting may not be successful in identifying product candidates that are useful in treating cancer or other diseases. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including: • potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval or achieve market acceptance; or • potential product candidates may not be effective in treating their targeted diseases. Research programs to identify new product candidates require substantial technical, financial and human resources. We may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful. If we are unable to identify suitable product candidates for preclinical and clinical development, we will not be able to obtain revenues from sale of products in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price. We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do. The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face and will continue to face competition from third parties that use protein degradation, antibody therapy, inhibitory nucleic acid, gene editing or gene therapy development platforms and from companies focused on more traditional therapeutic modalities, such as small molecule inhibitors. The competition is likely to come from multiple sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, government agencies and public and private research institutions. We are aware of several biotechnology companies focused on developing chimeric small molecules for protein degradation including Accutar Biotechnology, Inc., C4 Therapeutics, Inc., Cullgen Inc., Foghorn Therapeutics, Inc., Kymera Therapeutics, Inc., Nurix Therapeutics, Inc. and Proteovant Therapeutics, Inc. Further, several large pharmaceutical companies have disclosed preclinical investments in this field, including AbbVie **Inc.** , Amgen Inc., AstraZeneca plc, Boehringer Ingelheim **, C. H.** , Bristol Myers Squibb Company, GlaxoSmithKline plc, Genentech, Novartis ~~International~~ AG and Sanofi ~~SA~~ . Since 2020, some of these biotechnology and pharmaceutical companies have announced the initiation of clinical trials for targeted protein degraders. Additionally, other novel targeting mechanisms could ultimately address similar patient populations, such as CYP11A1 inhibitor (which is being developed by Orion ~~/~~ **Corporation in collaboration with** Merck **& Co., Inc.**) and an AR N- Terminal Domain inhibitor (which is being developed by ESSA Pharma **Inc.**) in ~~Prostate~~ **prostate** ~~Cancer~~ **cancer** . Many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early- stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third- party payors seeking to encourage the use of generic products. There are generic products currently on the market for certain of the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our product candidates are approved, we expect that they will be priced at a significant premium over competitive generic products. Risks Related to Dependence on Third Parties If our collaboration with Pfizer is not successful, we may not be able to capitalize on the market potential of **vepdegestrant (** ARV- 471 **)** . In July 2021, we entered into a collaboration agreement with Pfizer, or the ARV- 471 Collaboration Agreement, pursuant to which we granted Pfizer worldwide co- exclusive rights to develop and commercialize products containing our proprietary compound ARV- 471, or the Licensed Products. Although pursuant to the terms of the ARV- 471 Collaboration Agreement, we and Pfizer share equally (50 / 50) all development costs, including costs for conducting clinical trials, for the Licensed Products, subject to certain exceptions, our control over the amount and timing of resources that Pfizer dedicates to the development or commercialization of the Licensed Products is limited. Our ability to generate revenues

from the ARV- 471 Collaboration Agreement will depend, in part, on Pfizer' s ability to successfully perform the functions assigned to it in such agreement. We cannot predict the success of this collaboration with Pfizer, and we cannot guarantee that this collaboration will lead to development or commercialization of the Licensed Products in the most efficient manner or at all. If this collaboration with Pfizer does not result in the successful development and commercialization of Licensed Products, or if Pfizer terminates the ARV- 471 Collaboration Agreement, which it may do for convenience subject to certain notice periods, we may not receive any of the $ 1. 4 billion in contingent payments based on specified regulatory and sales- based milestones for the Licensed Products under the ARV- 471 Collaboration Agreement. We currently depend, and expect to continue to depend, on collaborations with third parties for the research, development, and the potential future commercialization of certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to capitalize on the market potential of those product candidates. We currently have, and anticipate in the future seeking additional, third- party collaborators for the research, development, and potential future commercialization of some of our PROTAC programs. For example, in September 2015 we entered into a research collaboration with Genentech, which we amended and restated in November 2017; in December 2017 we entered into a research collaboration with Pfizer; in July 2019 we entered into a research collaboration with Bayer; and in July 2021 we entered into a development and commercialization collaboration with Pfizer. Our likely collaborators for any other collaboration arrangements include large and mid- size pharmaceutical companies and biotechnology companies. Any such arrangements with third parties will likely limit our control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of any product candidates we may seek to develop with them. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into. Any collaborations involving our research programs or any product candidates we may develop, including our current collaborations with Pfizer, Genentech and Bayer, pose the following risks to us: • Collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations. For example, our collaboration with Genentech is managed by a joint research committee and joint project team, which is composed of representatives from us and Genentech, with Genentech having final decision- making authority. Similarly, our research collaborations with Pfizer and Bayer are managed by joint research committees composed of an equal number of representatives from us and our respective collaborative partners, with the collaborative partner having final decision- making authority. • Collaborators may not pursue development and commercialization of any product candidates we may develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator' s strategic focus or available funding or external factors such as an acquisition or business combination that diverts resources or creates competing priorities. • Genentech, Pfizer and Bayer have broad rights to select any target for protein degradation development on an exclusive basis, even as to us, so long as not excluded by us under the terms of each collaboration and may select targets we are considering but have not taken sufficient action to exclude under the collaboration. • Collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing. • Collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours. • Collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products. • Collaborators may not properly obtain, maintain, enforce, or defend our intellectual property or proprietary rights or may use our proprietary information in such a way that could jeopardize or invalidate our proprietary information or expose us to potential litigation. For example, Pfizer, Genentech and Bayer have the first right to enforce or defend certain intellectual property rights under the applicable collaboration arrangement with respect to particular licensed programs, and although we may have the right to assume the enforcement and defense of such intellectual property rights if the collaborator does not, our ability to do so may be compromised by their actions. • Disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources. • We may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control. • Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates. For example, each of Genentech, Pfizer and Bayer can terminate its agreement with us in its entirety or with respect to a specific target for convenience subject to specified notice periods, in certain cases as short as 60 days, or in connection with a material breach of the agreement by us that remains uncured for a specified period of time. • Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished, or terminated. If our collaborations do not result in the successful development and commercialization of products, or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of product candidates could be delayed, and we may need additional resources to develop product candidates. In addition, if one of our collaborators terminates its agreement with us, we may find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, marketing approval, and commercialization described in this Annual Report on Form 10- K apply to the activities of our collaborators. We may ~~in the future decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of any~~

~~product candidates we may develop. These relationships, or those like them, may require us to incur non- recurring and other charges, increase our near- and long- term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators, and the negotiation process is time- consuming and complex. Our ability to reach a definitive collaboration agreement will depend, among other things, upon our assessment of the collaborator' s resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator' s evaluation of several factors. If we license rights to any product candidates we or our collaborators may develop, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture. We may~~ seek to establish additional collaborations. If we are not able to establish collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans. To realize the full potential of our PROTAC Discovery Engine and accelerate the development of additional PROTAC programs, we plan to continue to selectively pursue collaborations with leading biopharmaceutical companies with particular experience, including development and commercial expertise and capabilities. We face significant competition in attracting appropriate collaborators to advance the development of any product candidates for which we may seek a collaboration. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator' s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator' s evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or other regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, the terms of any existing collaboration agreements, and industry and market conditions generally. The collaborator may also have the opportunity to collaborate on other product candidates or technologies for similar indications and will have to evaluate whether such a collaboration could be more attractive than one with us. Collaborations are complex and time- consuming to negotiate, document and execute. In addition, consolidation among large pharmaceutical companies has reduced the number of potential future collaborators. Our existing collaboration agreements limit our ability to enter into future agreements on certain terms with potential collaborators. For example, we have granted exclusive rights to Genentech, Pfizer and Bayer for the discovery, development and commercialization of PROTAC targeted protein degraders directed to certain protein targets, and during the terms of those agreements, we will be restricted from granting rights to other parties to use our PROTAC technology for those targets. Any collaboration we enter into may limit our ability to enter into future agreements on particular terms or covering similar target indications with other potential collaborators. We may not be able to negotiate collaborations on a timely basis, on acceptable terms or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, 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. If we elect to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate revenue from product sales, which could have an adverse effect on our business, prospects, financial condition and results of operations. We rely and expect to continue to rely on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials. We currently rely and expect to continue to rely on third- party CROs to conduct our ongoing and planned clinical trials. We currently do not plan to independently conduct any clinical trials of ~~bavdegalutamide,~~ **vepdegestrant (** ARV- 471 **)** and ARV- 766 or of our other product candidates **, including ARV- 393 and ARV- 102 and have not independent conducted any clinical trials of our product candidates, including bavdegalutamide, to date** . Agreements with these third parties might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, that would delay our product development activities. Our reliance on these third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols in the applicable IND. Moreover, the FDA requires compliance with standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Furthermore, these third parties may have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. We rely on third-party CMOs for the manufacture of both drug substance and finished drug product for our product candidates for preclinical testing and clinical trials and expect to continue to do so for commercialization. This reliance on third parties may increase the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely on and expect to continue to rely on third- party CMOs for both drug substance and finished drug product as well as the building blocks used to manufacture drug substance. This reliance on third parties may increase the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. We may be unable to establish agreements with third- party manufacturers or to do so on acceptable

