**Risk Factors Comparison 2023-03-27 to 2022-03-25 Form: 10-K**

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

In addition to other information contained in this Annual Report on Form 10- K, the following risks should be considered in evaluating our business and future prospects and an investment in our common stock. The risks and uncertainties described below are not the only ones we face. If any of the following risks and uncertainties develops into actual events, our business, financial condition, results of operations and cash flows could be materially adversely affected. In that case, the price of our common stock could decline and you may lose all or part of your investment. Risks Related to Our Business **Our exploration of strategic alternatives may not be successful. Given the Company' s current focus to explore growth through strategic transactions with potential partners, the Company' s ability to execute its current business plan depends on its ability to obtain additional funding via a strategic transaction or a series of strategic transactions, or to obtain funding to support such a transaction. We currently have no source of revenues or committed financing, and our financial resources are limited to our cash and cash equivalents. With respect to our efforts to maximize value from historical assets, while those efforts are continuing, based on the interest we have received to date we do not think it is likely they will generate significant value, at least in the near term. The Company plans to continue actively pursuing strategic alternatives, however, there can be no assurance that the Company will have sufficient resources or obtain additional financing necessary to complete this effort. Even if we do have such resources or can obtain financing, we may not be able to consummate such a transaction in a timely manner or at all or in a manner that would not adversely impact our business. The accompanying financial statements do not include any adjustments that might result from the outcome of this uncertainty. Strategic transactions are complex and time- consuming to identify, evaluate, negotiate and consummate in compliance with applicable laws and Nasdaq requirements. Our board and management do not have meaningful experience executing this type of endeavor in the U. S. public markets. Even if we are successful in entering into a strategic transaction, the terms and conditions of that transaction may restrict us from entering into future agreements with other potential collaborators. Additionally, such strategic transactions may not be favorable to investors nor deliver any anticipated benefits by the time of business integration. We need to obtain substantial funding in the near term in order to continue operations and our exploration of strategic alternatives. We require significant capital resources in order to continue to operate our business and conduct our exploration of strategic alternatives, and our limited liquidity could materially and adversely affect our business operations. Because we have no current source of revenue or committed financing, our current available cash and cash equivalents provide us with limited liquidity. We believe that our existing cash and cash equivalents could allow us to fund our business operations into early in the fourth quarter of 2023; however, it is very difficult to project our current monthly cash burn rate given the transitional status of the Company and this estimate may prove inaccurate and we may expend our limited resources sooner. Any such required additional capital may not be available on reasonable terms, if at all, due to a variety of factors, including uncertainty about the future direction of the Company and investor reaction to our new controlling stockholder and board composition, as well as broader conditions in the economy and capital markets, including recent volatility caused by inflation, questions about bank stability and other factors. The Company has already engaged in significant cost reductions, so our ability to further cut costs and extend our operating runway is limited. Without sufficient additional capital funding in the near term, we may be required, among other things, to seek bankruptcy protection. Our status as a " controlled company " could make our Common Stock less attractive to some investors or otherwise harm the trading price of our Common Stock. More than 50 % of our voting power is held by CBI USA. As a result, we are a " controlled company " under the corporate governance rules for Nasdaq- listed companies and may elect not to comply with certain Nasdaq corporate governance requirements with respect to board independence and compensation and nominating committee functions. We are relying on these exceptions. Following the closing of the Private Placement, our board includes 6 members, 5 of whom are affiliated or associated with CBI USA or were otherwise delegated by CBI USA. Investors may be hesitant to invest in the Company absent compliance with these governance requirements. In addition, should the interest or interests of our controlling stockholder differ from those of other stockholders, the other stockholders may not have the same protections afforded to stockholders of companies that are subject to all of the corporate governance rules for Nasdaq- listed companies. Our status as a controlled company could make our Common Stock less attractive to some investors, including but not limited to potential strategic partners, or otherwise harm our stock price. Additionally, it is possible we could pursue strategic or financing transactions with our controlling stockholder or its affiliates. The interests of the controlling stockholder and other stockholders would diverge in this case, and the lack of an independent board to evaluate such a transaction could adversely impact other stockholders. These conflicts of interest (or the perception that they could occur) might adversely affect our business and prospects for obtaining financing or completing a strategic transaction. For so long as CBI USA owns a majority of our Common Stock, it will have sufficient votes to elect all of our directors and to approve any other corporate action requiring the affirmative vote of holders of a majority of the outstanding shares of our Common Stock. Our control by a single stockholder, and our reliance on the Nasdaq controlled company exemptions, could deter investment in the Company and adversely impact our stock price and ability to obtain financing. These impacts may be more pronounced in the near term as investors assess the direction of the Company under the control of CBI USA and the actions of the new board. Potential partners considering engaging in a strategic transaction with the Company could have similar concerns.**

**Given our urgent need for additional funding and / or to complete a strategic transaction, it is imperative that our controlling stockholder and our board earn the confidence of investors and potential partners in the near term and there is no assurance this will occur Our controlling stockholder, and new members of our board, have limited experience controlling or governing a public company operating in the United States. Our controlling stockholder has not previously controlled a U. S. public company. In addition, the majority of our board is made of up Korean citizens, and none of the new members of the board have experience serving as directors or management of a U. S. publicly traded company. This could make it difficult to ensure that the Company complies with all applicable laws and stock exchange requirements, maintains adequate internal and disclosure controls and appropriately assesses and manages risk. This concern is exacerbated by the limited resources the Company has following recent reductions in force, and if there are further reductions in force or members of management leave the Company, it may be very difficult to manage this risk. The transitional state of the Company and ongoing exploration of