terms. Even if we are able to establish agreements with third- party manufacturers, reliance on third- party manufacturers entails additional risks, including: • reliance on the third party for regulatory, compliance and quality assurance; • the possible breach of the manufacturing agreement by the third party; • the possible misappropriation of our proprietary information, including our trade secrets and know- how; and • the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us. We have only limited technology transfer agreements in place with respect to our product candidates, and these arrangements do not extend to commercial supply. We acquire many key materials on a purchase order basis. As a result, we do not have long term committed arrangements with respect to our product candidates and other materials. If we receive marketing approval for any of our product candidates, we will need to establish an agreement for commercial manufacture with a third party. Third- party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our third- party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. As a result, we may not obtain access to these facilities on a priority basis or at all. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. Some of our manufacturers are based outside of the United States, including the manufacturers of the building blocks for our drug substances which are based in China and India. ~~As~~ **For example, as** a result of the **recent** COVID- 19 pandemic ~~, there has been an increased risk of supply interruption with our manufacturers and~~ , in the first quarter of 2020, the production of certain building blocks for the drug substance used in the manufacture of ARV-471 was delayed at one of our China- based manufacturers. While this production delay did not delay the overall clinical development of our product candidates, other delays in the manufacture of building blocks, drug substance or drug products for our product candidates could arise, which could have a material adverse effect on our clinical development. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement manufacturer or be unable to reach agreement with any alternative manufacturer. Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis. Risks Related to the Commercialization of Our Product Candidates Even if any of our product candidates 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. If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third- party payors and others in the medical community. For example, current cancer treatments, such as chemotherapy and radiation therapy, are well established in the medical community, and doctors may continue to rely on these treatments. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant revenue from product sales and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including, but not limited to: • the efficacy and potential advantages as compared to alternative treatments; • the prevalence and severity of any side effects of our product candidates, in particular as compared to alternative treatments; • our ability to offer our products for sale at competitive prices; • the convenience and ease of administration compared to alternative treatments; • the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies; • the strength of marketing, sales and distribution support; • the availability of third-party coverage and adequate reimbursement; • the timing of any marketing approval in relation to other product approvals; • support from patient advocacy groups; and • any restrictions on the use of our products together with other medications. If we are unable to establish sales and marketing capabilities, we may not be successful in commercializing our product candidates if and when they are approved. ~~We~~ **Though we are working to build, we** do not currently have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of biopharmaceutical products. To achieve commercial success for any product for which we obtain marketing approval, we will need to establish sales, marketing and distribution capabilities, either ourselves or through collaboration or other arrangements with third parties. We currently expect that we would **continue to** build our own focused, specialized sales ~~and~~ **,** marketing **and market access** organization to support the commercialization of **our** product candidates in the United States for which we receive marketing approval and that can be commercialized with such capabilities. There are risks involved with establishing our own sales and marketing capabilities. For example, recruiting and training a sales force is expensive and time- consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. Factors that may inhibit our efforts to commercialize our products on our own include: • our inability to recruit, train and retain adequate numbers of effective, knowledgeable and experienced sales and marketing personnel; • the inability of such sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products; • the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage to companies with more extensive product lines; and • unforeseen costs and expenses associated with creating an independent sales and marketing organization. If we are unable to establish our own sales and marketing capabilities or enter into arrangements with third parties to perform these services, our revenue from product sales and our profitability, if any, are likely to be lower than if we were to

market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to market and sell our product candidates or may be unable to do so on terms that are acceptable to us. We likely will have little control over such third parties, and any of these third parties may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates. Even if we are able to commercialize any product candidates, the products may become subject to unfavorable pricing regulations, third- party reimbursement practices or healthcare reform initiatives, which would harm our business. The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. 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 product licensing approval is granted. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues, if any, we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval. Our ability to commercialize any product candidates successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government healthcare programs, private health insurers and other organizations. Government authorities and third- party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U. S. healthcare industry and elsewhere is cost containment. Government authorities and third- party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, government authorities and third- party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Reimbursement may affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval. There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the FDA or similar regulatory authorities approve the drug outside of the United States. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, intellectual property, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third- party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and adequate reimbursement rates from both government- funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition. Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop. We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in: • decreased demand for any product candidates or products that we may develop; • termination of clinical trials; • withdrawal of any marketing approval, recall, restriction on the approval or a " black box " warning or contraindication for an approved drug; • failure to enroll clinical trial participants or withdrawal of clinical trial participants; • significant costs to defend the related litigation; • substantial monetary awards to trial participants or patients; • loss of revenue; • injury to our reputation and significant negative media attention; • reduced resources of our management to pursue our business strategy; and • the inability to commercialize any products that we may develop. We currently hold $ 10. 0 million in product liability insurance coverage in the aggregate, with a per incident limit of $ 10. 0 million, which may not be adequate to cover all liabilities that we may incur. We will need to increase product liability insurance coverage as we expand our clinical trials and if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. Risks Related to Our Intellectual Property If we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired, and we may not be able to compete effectively in our market. Our commercial

success depends in part on our ability to obtain and maintain patent and other proprietary protection in the United States and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing patent applications in the United States and other jurisdictions related to our novel technologies and product candidates. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. Moreover, the patent applications we own, co- own or license may fail to result in issued patents in the United States or in other foreign countries. The patent prosecution process is expensive and time- consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or at all. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, 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 that we license from third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has, in recent years, been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned, co- owned or licensed patents or pending patent applications, or that we were the first inventors to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. Moreover, we may be subject to a third- party preissuance submission of prior art to the United States Patent and Trademark Office, or the USPTO, or in addition to interference proceedings, may become involved in opposition, derivation, reexamination, inter partes review, post- grant review or other post- grant proceedings challenging our or our licensors' patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third- party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Our owned, co- owned and licensed patent estate includes patent applications, many of which are at an early stage of prosecution. Even if our owned, co-owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned, co- owned or licensed patents by developing similar or alternative technologies or products in a non- infringing manner. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned, co- owned and licensed patents may be challenged in the courts or patent offices in the United States and other jurisdictions. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned, co- owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Changes in patent laws or patent jurisprudence could diminish the value of our patents in general, thereby impairing our ability to protect our product candidates. Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy- Smith America Invents Act, or the Leahy- Smith Act, was signed into law. The Leahy- Smith Act includes a number of significant changes to United States patent law. These changes include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The USPTO developed new regulations and procedures to govern administration of the Leahy- Smith Act, and many of the substantive changes to patent law associated with the Leahy- Smith Act, and in particular, the first- inventor- to- file provisions, became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy- Smith Act will have on the operation of our business. However, the Leahy- Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition. Furthermore, for applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. Additionally, the U. S. Supreme Court has ruled on several patent cases in recent years limiting where a patentee may file a patent infringement suit, narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations, and there are other open questions under patent law that courts have yet to decisively address. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by Congress, the federal courts and the USPTO, the laws and regulations

governing patents could change in unpredictable ways and could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. In addition, the European patent system is relatively stringent in the type of amendments that are allowed during prosecution, but the complexity and uncertainty of European patent laws has also increased in recent years. Complying with these laws and regulations could limit our ability to obtain new patents in the future that may be important for our business. We may become involved in lawsuits to protect or enforce our patents, the patents of our licensors, or other intellectual property, which could be expensive, time- consuming and unsuccessful. Competitors may infringe our issued patents, the patents of our licensors, or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive, time- consuming and unpredictable. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours or our licensors is invalid or unenforceable, in whole or in part, construe the patent' s claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly. Even if we successfully assert our patents, a court may not award remedies that sufficiently compensate us for our losses. We may need to license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms or at all. A third party may hold intellectual property, including patent rights, that are important or necessary to the development of our products. It may be necessary for us to use the patented or proprietary technology of a third party to commercialize our own technology or products, in which case we would be required to obtain a license from such third party. A license to such intellectual property may not be available or may not be available on commercially reasonable terms, which could have a material adverse effect on our business and financial condition. The licensing and acquisition of third-party intellectual property rights is a competitive practice, and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third- party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. We may not be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire. Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, reexamination, and inter partes review proceedings before the USPTO and oppositions and other comparable proceedings in foreign jurisdictions. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference, derivation, reexamination or inter partes review proceedings before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. There may be third- party patents of which we are currently unaware with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If we are found by a court of competent jurisdiction to infringe a third party' s intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. In addition, even if we were able to obtain a license, it could be non- exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business. If we fail to comply with our obligations in our current and future intellectual property licenses and funding arrangements with third parties, we could lose rights that are important to our business. We are party to a license agreement with Yale that provides us with the foundational intellectual property rights for our PROTAC targeted protein degradation technology. This license agreement imposes diligence, development and commercialization timelines and milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations, including achieving specified milestone events, Yale may have the right to terminate this license, in which event we might not be able to develop, manufacture or market any product that is covered by the intellectual property we in- license from Yale and may face other penalties. Such an occurrence would materially adversely affect our business prospects. For a variety of purposes, we will likely enter into additional licensing and funding arrangements with third parties that may also impose similar obligations on us. Termination of any of our current or future in- licenses would reduce or eliminate our rights under these agreements and may result in our having to negotiate new or reinstated agreements with less favorable terms or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology. Any of the foregoing could prevent us from commercializing our other product candidates, which could have a material adverse effect on our operating results and overall

financial condition. In addition to the above risks, intellectual property rights that we license in the future may include sublicenses under intellectual property owned by third parties, in some cases through multiple tiers. The actions of our licensors may therefore affect our rights to use our sublicensed intellectual property, even if we are in compliance with all of the obligations under our license agreements. Should our licensors or any of the upstream licensors fail to comply with their obligations under the agreements pursuant to which they obtain the rights that are sublicensed to us, or should such agreements be terminated or amended, our ability to develop and commercialize our product candidates may be materially harmed. Further, we do not have the right to control the prosecution, maintenance and enforcement of all of our licensed and sublicensed intellectual property, and even when we do have such rights, we may require the cooperation of our licensors and upstream licensors, which may not be forthcoming. For example, under the Yale license, any patent applications and issued patents under the agreement remain the property of Yale, and Yale has the right to choose patent counsel. Our business could be adversely affected if we or our licensors are unable to prosecute, maintain and enforce our licensed and sublicensed intellectual property effectively. We may be subject to claims by third parties asserting that our employees, consultants, contractors or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property. We employ individuals who were previously employed at universities as well as other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We have received confidential and proprietary information from collaborators, prospective licensees and other third parties. Although we try to ensure that our employees do not use the proprietary information or know- how of others in their work for us, we may be subject to claims that these employees or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee' s former employer. We may also be subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. We may not be successful in defending these claims, and if we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Even if we are successful, litigation could result in substantial cost and reputational loss and be a distraction to our management and other employees. In addition, while it is our policy to require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Such assignment agreements may not be self- executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace. Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by governmental patent offices, and our patent protection could be reduced or eliminated for non- compliance with these requirements. Periodic maintenance fees on any issued patent are due to be paid to the USPTO and patent offices in foreign countries in several stages over the lifetime of the patent. The USPTO and patent offices in foreign countries require compliance with a number of procedural, documentary, fee payment and other requirements during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of a patent or patent rights in the relevant jurisdiction. Non- compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non- payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business. If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets, including unpatented know- how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non- disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time- consuming, and the outcome is unpredictable. In addition, some courts inside and outside of the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed. If we are not able to obtain patent term extensions in the

United States under the Hatch- Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of our marketing exclusivity for our product candidates, our business may be impaired. Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one of the U. S. patents covering each of such product candidates or the use thereof may be eligible for a patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or Hatch- Waxman Act. The period of extension may be up to five years beyond the expiration date of a patent but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. The Hatch- Waxman Act allows a maximum of one patent to be extended per FDA- approved product. Similar patent term extension also may be available in certain foreign countries upon regulatory approval of our product candidates. Nevertheless, we may not be granted patent term extension either in the United States or in any foreign country because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request. If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product may be shortened and our competitors may obtain approval of competing products following our patent expiration sooner, and our revenue could be reduced, possibly materially. We only have limited geographical protection with respect to certain patents and we may not be able to protect our intellectual property rights throughout the world. Filing, prosecuting and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In- licensing patents covering our product candidates in all countries throughout the world may similarly be prohibitively expensive, if such opportunities are available at all. And in- licensing or filing, prosecuting and defending patents even in only those jurisdictions in which we develop or commercialize our product candidates may be prohibitively expensive or impractical. Competitors may use our and our licensors' technologies in jurisdictions where we have not obtained patent protection or licensed patents to develop their own products and, further, may export otherwise infringing products to territories where we and our licensors have patent protection, but enforcement is not as strong as that in the United States or the European Union. These products may compete with our product candidates, and our or our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. In addition, we may decide to abandon national and regional patent applications while they are still pending. The grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications may be rejected by the relevant patent office, while substantively similar applications are granted by others. For example, relative to other countries, China has a heightened detailed description requirement for patentability. Furthermore, generic drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' patents, requiring us or our licensors to engage in complex, lengthy and costly litigation or other proceedings. Generic drug manufacturers may develop, seek approval for and launch generic versions of our products. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology. The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or regulations in the United States and the European Union, and many companies have encountered significant difficulties in protecting and defending proprietary rights in such jurisdictions. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets or other forms of intellectual property, which could make it difficult for us to prevent competitors in some jurisdictions from marketing competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, are likely to result in substantial costs and divert our efforts and attention from other aspects of our business, and additionally could put our or our licensors' patents at risk of being invalidated or interpreted narrowly, could increase the risk of our or our licensors' patent applications not issuing, or could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, while damages or other remedies may be awarded to the adverse party, which may be commercially significant. If we prevail, damages or other remedies awarded to us, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition in those jurisdictions. In some jurisdictions, compulsory licensing laws compel patent owners to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties under patents relevant to our business, or if we or our licensors are prevented from enforcing patent rights against third parties, our competitive position may be substantially impaired in such jurisdictions. Risks Related to Regulatory Approval and Marketing of Our Product Candidates and Other Legal and Compliance Matters The regulatory approval process of the FDA is lengthy, time- consuming and inherently unpredictable, and if we are ultimately unable to obtain marketing approval for our product candidates, our business will be substantially harmed. The time required to obtain approval by the FDA is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a