strategic alternatives also exacerbates the challenging environment in this respect. If the board of directors does not successfully or efficiently manage their new roles and responsibilities, including the significant regulatory oversight and reporting obligations under the federal securities laws and the continuous scrutiny of investors, our prospects may be adversely impacted. In addition, against this backdrop, it may be difficult to earn the confidence of prospective investors or strategic partners, threatening our ability to obtain much needed financing and hindering our exploration of strategic alternatives. Turnover of senior management, and any inability to attract and retain qualified management and other key personnel, could impair our ability to implement our business plan. As we continue our exploration of strategic alternatives, and potentially pursue transactions involving new business lines or industries, we expect significant turnover in senior management, including in the near term. Departures of members of our senior management team, coupled with the recent turnover in our board, will create significant continuity risks and challenges to our ability to operate our business, assess and manage risks and comply with applicable laws. If key members of our senior management team depart, which we believe is likely in the near term, it will be important that we attract and retain qualified managers promptly and develop and implement an effective succession plan. We expect to face significant competition in attracting experienced executives and other key personnel, and there can be no assurance that we will be able to do so. In addition, there are significant uncertainties as to how our controlled company status, transitional state of operations, financial condition and related matters will impact our ability to attract the necessary personnel and manage these succession risks. Depending on the circumstances of any management departures, it is also possible that we will be required to pay significant severance, adverse impacting our financial condition. Our urgent need to raise capital and engage with potential partners in strategic transactions magnify these risks. If we are unable to adequately address these concerns in the near term, and earn the confidence of potential investors and / or business partners, our prospects and financial condition would be adversely impacted.** Our consolidated financial statements have been prepared assuming that we will continue as a going concern. ~~We have incurred recurring losses~~ **Our ability to continue as a going concern will require us to obtain additional funding. Based on our current operating plans and existing working capital at December 31, 2022, our current liquidity is not sufficient to fund operations over the next twelve months** from ~~operations since inception which raises~~ **the date of the issuance of the accompanying consolidated financial statements. As a result, there is** substantial doubt about our ability to continue as a going concern. ~~accompanying consolidated financial statements.As a result,there is substantial~~ **Substantial** ~~doubt about our ability to continue as a going concern.We have no committed sources of additional capital at this time and substantial~~ additional financing will be needed by us to fund our operations **and exploration of strategic alternatives in the near term** . ~~We~~ **Although we currently estimate that available funds could be sufficient into early in the fourth quarter of 2023,we** have based these estimates ~~,however,~~ on assumptions that may prove to be wrong,and we could spend our available financial resources much faster than we currently expect ~~and need~~ **.It is very difficult** to ~~raise additional funds sooner than~~ **project our current monthly cash burn rate given the transitional status of the Company as** we ~~anticipate~~ **explore strategic alternatives** .The perception of our ability to continue as a going concern may make it more difficult for us to obtain financing for the continuation of our operations and could result in the loss of confidence by investors ~~,suppliers~~ and employees. ~~If we are~~ If we are unable to ~~obtain sufficient funding,~~ **raise capital when needed** ~~our~~ **or** ~~business~~ **on acceptable terms** , **we will be unable to continue** ~~prospects, financial condition and results of~~ operations ~~will be materially~~ and ~~adversely~~ **may need to seek bankruptcy protection in the near term. Our common stock may be delisted from The Nasdaq Capital Market which could negatively impact the price of our common stock, liquidity and our ability to access the capital markets. Our common stock is currently listed on The Nasdaq Capital Market under the symbol " XCUR. " As previously disclosed, the Company has received numerous deficiency notes with respect to various Nasdaq listing requirements in the past year. These related to: • Compliance with Nasdaq' s minimum bid price rule due to the Company' s stock trading below $ 1. 00 for a sustained period of time. The Company** ~~affected~~ **effected a one- for- thirty reverse stock split on June 29 , 2022 in order** ~~and we may be unable~~ to ~~continue~~ **attempt to raise the stock price. As of March 23, 2023, the Company' s stock price closed at $ 0. 9761. • Compliance with Nasdaq' s rule requiring stockholders' equity of at least $ 2, 500, 000 based on the Company' s balance sheet** as **of June 30** ~~a going concern. If we are unable to continue as a going concern~~ , **2022. The Company believes** ~~we may have to liquidate our assets and may receive less than the value at which those assets are carried on our audited financial statements, and~~ it is ~~likely~~ **in compliance with this requirement based on its December 31, 2022 balance sheet, but there can be no assurance it will remain in compliance. • Compliance with Nasdaq' s corporate governance requirements with respect to board and committee composition due to (i) the lack of a majority independent board, (ii) the lack of an audit committee comprised of three independent directors and (iii) the lack of a compensation committee comprised of at least two independent directors. With respect to the majority independence and the audit committee requirements, Nasdaq informed the Company** that ~~investors~~ **it was not entitled to a cure period and must**

**submit a plan to regain compliance no later than April 10, 2023. Following the closing of the Private Placement, the Company qualifies for Nasdaq' s controlled company exemptions from the requirements to have a majority independent board and independent compensation committee. The Company still must have an audit committee comprised of three independent directors. Even if the Company regains compliance with Nasdaq' s listing requirements and addresses the outstanding deficiency notices to Nasdaq' s satisfaction, there can be no assurance that the Company** will ~~lose all~~ **remain in compliance with Nasdaq' s requirements and will not be delisted. If Nasdaq delists** ~~or~~ **our** ~~a part~~ **securities from trading on its exchange for failure to meet the listing standards, we and our stockholders could face significant negative consequences including: • limited availability** of **market quotations and liquidity for our securities; • a determination that the common stock is a " penny stock " which would require brokers trading in the common stock to adhere to more stringent rules, possibly resulting in a reduced level of trading activity in the secondary trading market for shares of common stock; • a limited amount of analyst coverage, if any; and • a decreased ability to issue additional securities or obtain additional financing in the future. Delisting from The Nasdaq Capital Market could also result in** ~~their~~ **other** ~~investment~~ **negative consequences, including the potential loss of institutional investor interest and make obtaining new financing much more challenging** . In addition, **fewer strategic opportunities** ~~if there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources~~ may be **available** ~~unwilling to provide additional funding to us on commercially reasonable terms~~ , ~~or at all~~ **particularly from counterparties that are interested in combining with a listed company** . We **have** ~~are a biotechnology company with~~ a history of losses. We expect to continue to incur significant losses for the foreseeable future and may never achieve or maintain profitability, which could result in a decline in the market value of our common stock. ~~We are a biotechnology company developing nucleic acid therapies targeting ribonucleic acid against validated targets to neurological disorders and hair loss.~~ Since our inception in June 2011, we have devoted our resources to the development of SNA technology **, and are currently exploring out- licensing opportunities and strategic alternatives to maximize stockholder value** . We have had significant operating losses since our inception. As of December 31, ~~2021~~ **2022** , we have generated an accumulated deficit of $ ~~188~~ **191** . ~~9~~ **5** million. For the years ended December 31, **2022 and** 2021 ~~and 2020~~ , our net loss was $ **2. 6 million and $** 64. 1 ~~million and $ 24. 7~~ million, respectively. Substantially all of our losses have resulted from expenses incurred in connection with our research programs and from general and administrative costs associated with our operations. ~~Our technology and therapeutic candidates are in early stages of development, and we are subject to the risks of failure inherent in the development of therapeutic candidates based on novel technologies.~~ We have not generated, and do not expect to generate, any product revenue for the foreseeable future **and currently have no source of revenue or committed financing** , and we expect to continue to incur significant operating losses for the foreseeable future ~~due to the cost of research and development, preclinical studies, clinical trials, and the regulatory approval process for therapeutic candidates~~ . The amount of future losses is uncertain. Our ~~ability to achieve profitability~~ **future financial performance and condition are substantially dependent on the results of our ongoing exploration of strategic alternatives** , ~~if ever,~~ **and we cannot predict whether we** will **be** ~~depend on, among other things, us, or any current or future collaborators, successfully~~ -- **successful** ~~developing therapeutic candidates~~ **. We are pursuing asset out- licenses** , **asset** ~~obtaining regulatory approvals to market and commercialize therapeutic candidates, manufacturing any approved products on commercially reasonable terms, establishing a~~ sales and ~~marketing organization~~ **similar strategic transactions with respect to** ~~or~~ **our** ~~suitable third- party~~ **historical assets. There can be no assurance that we will be successful in executing such a strategic transaction. We continue to seek strategic** alternatives for **our therapeutic portfolios, with the goal of maximizing stockholder value of these assets. These strategic alternatives may include a variety of different business arrangements, such as the sale of certain of our assets, out- licensing, strategic partnerships, joint ventures, restructurings, divestitures, investments and other alternatives. We may not be able to identify or consummate a suitable transaction as a result of this review, or** any **transactions that** ~~approved product and raising sufficient funds to finance business activities. If~~ we ~~,~~ **are able to identify and consummate may not provide material benefits to** ~~or~~ **our stockholders. Based on the interest in these assets that we have seen to date, we do not currently expect** any **such transaction** ~~current or future collaborators, are unable~~ to **provide significant value** ~~develop and commercialize one or more of our therapeutic candidates or if sales revenue from any therapeutic candidate that receives approval is insufficient~~ , ~~we will not achieve profitability, which could have a material adverse effect on our business, financial condition, results of operations and prospects. Management has identified certain conditions or events, which, considered in the aggregate, raise substantial doubt about our ability to continue as a going concern, including the risk that we will be unable to raise adequate additional capital to fund our operations through~~ at least **in** ~~the twelve months following the filing date of this Annual Report on Form 10- K. Substantial doubt about our ability to continue as a going concern may create negative reactions to the price of our common stock. If we are unable to raise capital, we may be required to delay, reduce the scope of, or eliminate research and development programs, or obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain drug candidates that we might otherwise seek to develop or commercialize independently. In addition, if we are unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those~~ -- **the near term** ~~assets are carried on our financial statements, and it is likely that investors will lose all or a part of their investment~~ . **Our** ~~Further, the perception that we may be unable to continue as a going concern may impede our ability to pursue strategic opportunities or operate our~~ business **could be adversely affected** ~~due to concerns regarding our ability to discharge our contractual obligations. Our approach to the discovery and development of innovative therapeutic treatments based on our technology is unproven and may not result in marketable products. We plan to develop a pipeline of therapeutic candidates based on our proprietary SNA technology. We believe that therapeutic candidates identified with our therapeutic discovery technology may offer an improved therapeutic approach compared to small molecules and antibodies, as well as several advantages over linear oligonucleotide- based therapeutics. However, the scientific research that forms the basis of our efforts to develop therapeutic candidates based on our SNA technology and the identification and~~

optimization of SNA- based therapeutic candidates is relatively new. Further, the scientific evidence to support the feasibility of developing therapeutic treatments based on SNA technology is both preliminary and limited. Therapeutic candidates based on SNA technology have not been extensively tested in humans, and a number of clinical trials conducted by other companies using oligonucleotide technologies have not been successful. We may discover that the SNA- based therapeutic candidates do not possess certain properties required for therapeutic treatment to be effective, such as the ability to remain stable in the human body for the period of time required for the therapeutic candidate to reach the target tissue or the ability to cross the cell membrane and enter into cells within the target tissue for effective delivery. We currently have only limited data, and no conclusive evidence, to suggest that we can introduce these necessary drug- like properties into SNA- based therapeutic candidate. We may spend substantial funds attempting to introduce these properties and may never succeed in doing so. In addition, therapeutic candidates based on SNA technology may demonstrate different chemical and pharmacological properties in patients than they - **the effects** do in laboratory studies. Even if therapeutic candidates have successful results in animal studies, they may not demonstrate the same chemical and pharmacological properties in humans and may interact with human biological systems in unforeseen, ineffective or harmful ways. As a result, we may never succeed in developing a marketable therapeutic, we may not become profitable and the value of **health epidemics** our common stock would decline. Further, the U. S. Food and Drug Administration, or FDA, and equivalent foreign regulatory authorities