product candidate' s clinical development and may vary among jurisdictions. We have not obtained marketing approval for any product candidate to date and it is possible that none of our existing product candidates, or any product candidates we may seek to develop in the future, will ever obtain marketing approval. Our product candidates could fail to receive marketing approval for many reasons, including the following: • the FDA may disagree with the design or implementation of our clinical trials; • we may be unable to demonstrate to the satisfaction of the FDA that a product candidate is safe and effective for its proposed indication; • results of clinical trials may not meet the level of statistical significance required by the FDA for approval; • we may be unable to demonstrate that a product candidate' s clinical and other benefits outweigh its safety risks; • the FDA may disagree with our interpretation of data from preclinical studies or clinical trials; • data collected from clinical trials of our product candidates may not be sufficient to support the submission of a New Drug Application, or NDA, to the FDA or other submission or to obtain marketing approval in the United States; • the FDA may find deficiencies with or fail to approve the manufacturing processes or facilities of third- party manufacturers with which we contract for clinical and commercial supplies; and • the approval policies or regulations of the FDA may significantly change in a manner rendering our clinical data insufficient for approval. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations and prospects. The FDA has substantial discretion in the approval process, and determining when or whether regulatory approval will be obtained for any of our product candidates. Even if we believe the data collected from clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA. In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post- marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates. 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 from obtaining approvals for the commercialization of any or all of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired. Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, export and import are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and similar regulatory authorities outside of the United States. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not submitted an application for or received marketing approval for any of our product candidates in the United States or in any other jurisdiction. As a company, we do not have experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third- party clinical research organizations or other third- party consultants or vendors to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate' s safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. New oncology drugs frequently are indicated only for patient populations that have not responded to an existing therapy or have relapsed. The process of obtaining marketing approvals, both in the United States and in other jurisdictions, is expensive, 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 product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may increase costs or cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post- approval commitments that render the approved product not commercially viable. **Further, under the Pediatric Research Equity Act, or PREA, an NDA, or supplement to an NDA for certain drugs and biological products must contain data to assess the safety and effectiveness of the drug or biological product in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the sponsor receives a deferral or waiver from the FDA. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. The applicable legislation in the EU also requires sponsors to either conduct clinical trials in a pediatric population in accordance with a Pediatric Investigation Plan approved by the Pediatric Committee of the EMA or to obtain a waiver or deferral from the conduct of these studies by this Pediatric Committee. For any of our product candidates for which we are seeking regulatory approval in the U. S. or the European Union, we cannot guarantee that we will be able to obtain a waiver or alternatively complete any required studies and other requirements in a timely manner, or at all, which could result in associated reputational harm and subject us to enforcement action** If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be

materially impaired. Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed outside of the United States and may limit our ability to generate revenue from product sales. In order to market and sell our products in the European Union and in other jurisdictions outside of the United States, we, and any 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. We, and any 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 United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. In many countries outside the United States, a product 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 products, 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 collaborators and could delay or prevent the introduction of our product candidates in certain countries. In addition, if we or any collaborators fail to obtain the non- U. S. approvals required to market our product candidates outside the United States or if we or any 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 product candidates will be harmed and our business, financial condition, results of operations and prospects may be adversely affected. Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the withdrawal of the United Kingdom from the EU, commonly referred to as Brexit. The United Kingdom is no longer part of the European Single Market and European Union Customs Union. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland will continue to be subject to European Union rules under the Northern Ireland Protocol. The ~~MHRA will rely on~~ **United Kingdom and EU have however agreed to** the **Windsor Framework which fundamentally changes** ~~Human Medicines Regulations 2012 (SI 2012 / 1916) (as amended), or~~ the ~~HMR, as~~ **existing system under** the ~~basis for~~ **Northern Ireland Protocol, including with respect to the** ~~regulating~~ **regulation** ~~medicines. The HMR has been incorporated into the domestic law~~ of ~~the body of European Union law instruments governing~~ medicinal products **in** ~~that pre- existed prior to~~ the United Kingdom **Once implemented, the changes introduced by the Windsor Framework will see the MHRA be responsible for approving all medicinal products destined for the United Kingdom market), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. 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 ~~withdrawal from~~ **proposal for revision of several legislative instruments related to medicinal products (potentially reducing the duration of regulatory data protection, revising the eligibility for expedited pathways, etc.) was published on April 26, 2023. The proposed revisions remain to be agreed and adopted by** the European **Parliament** ~~Union. Any delay in obtaining, or an~~ **and European Council and** ~~inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in~~ the ~~United Kingdom for our product candidates~~ **proposals may therefore be substantially revised before adoption** , which ~~could~~ **is not anticipated before early 2026. The revisions may however have a** ~~significantly~~ **significant impact on the pharmaceutical industry** and ~~materially harm~~ our business **in the long term** . We expect that we will be subject to additional risks in commercializing any of our product candidates that receive 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 outside of the United States; 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. Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, and, as a result, 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 product 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. Disruptions at the FDA **, EMA** and other agencies may also slow the time necessary for new **drugs** ~~product candidates~~ to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. For example, **in recent** ~~over the last several~~ years **, including in 2018 and 2019,** 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. **In addition** ~~If a prolonged government shutdown occurs~~ , **disruptions may result also events similar** ~~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. Separately, in response~~ 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** ~~As of May 26, 2021,~~ the **event** ~~FDA noted it was continuing to ensure timely reviews~~ of **a similar public health emergency** ~~applications for medical products during the ongoing COVID- 19 pandemic~~ in **the future** ~~line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. However~~ , the FDA may not be able to continue its current pace and review timelines could be extended ~~, thus, the FDA may be unable to complete such required inspections during the review period~~ . Regulatory authorities outside the ~~U. S.~~ **United States facing similar circumstances** may adopt similar restrictions or other policy measures in response to ~~the COVID- 19 pandemic~~ **a similar public health emergency** and may **also** experience delays in their regulatory 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. Even if we, or any collaborators, obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue. Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any collaborators, must therefore comply with requirements concerning advertising and promotion for any of our product candidates for which we or they obtain marketing approval. Promotional communications with respect to prescription drugs 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, and any collaborators will not be able to promote any products we develop for indications or uses for which they are not approved. In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our third- party manufacturers, any collaborators and their third- party manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs. Accordingly, assuming we, or any collaborators, receive marketing approval for one or more of our product candidates, we, and any collaborators, and our respective third- party 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 any collaborators, are not able to comply with post- approval regulatory requirements, we, and any collaborators, could have the marketing approvals for our products withdrawn by regulatory authorities and our, or any 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 certain designations for our product candidates, including Breakthrough Therapy, Fast Track and Priority Review designations in the United States, 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 one or more of our product candidates 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 products 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. 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. We may also seek a priority review designation for one or more of our product candidates. If the FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. These designations are within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for these designations, the FDA may disagree and instead determine not to make such designation. Further, even if we receive a designation, the receipt of such designation for a product 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, including the Fast Track designation we received in May 2019 for bavdegalutamide for mCRPC **and the Fast Track designation we received in the first quarter of 2024 for vepdegestrant for ER / HER2- breast cancer** . In addition, even if one or more of our product candidates qualifies for these designations, the FDA may later decide that the product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. ~~Any~~ **Even if we obtain regulatory approval for a** product candidate **, our products will remain subject to regulatory oversight. Even if we obtain any regulatory approval for our product candidates, they will be subject to ongoing**

regulatory requirements for manufacturing, labeling, packaging, storing, advertising, promoting, sampling, record - keeping and submitting safety and other post - market information. Any regulatory approvals that we receive for our product candidates also may be subject to a Risk Evaluation and Mitigation Strategy, or REMS, limitations on the approved indicated uses for which ~~we, the~~ **the product may be marketed or to the conditions of approval or contain requirements** ~~or~~ **for potentially costly post - marketing testing, including post- marketing clinical trials, and surveillance to monitor the quality, safety and efficacy of the product. For example, the holder of an approved NDA is obligated to monitor and report adverse events and** any **failure of a product to meet the specifications in the NDA. FDA guidance advises that patients treated with some types of gene therapy undergo follow - up observations for potential adverse events for as long as 15 years. The holder of an approved NDA also must submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws. In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the NDA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured or such regulatory authority disagrees with the promotion, marketing or labeling of that product, the regulatory authority may impose restrictions relative to that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. If we fail to comply with applicable regulatory requirements following approval of any of our product candidates, a regulatory authority may: • issue a warning letter asserting that we are in violation of the law; • seek an injunction or impose administrative, civil or criminal penalties or monetary fines; • suspend or withdraw regulatory approval; • suspend any ongoing clinical trials; • refuse to approve a pending NDA or comparable foreign marketing application, or any supplements thereto, submitted by us or our** ~~collaborators~~ **collaboration partners; • restrict the marketing or manufacturing of the product; • seize or detain the product or otherwise require the withdrawal of the product from the market; • refuse to permit the import or export of products; or • refuse to allow us to enter into supply contracts , including government contracts. Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and adversely affect our business, financial condition, results of operations and prospects. Further, our ability to develop and market new drug products may be impacted by ongoing litigation challenging the FDA' s approval of mifepristone. Specifically, on April 7, 2023, the U. S. District Court for the Northern District of Texas stayed the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various conditions adopted under a REMS. In reaching that decision, the district court made a number of findings that may negatively impact the development, approval and distribution of drug products in the U. S. Among other determinations, the district court held that plaintiffs were likely to prevail in their claim that FDA had acted arbitrarily and capriciously in approving mifepristone without sufficiently considering evidence bearing on whether the drug was safe to use under the conditions identified in its labeling. Further, the district court read the standing requirements governing litigation in federal court as permitting a plaintiff to bring a lawsuit against the FDA in connection with its decision to approve an NDA or establish requirements under a REMS based on a showing that the plaintiff or its members would be harmed to the extent that FDA' s drug approval decision effectively compelled the plaintiffs to provide care for patients suffering adverse events caused by a given drug. On April 12, 2023, the U. S. District Court for the Northern District of Texas' s 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 of the district court' s decision, in its entirety, pending disposition of the appeal of the district court decision in the U. S. Court of Appeals for the Fifth Circuit and the disposition of any petition for a writ of certiorari to or the U. S. Supreme Court. The U. S. Court of Appeals for the Fifth Circuit held oral argument in the case on May 17, 2023 and, on August 16, 2023, issued its decision. The U. S. Court of Appeals for the Fifth Circuit declined to order the removal of mifepristone from the market, finding that a challenge to the FDA' s initial approval in 2000 is barred by the statute of limitations. But the U. S. Court of Appeals for the Fifth Circuit did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone that FDA authorized in 2016 and 2021 were arbitrary and capricious. On September 8, 2023, the Justice Department and a manufacturer of mifepristone filed petitions for a writ of certiorari, requesting that asked the U. S. Supreme Court to review the U. S. Court of Appeals for the Fifth Circuit' s decision. On December 13, 2023, the U. S. Supreme Court granted these petitions for writ of certiorari for the U. S. Court of Appeals for the Fifth Circuit' s decision. In addition, FDA policies, and those of equivalent foreign regulatory agencies, may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U. S. or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would harm our business, financial condition, results of operations and prospects. The FDA, EMA and other regulatory authorities actively enforce the laws and regulations prohibiting the promotion of off- label uses. We must also comply with requirements concerning advertising and promotion for any of our product candidates for which we** obtain marketing approval ~~could~~ **. Promotional communications with respect to prescription products are subject to a variety of legal and**

regulatory restrictions and must be **consistent with** ~~subject to post- marketing restrictions or withdrawal from~~ the ~~market and we~~ **information in the product' s approved labeling. Thus** , ~~or~~ **we will not be able to promote** any **products** ~~collaborators, may be subject to substantial penalties if~~ we ~~,~~ **develop** ~~or~~ **for indications or uses for which** they ~~, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our products when and if any of them~~ are **not** approved ~~. Any product candidate for which we, or any collaborators, obtain marketing approval, as well as the manufacturing processes, post- approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA, EMA and other regulatory authorities. These requirements include submissions of safety and other post- marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a risk evaluation and mitigation strategy. New cancer drugs frequently are indicated only for patient populations that have not responded to an existing therapy or have relapsed. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our drug in this way, which could limit sales of the product~~ . The FDA ~~may also impose requirements for costly post- marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product, including the adoption and implementation of risk evaluation and mitigation strategies. The FDA~~ and other agencies, including the Department of Justice ~~, or the DOJ~~ , closely regulate and monitor the post- approval marketing and promotion of ~~drugs~~ **products** to ensure **that** they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. ~~The~~ **In September 2021, the** FDA ~~and DOJ impose stringent~~ **published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug or biologic. Notwithstanding the regulatory** restrictions on ~~manufacturers' communications regarding~~ off- label **promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non- misleading, and non- promotional scientific communications concerning their products in certain circumstances. For example, in October 2023, the FDA published draft guidance outlining the agency' s non-binding policies governing the distribution of scientific information on unapproved uses to healthcare providers. This draft guidance calls for such communications to be truthful, non- misleading, factual, and unbiased and include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved** use **. In addition** , **under some relatively recent guidance from the FDA and the Pre-Approval Information Exchange Act, signed into law as part of the Consolidated Appropriations Act of 2023, companies may also promote information that is consistent with the prescribing information and proactively speak to formulary committee members of payors regarding data for** ~~and~~ **an** ~~if we do not market~~ **unapproved drug or unapproved uses of an approved drug. We may engage in these discussions and communicate with healthcare providers, payors and other constituencies in compliance with all applicable laws, regulatory guidance and industry best practices. We will 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 ~~for their approved indications, we may be subject to enforcement action for off- label marketing~~ . Violations of the Federal Food, Drug, and Cosmetic Act **, or the FDCA,** and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription ~~drugs~~ **products** may lead to investigations and enforcement actions alleging violations of federal and state ~~healthcare~~ **health care** fraud and abuse laws, as well as state consumer protection laws. ~~In addition, later discovery of previously unknown side effects or other problems with our products or their manufacturers or manufacturing processes, or failure~~ **Failure** to comply with regulatory requirements, may yield various results, including: • restrictions on such products, manufacturers or manufacturing processes; • restrictions ~~and~~ **or** warnings on the labeling or marketing of a product; • restrictions on product 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; • 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 or detention; • injunctions or the imposition of civil or criminal penalties** ; • damage to relationships with any potential collaborators; • unfavorable press coverage and damage to our reputation; ~~• refusal to permit the import or export of our products; • product seizure; • injunctions or the imposition of civil or criminal penalties;~~ or • litigation involving patients using our products. ~~In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs applicable to drug manufacturers or quality assurance standards applicable to medical device manufacturers, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, and any contract manufacturers we may engage in the future, our collaborators and their contract manufacturers will also be subject to other regulatory requirements, including submissions of safety and other post- marketing information and reports, registration and listing requirements, requirements regarding the distribution of samples to clinicians, recordkeeping, and costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product such as the requirement to implement a risk evaluation and mitigation strategy.~~ Similar restrictions apply to the approval of our products in the ~~EU~~ **European Union** . The holder of ~~a~~ **the** marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. **If we are found to have promoted such off- label uses, we may become subject to significant liability.** ~~These~~ -- **The** ~~include: compliance with the EU' s stringent pharmacovigilance~~ **U. S. federal government has levied large civil and criminal fines against companies** ~~or for safety reporting rules,~~ **alleged improper promotion of off- label use and has enjoined several companies from engaging in off-**