have limited experience with SNA- based therapeutics. No regulatory authority has granted approval to any person or entity , including us, to market and commercialize SNA- based therapeutics, which may increase the complexity **global COVID - 19 pandemic** , **in regions where we** uncertainty and length of the regulatory approval process for - **or** our therapeutic candidates. We and any current or future collaborators may never receive approval to market and commercialize any therapeutic candidate. Even if we or a future collaborator obtain regulatory approval, the approval may be for disease indications or patient populations that are not as broad as we intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. We or a future collaborator may be required to perform additional or unanticipated clinical trials to obtain approval or be subject to post- marketing testing requirements to maintain regulatory approval. If our SNA technology proves to be ineffective, unsafe or commercially unviable, our technology and pipeline would have little, if any, value, which could have a material adverse effect on our business, financial condition, results of operations and prospects. Our therapeutic candidates are in early stages of development and may fail in development or suffer delays that materially and adversely affect their commercial viability. We have no therapeutics on the market and all of our therapeutic candidates are in early stages of development. Our ability to achieve and sustain profitability depends on obtaining regulatory approvals, including an institutional review board, or IRB, approval to conduct clinical trials at particular sites for, and successfully commercializing, our therapeutic candidates, either alone or with third parties **on which** . Before obtaining regulatory approval for the commercial distribution of our therapeutic candidates, we or **rely have business operations. Our business** an **and operations could be adversely** existing or a future collaborator must conduct extensive preclinical studies and clinical trials to demonstrate the safety and efficacy in humans of our therapeutic candidates. Preclinical studies and clinical trials are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. The start or end of a clinical trial is often delayed or halted due to changing regulatory requirements, manufacturing challenges, required clinical trial administrative actions, slower than anticipated patient enrollment, changing standards of care, availability or prevalence of use of a comparative therapeutic or required prior therapy, clinical outcomes or financial constraints. For instance, delays or difficulties in patient enrollment or difficulties in retaining trial participants can result in increased costs, longer development times or termination of a clinical trial. Clinical trials of a new therapeutic candidate require the enrollment of a sufficient number of patients, including patients who are suffering from the disease the therapeutic candidate is intended to treat and who meet other eligibility criteria. Rates of patient enrollment are affected by many factors **the effects of health epidemics** , including the size of the patient population, the eligibility criteria for the clinical trial, the age and condition of the patients, the stage and severity of disease, the nature of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease, and COVID- 19- related developments including the extent to which they may interact with any of the foregoing factors. For example, the continuing effects of the COVID- 19 pandemic contributed to delays that began in the third quarter of 2020 and continued into the second half of 2021 in our enrollment plans and clinical trial site start- ups for the Phase 2 dose expansion phase of the Phase 1b / 2 clinical trial for our eavrotolimod (AST- 008) clinical program. A therapeutic candidate can unexpectedly fail at any stage of preclinical and clinical development. The historical failure rate for therapeutic candidates is high due to scientific feasibility, safety, efficacy, changing standards of medical care and other variables. The results from preclinical studies or early clinical trials of a therapeutic candidate may not predict the results that will be obtained in later phase clinical trials of the therapeutic candidate. We, the FDA, an IRB, an independent ethics committee, or other applicable regulatory authorities may suspend clinical trials of a therapeutic candidate at any time for various reasons, including a finding that subjects participating in such trials are being exposed to unreasonable and significant risk of illness or injury. Similarly, an IRB or ethics committee may suspend a clinical trial at a particular trial site. We may not have the financial resources to continue development of, or to enter into collaborations for, a therapeutic candidate if we experience any problems or other unforeseen events that delay or prevent regulatory approval of, or our ability to commercialize, therapeutic candidates, including: • negative or inconclusive results from our clinical trials or the clinical trials of others for therapeutic candidates similar to ours, leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program; • therapeutic- related side effects experienced by participants in our clinical trials or by individuals using therapeutics similar to our therapeutic candidates; • delays in submitting INDs or clinical trial applications, or CTAs, or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators or IRBs or ethics committees to commence a clinical trial, or a suspension or termination of a clinical trial once commenced; • conditions imposed by the FDA or comparable foreign authorities, such as the European Medicines Agency, or EMA, or European Union national competent authorities, regarding the scope or design of our clinical trials; •

further delays in enrolling research subjects in clinical trials; • high drop- out rates of research subjects; • inadequate supply or quality of therapeutic candidate components or materials or other supplies necessary for the conduct of our clinical trials; • greater than anticipated clinical trial costs; • poor effectiveness of our therapeutic candidates during clinical trials; • unfavorable FDA or other regulatory agency inspection and review of a clinical trial site; • failure of our third- party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all; • delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular, especially in light of the novelty of our therapeutic candidates; • varying interpretations of data by the FDA and similar foreign regulatory agencies; or • refusal of the FDA to accept data from clinical trials conducted outside the United States, or acceptance of these data subject to certain conditions by the FDA. Product development involves a lengthy and expensive process with an uncertain outcome, and results of earlier preclinical studies and clinical trials may not be predictive of future clinical trial results. Clinical testing is expensive and generally takes many years to complete, and the outcome is inherently uncertain. Failure can occur at any time and at any stage during the clinical trial process. The results of preclinical studies and early clinical trials of our therapeutic candidates may not be predictive of the result of any subsequent clinical trials. Therapeutic candidates that have shown promising results in early stage clinical trials may still suffer significant setbacks in subsequent clinical trials. We will have to conduct trials in our proposed indications to verify the results obtained to date and to support any regulatory submissions for further clinical development. A number of companies in the biopharmaceutical industry have suffered significant setbacks in clinical trials due to lack of efficacy or adverse safety profiles despite promising results in earlier clinical trials. Moreover, clinical data is often susceptible to varying interpretations and analyses. We do not know whether Phase 1, Phase 2, Phase 3, or other clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety with respect to the proposed indication for use sufficient to receive regulatory approval or market our therapeutic candidates. If we experience delays in the completion of, or termination of, any clinical trial of our therapeutic candidates, the commercial prospects of our therapeutic candidates may be harmed, and our ability to generate product revenues from any of these therapeutic candidates will be delayed. In addition, any delays in completing clinical trials will increase our costs, slow down our therapeutic candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences could materially and adversely affect our business, financial condition, results of operations or prospects. Additionally, some of the clinical trials we conduct may be open- label in study design and may be conducted at a limited number of clinical sites on a limited number of patients. An " open- label " clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open- label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open- label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open- label clinical trials are aware when they are receiving treatment. Open- label clinical trials may be subject to a " patient bias " where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. Moreover, patients selected for early clinical studies often include the most severe sufferers and their symptoms may have been bound to improve notwithstanding the new treatment. In addition, open- label clinical trials may be subject to an " investigator bias " where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. We will need substantial additional funds to advance the development of our therapeutic candidates, and we cannot guarantee that we will have sufficient funds available in the future to develop and commercialize our current or future therapeutic candidates. If our existing therapeutic candidates or our future therapeutic candidates enter and advance through preclinical studies and clinical trials, we will need substantial additional funds to expand our development, regulatory, manufacturing, marketing, and sales capabilities or contract with other organizations to provide these capabilities for us. We have used substantial funds to develop our therapeutic candidates and will require significant funds to conduct further research and development and preclinical studies and clinical trials of our therapeutic candidates, to seek regulatory approvals for our therapeutic candidates and to manufacture and market products, if any, that are approved for commercial sale. As of December 31, 2021, we had $ 43. 8 million in cash, cash equivalents, and restricted cash and $ 4. 5 million in short- term investments. Based on our current operating plans and existing working capital at December 31, 2021, it is uncertain whether our current liquidity is sufficient to fund operations over the next twelve months from the date of the issuance of the accompanying consolidated financial statements. As a result, there is substantial doubt about our ability to continue as a going concern. We have no committed sources of additional capital at this time and substantial additional financing will be needed by us to fund our operations. Our future capital requirements and the period for which we expect our existing resources to support our operations may vary significantly from what we expect. Our monthly spending levels vary based on new and ongoing development and corporate activities. Since the length of time and activities associated with successful development of our therapeutic candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. To execute our business plan, we will need, among other things: • to obtain the human and financial resources necessary to develop, test, obtain regulatory approval for, manufacture and market our therapeutic candidates; • to build and maintain a strong intellectual property portfolio and avoid infringing the intellectual property of third parties; • to establish and maintain successful licenses, collaborations and alliances; • to satisfy the requirements of clinical trial protocols, including patient enrollment; • to establish and demonstrate the clinical efficacy and safety of our therapeutic candidates; • to obtain regulatory approvals; • to manage our spending as costs and expenses increase due to preclinical studies and clinical trials, regulatory approvals, and commercialization; • to obtain additional capital to support and expand our operations; and • to market our products to achieve acceptance and use by the medical community in general. If we are unable to obtain funding on a timely basis or on acceptable terms, we may have to delay, reduce or terminate our research and development programs and preclinical studies or clinical

trials, if any, limit strategic opportunities or undergo reductions in our workforce or other corporate restructuring activities. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technology or therapeutic candidates that we would otherwise pursue on our own. We do not expect to realize revenue from product sales, milestone payments or royalties in the foreseeable future, if at all. Our revenue sources are, and will remain, extremely limited unless and until our therapeutic candidates are clinically tested, approved for commercialization and successfully marketed. To date, we have primarily financed our operations through the sale of equity securities, payments received in connection with our collaboration, option, and license agreement with AbbVie Inc., or AbbVie, our collaboration, option and license agreement with Ipsen Biopharm Limited, or Ipsen, our research collaboration, license, and option agreement with Purdue Pharma L. P., or Purdue, our license and development agreement with Dermelix LLC, or Dermelix, or as a primary contractor or as a subcontractor on government grants, proceeds from our credit and security agreement with MidCap Financial Trust, or MidCap, and proceeds from our loan agreement with Hercules Technology Growth Capital, or Hercules. We will be required to seek additional funding in the future and intend to do so through either collaborations, public or private equity offerings or debt financings, credit or loan facilities or a combination of one or more of these funding sources. Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. Additional funds may not be available to us on acceptable terms, or at all, and our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID- 19 pandemic . In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, may involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of equity securities received any distribution of corporate assets. Our business could be adversely affected by the effects of health epidemics, including the global COVID - 19 pandemic, in regions where we or third parties on which we rely have business operations and at our clinical trial sites, as well as the business or operations of our CROs or other third parties with whom we conduct business. The outbreak of the novel strain of coronavirus, SARS- CoV- 2, which causes coronavirus disease 2019, or COVID- 19, continues to negatively impact the global economy. Our business and operations could be adversely affected by the effects of health epidemics, including the ongoing COVID- 19 pandemic , on our business activities performed by us or by third parties with whom we conduct business , including our third party manufacturers, contract research organizations, or CROs, shippers and others . Such effects could be more pronounced in regions where we have concentrations of clinical trial sites or other business operations . Our company headquarters is located in Chicago, Illinois, our CROs are located globally, and our substance and drug product manufacturers are located in the United States and Europe. As of March 23, 2022, Illinois remains in " Phase 5 " of the Restore Illinois Plan. Certain jurisdictions have begun