label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which ~~can impose post- authorization studies and additional monitoring obligations;~~ **specified promotional conduct is changed or curtailed. If we cannot successfully manage** the ~~manufacturing~~ **promotion** of **our** ~~authorized medicinal products~~ **product candidates** , ~~for~~ **if approved, we could become subject to significant liability,** which **would materially adversely affect our business** ~~a separate manufacturer' s license is mandatory;~~ and **financial condition** ~~the marketing and promotion of authorized drugs, which are strictly regulated in the EU and are also subject to EU Member State laws~~ . Our relationships with health care providers, physicians and third- party payors will be subject to applicable anti- kickback, fraud and abuse and other health care laws and regulations, which could expose us to civil, criminal and administrative sanctions, contractual damages, reputational harm and diminished future profits and earnings. Health care providers, physicians and third- party payors will play a primary role in the recommendation and prescription of any drugs for which we obtain marketing approval. Our future arrangements with third- party payors, health care providers and physicians may expose us to broadly applicable state and federal fraud and abuse and other health care laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any drugs for which we obtain marketing approval. These include the following: • Anti- Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, or receiving remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchasing, ordering, leasing, arranging for, or recommending the purchasing, ordering, or leasing of, any good or service for which payment may be made, in whole or in part, under a federal health care program such as Medicare or Medicaid; • False Claims Act- the federal civil and criminal false claims laws, including the civil False Claims Act, and Civil Monetary Penalties Law, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, false or fraudulent claims for payment or knowingly making, using or causing to made or used a false record or statement material to a false or fraudulent claim or to avoid, decrease or conceal an obligation to pay money to the federal government, or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government; • HIPAA- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit, among other things, executing a scheme to defraud any health care benefit program or making false statements relating to health care matters, and apply regardless of the payor (e. g., public or private); • HIPAA and HITECH- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, which impose obligations on HIPAA covered entities and their business associates, including mandatory contractual terms and required implementation of administrative, physical and technical safeguards to maintain the privacy and security of individually identifiable health information; • Transparency Requirements- the federal physician transparency requirements known as the Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the ACA, which requires manufacturers of drugs, medical devices, biological and medical supplies covered by Medicare, Medicaid, or State Children' s Health Insurance Program to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and • Analogous State, Local and Foreign Laws- analogous state, local and foreign fraud and abuse laws and regulations, such as state anti- kickback and false claims laws, which may be broader than similar federal laws, can apply to claims involving health care items or services regardless of payor, and are enforced by many different federal and state agencies as well as through private actions. 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 and require drug manufacturers to report information related to payments and other transfers of value to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not pre- empted by HIPAA, thus complicating compliance efforts. Efforts to ensure that our business arrangements with third parties will comply with applicable health care 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 health care 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 / or administrative penalties, damages, fines, individual imprisonment, disgorgement, exclusion from government funded health care programs, such as Medicare and Medicaid, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non- compliance with these laws and the curtailment or restructuring of our operations. If any of the physicians or other health care providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded health care programs. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the European Union. The provision of benefits or advantages to physicians is governed by the national anti- bribery laws of European Union Member States. In addition, payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician' s employer, his or her competent professional organization and / or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment. **If the FDA or comparable foreign**

regulatory authorities approve generic versions of any of our future drug products that receive marketing approval through the NDA pathway, or such authorities do not grant such future products appropriate periods of data exclusivity before approving generic versions of our products, our sales 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 applicant generally must show that its product has the same active ingredient (s), dosage form, strength, route of administration and conditions of use or labeling 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 non- patent exclusivity for the reference- listed drug has expired. The FDCA provides a period of five years of non- patent exclusivity for a new drug containing a new chemical entity, or NCE. For the purposes of this provision, an NCE is a drug that contains an active moiety that has previously been approved by the FDA in any other NDA. This interpretation was confirmed with enactment of the Ensuring Innovation Act in April 2021. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. 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 applicant may submit its application four years following approval of the reference- listed drug. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical trials, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. Generic drug manufacturers may seek to launch generic products following the expiration of any applicable exclusivity period we obtain if our product candidates are approved, even if we still have patent protection for such product candidates. Competition that any such product candidates of ours may face from generic versions of such products could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we may make in those product candidates. Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could 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 **international** data privacy and protection laws and regulations that apply to ~~the~~ **our** collection, transmission, storage and use of personally ~~identifying~~ **identifiable** 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 UK~~ . 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~~ , **including** ~~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 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 expanded 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~~ **Certain other U. S. state laws impose similar privacy obligations, and we also anticipate that more U. S. states will increasingly enact legislation similar to the CCPA. The CCPA has prompted a number of proposals for new U. S. federal and U. S. state- level privacy legislation and in some states efforts to pass comprehensive privacy laws have been successful. For example, in** addition **to California** , **at least eleven** other states ~~, including Virginia, Colorado, Utah, and Connecticut already~~ have passed ~~state~~ **comprehensive** privacy laws **similar to the CCPA and CPRA** . **These** ~~Virginia' s privacy law~~ **laws** ~~also went into~~ **are either in** effect **or** ~~on January 1, 2023, and the laws in the other three states~~ will go into effect ~~later in~~ **sometime before the end of 2026. Like the CCPA and CPRA,** ~~the~~ **these** ~~year~~ **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 2023 legislative sessions that will go into effect in 2024 and beyond, including New Hampshire and New Jersey** . Other states will be considering these laws in the future, and Congress has also been debating passing a federal privacy law. **There are also states that are specifically regulating health information that may affect our business. For example, Washington state passed a health privacy law in 2023 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. Connecticut and Nevada have also passed similar laws regulating consumer health data and additional states (including Vermont) are considering such legislation for 2024.** 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. 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 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 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 EU to offer adequate data protection legislation, such as the U. S. 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 European Union, 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 transfers of personal data from the EEA to the U. S. While we were not self-certified under the Privacy Shield, this CJEU decision may lead to increased scrutiny on data transfers from the EEA to the U. S. generally and increase 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. ~~Additionally, in October 2022~~ **As a response to the CJEU decision** , President Joe Biden signed an executive order to implement the EU- U. S. Data Privacy Framework, which would serve as a replacement to the EU- U. S. Privacy Shield. The EU initiated the process to adopt an adequacy decision for the EU- U. S. Data Privacy Framework in December 2022. It is unclear if and when the framework will be finalized and whether it will be challenged in court. The uncertainty around this issue may further impact our business operations in the EU. 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. Any changes or updates to these adequacy decisions 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. Current and future legislation may increase the difficulty and cost for us and any collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain. In the United States and some 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 product candidates, restrict or regulate post- approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. The pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by legislative initiatives. 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 receive for any FDA approved product. In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for prescription drugs purchased through a pharmacy by the elderly and disabled and introduced a new reimbursement methodology based on average sales prices for physician- administered drugs. In addition, this statute provides authority for limiting the number of drugs that will be covered in any therapeutic class, subject to certain exceptions. Cost reduction initiatives and other provisions of this statute could decrease the coverage and price that we receive for any approved products. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors. In March 2010, then- President Obama signed into law the Patient Protection and Affordable Care Act, 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 **These changes include** ~~. In August 2011~~ , the Budget Control Act of 2011, **which,** among other things, **led** ~~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~~ Under current legislation** ~~the Coronavirus Aid~~ , ~~Relief, and Economic Security~~ **the actual reductions in Medicare payments may vary up to 4 %. The Consolidated Appropriations** Act, ~~or~~ **which was signed into law by President Biden in December 2022, made several changes to sequestration of** the ~~CARES~~ **Medicare program. Section 1001 of the Consolidated Appropriations** 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.** ~~These~~ -- **The Consolidated Appropriations 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** ~~reductions~~ - **reduction percentages in fiscal** ~~were reduced and suspended through June 2022 with the full 2 % cut resuming thereafter. 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 **2030** ~~. These laws may result in additional reductions in Medicare~~ and **2031** ~~other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used~~ . 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 for Jobs Act, or TCJA, in 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 TCJA, 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, dismissed this action **without specifically ruling on** ~~after finding that the plaintiffs do not have standing to challenge~~ the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results. The Trump Administration also took executive actions to undermine or delay implementation of 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 rescinded those orders and issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to 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 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 enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents. This Executive Order also directs HHS to create a special enrollment period for the Health Insurance Marketplace in response to the COVID- 19 pandemic **. In the EU, on December 13, 2021, Regulation No 2021 / 2282 on Health Technology**