re- opening only to return to restrictions in the face of increases in new COVID- 19 cases. The extent of and timing for lifting of government restrictions remains uncertain as the COVID- 19 pandemic continues to evolve. There is no guarantee that prior or new restrictions will not be reinstated in response to the continued spread of COVID- 19 or the introduction and spread of new variants of SARS- CoV- 2. In response to the ongoing COVID- 19 pandemic, we have taken and continue to take active measures designed to address and mitigate the impact of the COVID- 19 pandemic on its business. We continue to monitor closely the developments and continue to take active measures to protect the health of our employees and their families, and our communities. Our on- site activities continue with protocols for safely accessing and working within our facilities. While we continue to conduct research and development activities, the COVID- 19 pandemic has impacted, and may continue to impact, certain of our early- stage discovery efforts. We are working closely with our third- party manufacturers and other partners to manage our supply chain activities and mitigate potential disruptions as a result of the COVID- 19 pandemic. We have observed minor delays in receipt of key chemicals, reagents and materials as certain manufacturers have had supply disruptions related to the COVID- 19 pandemic. If the COVID- 19 pandemic continues to persist for an extended period of time and impacts essential distribution systems such as FedEx and postal delivery, we could experience future disruptions to our supply chain and operations and associated delays in the manufacturing and our clinical supply, which would adversely impact our preclinical and clinical development activities. In addition, if the COVID- 19 pandemic continues to persist for an extended period of time, we could experience further significant disruptions to our clinical and preclinical development timelines, which would adversely affect our business, financial condition, results of operations and growth prospects. The regions in which we operate are currently being affected by COVID- 19 and have become subject to additional government- imposed mitigation measures to prevent the ongoing spread of COVID- 19. Further, timely enrollment in our clinical trials is dependent upon clinical trial sites which may be adversely affected by the COVID- 19 pandemic or its impact or effects. Quarantines, shelter- in- place, safer- at- home, social distancing requirements and similar government orders, business shutdowns and closures, phased re- openings or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could continue to occur, related to COVID- 19 or other infectious diseases could impact personnel at third- party manufacturing facilities and CROs in the United States and other countries, or the availability or cost of materials, which would disrupt our supply chain. Additionally, our clinical trials may involve immunocompromised patients who are at higher risk for COVID- 19 and who are therefore more likely to avoid hospitals or other high risk areas. The effects of the executive orders and our work- from- home policies may negatively impact productivity, disrupt our business and delay our clinical programs and timelines (for example, our timelines for any of our product candidates), the magnitude of which will continue to depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. As a result of the COVID- 19 outbreak, or similar pandemics, we may experience further disruptions that could severely impact our business, clinical trials and preclinical studies, including: • further delays or difficulties in enrolling or maintaining patients in our clinical trials, including patients who may not be able to comply with clinical trial protocols if quarantines, shelter- in- place or safer- at- home restrictions, or social distancing practices or

~~requirements, business shutdowns and closures, among other similar requirements or government orders, continue to impede patient movement or interrupt healthcare services; • increased rates of patients withdrawing from our clinical trials following enrollment as a result of contracting COVID- 19, being forced to quarantine, or being unable to visit clinical trial locations; • delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff who may have heightened exposure to COVID- 19 or experience additional restrictions by their institutions, city, or state; • delays or disruptions in non- clinical experiments and investigational new drug application- enabling good laboratory practice standard toxicology studies due to unforeseen circumstances in supply chain; • diversion or prioritization of healthcare resources away from the conduct of clinical trials and towards the COVID- 19 pandemic, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials, and because, who, as healthcare providers, may have heightened exposure to COVID- 19 and adversely impact our clinical trial operations; • interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others; • interruption of our key clinical trial activities, such as clinical assessments at pre-specified time points during the trial and clinical trial site data monitoring, due to limitations on travel imposed or recommended by governmental entities, employers and others or interruption of clinical trial subject visits and study procedures (particularly any procedures that may be deemed non- essential), which may impact the integrity of subject data and clinical study endpoints; • interruption or delays in the operations of the FDA, European Medicines Agency, or EMA, and comparable foreign regulatory agencies or their refusal to accept data from clinical trials in affected geographies, which may impact approval timelines; • delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees; and • limitations in employee resources that would otherwise be focused on the conduct of our clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people. For our clinical trials that we might conduct at sites outside the United States, in addition to the risks listed above, we may also experience the following adverse impacts, particularly in countries which are experiencing heightened impact from the COVID- 19 pandemic: • delays in receiving approval from local regulatory authorities to initiate our planned clinical trials; • delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials; • interruption in global shipping that may affect the transport of clinical trial materials, such as investigational drug product and comparator drugs used in our clinical trials; • changes in local regulations as part of a response to the ongoing COVID- 19 pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether; • the refusal of the FDA to accept data from clinical trials in these affected geographies~~ . The spread of COVID- 19, which continues to cause broad global impact, may materially affect us economically. The trading price for our shares as well as the trading prices of other biopharmaceutical companies, as well as the broader equity and debt markets overall, have been highly volatile as a result of the COVID- 19 pandemic and the resulting impact on U. S. economic activities. Although the potential economic impact brought by, and the duration or subsequent reoccurrence of, the COVID- 19 pandemic may be difficult to assess or predict, a widespread and prolonged pandemic could continue to result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, even after the COVID- 19 pandemic has subsided, a recession or market correction that has occurred or may occur in the future because of the COVID- 19 could materially affect our business and the value of our common stock. **These conditions could challenge our ability to raise needed capital and our ability to identify and consummate strategic transactions to create value for stockholders.