Assessment, or HTA, amending Directive 2011 / 24 / EU, was adopted. While the Regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation- related steps to take place in the interim. Once applicable, it will have a phased implementation depending on the concerned products. The Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products as well as certain high- risk medical devices, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non- clinical (e. g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement . 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 product candidates 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 product candidates. 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 drug products, if and when approved. The prices of prescription pharmaceuticals have also 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, 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. ~~The final rule is currently~~ **That regulation was challenged in a lawsuit by** the ~~subject~~ **Pharmaceutical Research and Manufacturers** of ~~ongoing litigation~~ **America, or PhRMA** , but ~~at least six~~ **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** states (~~Vermont,~~ Colorado, Florida, Maine **, New Hampshire** , New Mexico, **North Dakota, Texas, Vermont** and **Wisconsin** ~~New Hampshire~~) have passed laws allowing for the importation of drugs from Canada ~~with~~ **. Certain of** ~~the~~ **these** ~~intent of developing SIPs for review~~ **states have submitted Section 804 Importation Program proposals** and **are awaiting FDA** approval ~~by~~ **. On January 5, 2023,** the FDA **approved Florida' s plan for Canadian drug importation** . 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** ~~implementation of the~~ 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** has been delayed by **Congress to** ~~the Biden administration from~~ January 1, ~~2022~~ - **2032** ~~to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point- of- sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have been delayed until January 1, 2026 by the Infrastructure Investment and Jobs Act~~ . More recently, on August 16, 2022, the 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 enrolling in a plan providing 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 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). 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 and biologic 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 additional Part D drugs in 2027, 15 additional Part B or Part D drugs in 2028, and 20 additional 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 and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics 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. 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 beneficiaries' out- of- pocket drug costs at an estimated $ 4, 000 a year in 2024 and, thereafter beginning in 2025, at $ 2, 000 a year. **On June 6, 2023, Merck & Co. filed a lawsuit against 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, the PhRMA, Astellas Pharma Inc., Novo Nordisk Inc., Janssen Pharmaceuticals, Inc., Novartis AG, AstraZeneca plc and C. H. Boehringer Sohn AG & Co. KG, also filed lawsuits in various courts with similar constitutional claims against HHS and CMS. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results.** At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, health care 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 health care 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 product candidates or additional pricing pressures. In other jurisdictions, particularly in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. **In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low- priced and high- priced member states, can further reduce prices, and in certain instances render commercialization in certain markets infeasible or disadvantageous from a financial perspective.** 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 drug to other available therapies. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, **the commercial launch of our products and / ~~our~~ or ~~business~~ product candidates** could be **delayed, possibly for lengthy periods of time, we or our collaborators may not launch at all in a particular country, we may not be able to recoup our investment in one or more product candidates, and there could be a ~~materially~~ material ~~harmed~~ adverse effect on our business** . We are subject to anti- corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, which could adversely affect our business, results of operations and financial condition. Our operations are subject to anti- corruption laws, including the FCPA, the Bribery Act, and other anticorruption laws that apply in countries where we do business and may do business in the future. The FCPA, the Bribery Act, and these other laws generally prohibit us, our officers and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential FCPA or Bribery Act violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the FCPA, the Bribery Act, or local anti- corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted. We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United States, United Kingdom, and authorities in the European Union, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, which we collectively refer to as Trade Control Laws. There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti- corruption laws, including the FCPA, the Bribery Act, or other legal requirements, including Trade Control Laws. If we are not in compliance with the FCPA, the Bribery Act, and other anti- corruption laws or Trade Control Laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. The Securities and Exchange Commission, or SEC, also may suspend or bar issuers from trading securities on U. S. exchanges, including the Nasdaq Stock Market, for violations of the FCPA' s accounting provisions. Likewise, any investigation of any potential violations of the FCPA, the Bribery Act, other anti- corruption laws or Trade Control Laws by U. S., U. K. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition. 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 significantly 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. Although 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 costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, but 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, which could adversely affect our business, financial condition, results of operations or prospects. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions. Risks Related to Employee Matters and Managing Growth Our future success depends on our ability to retain key executives and to attract, train, retain and motivate qualified personnel. We are highly dependent on the research, development and clinical expertise of our management and scientific teams. Although we have offer letters or employment agreements with each of our executive officers, each of them may terminate their employment with us at any time. We do not maintain " key person " insurance for any of our executives or other employees. Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain marketing approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms or at all given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategies. These consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract, train, retain and motivate high quality personnel, our ability to pursue our corporate growth strategy will be limited. We will need to grow the size of our organization, and we may experience difficulties in managing this growth, which could disrupt our operations. We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, manufacturing, regulatory and medical affairs and compliance and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Any future growth will impose significant added responsibilities on members of management, including, but not limited to: • identifying, recruiting, training, integrating, retaining and motivating additional employees; • managing our internal development efforts effectively, including the clinical and FDA review process for ~~bavdegalutamide,~~ **vepdegestrant (** ARV- 471 **)** , ARV- 766 and any product candidate we develop, while complying with our contractual obligations to contractors and other third parties, including our partners and collaborators; and • improving our managerial, operational and financial controls, reporting systems and procedures. Our future financial performance and our ability to advance the development of and, if approved, commercialize ~~bavdegalutamide,~~ **vepdegestrant (** ARV- 471 **)** , ARV- 766 and any other product candidate we develop will depend, in part, on our ability to effectively manage any future growth. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations. Our internal computer systems **and** ~~, or~~ those of ~~any~~ **our** collaborators, contractors, consultants ~~or~~ **and** other third parties ~~that we work with~~ **are vulnerable to cyber attacks** , **cyber intrusions and** ~~may fail or suffer~~ security breaches, which ~~could~~ **would not only materially disrupt our business operations and result in the loss of confidential information, but also** damage the integrity of our clinical trials, impact our regulatory filings, compromise our ability to protect our intellectual property, and subject us to regulatory actions that could result in significant fines or other penalties. Our internal computer systems and those of any collaborators, contractors, consultants or other third parties that we work with, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third- party vendors and / or business partners, or from cyber- attacks by malicious third parties. **In recent years,** ~~Cyber~~ **cyber** - attacks ~~are increasing~~ **have increased** in their frequency, sophistication and intensity, and have become increasingly difficult, time consuming and costly to detect and we have experienced certain attacks, though minor, related to third party vendors. Cyber- attacks could include the deployment of harmful malware, ransomware, denial- of- service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyber- attacks also could include phishing attempts or e- mail fraud to cause payments or information to be transmitted to an unintended recipient. **These types of incidents continue to be prevalent**