** The global outbreak of COVID- 19 continues to rapidly evolve. The extent to which the COVID- 19 pandemic or a similar pandemic will impact our business ~~, preclinical studies and clinical trials~~ will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration and severity of the outbreak, the possibility of additional periods of increases or spikes in the number of COVID- 19 cases, the introduction and spread of new variants of the virus, limitations on our ability to conduct our business in the ordinary course, any reopening plans and additional closures, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions for us, ~~our third party contractors~~ and the effectiveness of actions taken in the United States and other countries to contain and treat the disease, including, without limitation, the effectiveness and timing of vaccination initiatives in the United States and worldwide. The ultimate impact of the COVID- 19 pandemic or a similar health pandemic is highly uncertain and subject to change; we continue to monitor the COVID- 19 situation closely. ~~If we continue to experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be further delayed or prevented. We may not be able to initiate or continue conducting 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 the United States. 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 size and nature of the patient population; • the severity of the disease under investigation; • the eligibility criteria for, and design of, the trial in question; • the perceived risks and benefits of the product candidate under study; • competition in recruiting and enrolling patients in clinical trials; • the efforts to facilitate timely enrollment in clinical trials; • the patient referral practices of physicians; • the ability to monitor patients adequately during and after treatment; • the proximity and availability of clinical trial sites for prospective patients; and • delays or difficulties due to the COVID- 19 pandemic or its impact or effects. 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. We may encounter further difficulties and / or delays in completing our planned enrollments. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, or the inability to complete development of our product candidates, which would cause the value of our company to decline, limit our~~

ability to obtain additional financing, and materially impair our ability to generate revenues. Our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline. We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including: • variations in the level of expense related to our therapeutic candidates or future development programs; • results of clinical trials, or the addition or termination of clinical trials or funding support by us, or a future collaborator or licensing partner; • our execution of any collaboration, licensing or similar arrangement, and the timing of payments we may make or receive under such existing or future arrangements or the termination or modification of any such existing or future arrangements; • changes in estimates in total project hours in connection with the revenue recognition related to our collaboration agreements that may result in a significant adjustment of non- cash revenue; • any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved; • additions and departures of key personnel; • strategic decisions by us or our competitors, such as acquisitions, divestitures, spin- offs, joint ventures, strategic investments or changes in business strategy; • whether or not any of our therapeutic candidates receives regulatory approval, market acceptance and demand for such therapeutic candidates; • regulatory developments affecting our therapeutic candidates or those of our competitors; and • changes in general economic, industry, political and market conditions, including, but not limited to, the ongoing impact of the COVID- 19 pandemic. If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We may not successfully engage in strategic transactions, including any additional collaborations or out- licensing of cavrotolimod we seek, which could adversely affect our ability to develop and commercialize product candidates, impact our cash position, increase our expense and present significant distractions to our management. From time to time, we may consider strategic transactions, such as collaborations, acquisitions of companies, asset purchases and out- or in- licensing of product candidates or technologies. In particular, in addition to our current arrangements with Ipsen, which began in July 2021, AbbVie, which began in November 2019, and Dermelix, which began in February 2019, and Purdue, with which there no active therapeutic candidates in development and which has not indicated any further interest in development, we will evaluate and, if strategically attractive, seek to enter into additional collaborations, including with major biotechnology or pharmaceutical companies. For example, on July 30, 2021, we entered into a collaboration, option, and licensing agreement with Ipsen. The competition for collaborators is intense, and the negotiation process is time- consuming and complex. Any new collaboration may be on terms that are not optimal for us, and we may be unable to maintain any new or existing collaboration if, for example, development or approval of a therapeutic candidate is delayed, sales of an approved product do not meet expectations or the collaborator terminates the collaboration. Any such collaboration, or other strategic transaction, may require us to incur non- recurring or other charges, increase our near- and long- term expenditures and pose significant integration or implementation challenges or disrupt our management or business. On December 10, 2021, in connection with our announcement to implement strategic measures to reduce cash burn and prioritize our pipeline focus, we announced the wind- down of our immuno- oncology program cavrotolimod (AST- 008). We are currently engaged in out- licensing activities for cavrotolimod. These transactions entail numerous operational and financial risks, including exposure to unknown liabilities, disruption of our business and diversion of our management' s time and attention in order to manage a collaboration or develop acquired products, product candidates or technologies, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected collaboration, acquisition or integration costs, write- downs of assets or goodwill or impairment charges, increased amortization expenses, difficulty and cost in facilitating the collaboration or combining the operations and personnel of any acquired business, impairment of relationships with key suppliers, manufacturers or customers of any acquired business due to changes in management and ownership and the inability to retain key employees of any acquired business. Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks and have a material adverse effect on our business, results of operations, financial condition and prospects. Conversely, any failure to enter any collaboration or other strategic transaction that would be beneficial to us could delay the development and potential commercialization of our product candidates and have a negative impact on the competitiveness of any product candidate that reaches market. If third parties on which we depend to conduct our preclinical studies and clinical trials do not perform as contractually required, fail to satisfy regulatory or legal requirements, or miss expected deadlines, our development program could be delayed with materially adverse effects on our business, financial condition, results of operations and prospects. We rely on third- party clinical investigators, CROs, clinical data management organizations and consultants to design, conduct, supervise and monitor preclinical studies and clinical trials for our therapeutic candidates. Because we rely on third parties and do not have the ability to conduct preclinical studies or clinical trials independently, we have less control over the timing, quality and other aspects of preclinical studies and clinical trials than we would if we conducted them on our own. These investigators, CROs and consultants are not our employees and we have limited control over the amount of time and resources that they dedicate to our programs. These third parties may have contractual relationships with other entities, some of which may be our competitors, which may draw time and resources away from our programs. The third parties with which we contract might not be diligent, careful or timely in conducting our preclinical studies or clinical trials, resulting in the preclinical studies or clinical trials being delayed or unsuccessful. If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. In all events, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. The FDA requires preclinical studies to be conducted in accordance with applicable good laboratory practices, or GLPs, and