and pervasive across industries, including in our industry. In addition, we expect information security risks to continue to increase due to the proliferation of new technologies and the increased sophistication and activities of organized crime, hackers, terrorists and other external parties, including foreign state actors. We are increasingly dependent on information technology systems and infrastructure, including mobile technologies, to operate our business. In the ordinary course of our business, we collect, process, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such information. The size and complexity of our information technology systems, and those of third- party vendors with whom we contract, and the volume of data we retain, make such systems potentially vulnerable to breakdown, malicious intrusion, security breaches, ransomware, phishing, and other cyber- attacks. While we have not experienced any material system failure, accident or security breach to date, if such an event were to occur **, or if we were unable to implement satisfactory remedial measures** , it could result in diversion of management' s attention and a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be materially harmed and the further development and commercialization of our product candidates could be delayed. Our employees, independent contractors, vendors, principal investigators, CROs and consultants may engage in misconduct or other improper activities, including non- compliance with regulatory standards and requirements and insider trading laws, which could materially harm our business. We are exposed to the risk that our employees, independent contractors, vendors, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include: • intentional, reckless or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of the FDA or similar foreign regulatory authorities; • healthcare fraud and abuse laws and regulations in the United States and in other jurisdictions; • violations of U. S. federal securities laws, including those related to trading in our common stock; and • failures to report financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self- dealing and other abusive practices. These laws and regulations regulate a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Other forms of misconduct could involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could, among other things, result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct and implement other internal controls applicable to all of our employees, but it is not always possible to identify and deter misconduct by employees and other third parties. In addition, the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any legal, regulatory or administrative actions or proceedings are instituted against us, and we are not successful in defending ourselves or asserting our rights, such actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diversion of management attention, general costs of litigation or proceedings, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. Risks Related to Our Common Stock The price of our common stock is volatile and may fluctuate substantially, which could result in the loss of all or part of our stockholders' investment. Our stock price has been and likely will continue to be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including: • the degree of success of any competitive products or technologies; • results of or developments in preclinical studies and clinical trials of our product candidates or those of our competitors; • regulatory or legal developments in the United States and other countries; • developments or disputes concerning patent applications, issued patents or other proprietary rights; • the recruitment or departure of key personnel; • the level of expenses related to any of our product candidates or clinical development programs; • the results of our efforts to discover, develop, acquire or in- license additional technologies or product candidates; • actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts; • variations in our financial results or those of companies that are perceived to be similar to us; • changes in the structure of healthcare payment systems in the United States and other jurisdictions; • market conditions in the pharmaceutical and biotechnology sectors; • general economic, industry and market conditions **, including geopolitical conflicts, inflation and high interest rates** ; and • the other factors described in this " Risk Factors " section. If any of the foregoing factors 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. In addition, in the past, companies that have experienced volatility in the market price of their stock have frequently been the subject of securities class action and shareholder derivative litigation. Such litigation, if instituted against us, whether successful or not, could cause us to incur substantial costs to defend such claims and divert management' s attention and resources, which could seriously harm our business, financial condition, results of operations and prospects. Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to significantly influence or control all matters submitted to stockholders for approval. Our executive officers and directors, combined with our stockholders who own more than 5 % of

our outstanding common stock, in the aggregate, beneficially own shares representing approximately ~~53~~ **44** % of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence or control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could significantly influence or control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of ownership control may: • delay, defer or prevent a change in control; • entrench our management and the board of directors; or • impede a merger, consolidation, takeover or other business combination involving us that other stockholders may desire. Provisions in our organizational documents and under Delaware law may have anti- takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management. Provisions in our certificate of incorporation and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions: • provide for a classified board of directors such that only one of three classes of directors is elected each year; • allow the authorized number of our directors to be changed only by resolution of our board of directors; • limit the manner in which stockholders can remove directors from our board of directors; • provide for advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors; • require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent; • limit who may call stockholder meetings; • authorize our board of directors to issue" blank check" preferred stock, which could be issued without stockholder approval, may contain voting, liquidation, dividend and other rights superior to our common stock, and could be used to institute a " poison pill " that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and • require the approval of the holders of at least 75 % of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our charter or bylaws. Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15 % of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15 % of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline. The trading market for our common stock is influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our trials or operating results fail to meet the expectations of analysts, our stock price will likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline. If a significant portion of our total outstanding shares are sold into the market, the market price of our common stock could drop significantly, even if our business is doing well. 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 shares, could reduce the market price of our common stock. Holders of a significant portion of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. In July 2019, we issued 1, 346, 313 shares of our common stock to Bayer. On October 1, 2019, we filed a registration statement on Form S- 3 covering the resale of these shares. In September 2021, we issued 3, 457, 815 shares of our common stock to Pfizer. **In November 2023, in a private placement with certain institutional accredited investors, we issued an aggregate of 12, 963, 542 shares of our common stock and, to one investor, pre- funded warrants to purchase 3, 422, 380 shares of our common stock. On December 8, 2023, we filed a registration statement on Form S- 3 covering the resale of these shares.** We have a significant number of shares that are subject to outstanding options and restricted stock units, and in the future we may issue additional options, restricted stock units, or other derivative securities convertible into our common stock under our equity compensation plans. The exercise or vesting of any such options, restricted stock units, or other derivative securities, and the subsequent sale of the underlying common stock, could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. Such sales of our common stock could result in higher than average trading volume and may cause the market price for our common stock to decline. We currently have on file with the SEC **a** universal shelf registration ~~statements~~ **statement** on Form S- 3 which ~~allow~~ **allows** us to offer and sell registered common stock, preferred stock, debt securities, ~~depositary~~ **depository** shares, units and / or warrants from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale ~~. In October 2019, we entered into an Equity Distribution Agreement, or the Distribution Agreement, with Piper Sandler & Co. (formerly Piper Jaffray & Co.), or Piper Sandler, pursuant to which we sold 2, 593, 637 shares of common stock in at- the- market offerings for aggregate net proceeds of $ 64. 1 million. We terminated the Distribution Agreement in August 2021~~ . In August 2021, we entered into an Equity Distribution Agreement with Piper Sandler & Company, or Piper Sandler, and Cantor Fitzgerald & Co., or Cantor, as agents, pursuant to which we **we sold 1, 449, 275 shares of common stock in at- the- market offerings, resulting in net proceeds of approximately $ 36. 0 million. In November 2023, we amended and restated the**

Equity Distribution Agreement with Piper Sandler and Cantor, pursuant to which we may offer and sell from time to time, through the agents, up to **an additional approximately** $ ~~300~~ **262** . ~~0~~ **8** million of the common stock registered under ~~the~~ **our** universal shelf registration statement pursuant to one or more ~~"~~ **“** at- the- market ~~"~~ **”** offerings. During the year ended December 31, ~~2022~~ **2023 , since the amendment and restatement of the agreement** , no shares were issued under this agreement. Sales of substantial amounts of shares of our common stock or other securities by our stockholders under our universal shelf registration statement, including pursuant to our" at- the- market" offering program, or otherwise could also dilute our stockholders. We will continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices. As a public company, we incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes- Oxley Act of 2002, or Sarbanes- Oxley, the Dodd- Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Select Market and other applicable securities rules and regulations, including those promulgated by the SEC, impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time- consuming and costly. Pursuant to Section 404 of Sarbanes- Oxley, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. To achieve compliance with Section 404, we are engaged in a process to document and evaluate our internal control over financial reporting and internal controls, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and carry out a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in harm to our reputation or an adverse reaction in the financial markets and it could restrict our future access to the capital markets due to a loss of confidence in the reliability of our consolidated financial statements which would materially harm our business. Our certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders. Our certificate of incorporation further provides that the federal district courts of the United States are the sole and exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended. These choice of forum provisions could limit our stockholders’ ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees or other stockholders. Our certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty owed by our directors, officers, other employees or stockholders to the company or our stockholders, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law or as to which the Delaware General Corporation Law confers jurisdiction on the Court of Chancery of the State of Delaware, or any action asserting a claim arising pursuant to our certificate of incorporation or our bylaws or governed by the internal affairs doctrine. Our certificate of incorporation further provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended. These choice of forum provisions may limit a stockholder’ s ability to bring a claim in a judicial forum that such stockholder finds favorable for disputes with us or our directors, officers, other employees or other stockholders, which may discourage such lawsuits against us and our directors, officers, other employees or other stockholders. Alternatively, if a court were to find this provision in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition. Neither of these choice of forum provisions would affect suits brought to enforce any liability or duty created by the Exchange Act or the rules and regulations thereunder, jurisdiction over which is exclusively vested by statute in the United States federal courts, or any other claim for which United States federal courts have exclusive jurisdiction. Because we have never paid and do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be our stockholders’ sole source of gain. We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends in respect of our common stock in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors and will depend on various factors, including applicable laws, our results of operations, financial condition, future prospects, then applicable contractual restrictions and any other factors deemed relevant by our board of directors. As a result, capital appreciation, if any, of our common stock will be our stockholders’ sole source of gain for the foreseeable future.