clinical trials to be conducted in accordance with applicable FDA regulations and good clinical practices, or GCPs, including requirements for conducting, recording and reporting the results of preclinical studies and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. Any adverse development or delay in our preclinical studies or clinical trials could have a material adverse effect on our business, financial condition, results of operations and prospects. In addition, the operations of our CROs may be constrained or disrupted by the COVID- 19 pandemic. Clinical site closure and other activities that require visits to clinical sites, have been and may continue to be delayed due to prioritization of hospital resources toward the COVID- 19 pandemic or concerns among patients about participating in clinical trials during a pandemic. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our preclinical studies or clinical trials in accordance with regulatory requirements or our stated protocols, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may 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. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed. If any of our relationships with these third- party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms or in a timely manner. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays could occur, which could compromise our ability to meet our desired development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects. Because we rely on third- party manufacturing and supply partners, our supply of research and development, preclinical studies and clinical trial materials may become limited or interrupted or may not be of satisfactory quantity or quality. We rely on third- party partners to manufacture and supply the materials and components for our research and development, preclinical study and clinical trial supplies. We do not own manufacturing facilities or supply sources for such components and materials. Our manufacturing requirements include oligonucleotides and lipids. We procure our nonclinical toxicology and clinical development materials from a limited number of suppliers on a purchase order basis. There can be no assurance that our supply of research and development, preclinical study and clinical trial therapeutic candidates and other materials will not be limited, interrupted, restricted in certain geographic regions or of satisfactory quality or continue to be available at acceptable prices. In particular, any replacement of our drug product manufacturers could require significant effort and expertise because there may be a limited number of qualified replacements. The manufacturing process for a therapeutic candidate is subject to oversight by the FDA and foreign regulatory authorities. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory requirements, such as current good manufacturing practices, or cGMPs. In the event that any of our suppliers or manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third- party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our therapeutic candidates may be unique or proprietary to the original manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills or technology to another third- party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third- party manufacture our therapeutic candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop therapeutic candidates in a timely manner or within budget. We expect to continue to rely on third- party manufacturers if we receive regulatory approval for any therapeutic candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are unable to obtain or maintain third- party manufacturing for therapeutic candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our therapeutic candidates successfully. Our or a third- party' s failure to execute on our manufacturing requirements and comply with cGMPs could adversely affect our business in a number of ways, including: • an inability to initiate or continue preclinical studies or clinical trials of our therapeutic candidates under development; • delay in submitting regulatory applications, or receiving regulatory approvals, for therapeutic candidates; • loss of the cooperation of a future collaborator; • subjecting manufacturing facilities of our therapeutic candidates to additional inspections by regulatory authorities; • requirements to cease distribution or to recall batches of our therapeutic candidates; and • in the event of approval to market and commercialize a therapeutic candidate, an inability to meet commercial demands for our therapeutics. If our relationships with our manufacturers, suppliers or other vendors are terminated or scaled back as a result of the COVID- 19 pandemic or other health epidemics or pandemics, we may not be able to enter into arrangements with alternative suppliers or vendors or do so on commercially reasonable terms or in a timely manner. Further, if the COVID- 19 pandemic continues to persist for an extended period of time and impacts essential distribution systems such as FedEx and postal delivery, we could experience disruptions to our supply chain and operations, and associated delays in the manufacturing and supply of our product candidates. For example, we have observed

minor delays in receipt of key chemicals, reagents and materials as certain manufacturers have had supply disruptions related to the COVID-19 pandemic. Switching or adding additional suppliers or vendors involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new supplier or vendor commences work. As a result, delays may occur, which could adversely impact our ability to meet our desired clinical development and any future commercialization timelines. Although we carefully manage our relationships with our suppliers and vendors, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not harm our business. We face competition from entities that have developed or may develop therapeutic candidates for our target disease indications, including companies developing novel treatments and technology platforms based on modalities and technology similar to ours. If these companies develop technologies, including delivery technologies, or therapeutic candidates more rapidly than we do or their technologies are more effective, our ability to develop and successfully commercialize therapeutic candidates may be adversely affected. The development and commercialization of therapeutic candidates is highly competitive. We compete with a number of multinational pharmaceutical companies and specialized biotechnology companies, as well as technology being developed at universities and other research institutions. Our competitors have developed, are developing or will develop therapeutic candidates and processes competitive with our therapeutic candidates. Competitive therapeutic treatments include those that have already been approved and accepted by the medical community and any new treatments that enter the market. We believe that a significant number of therapeutics are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may try to develop therapeutic candidates. There is intense and rapidly evolving competition in the biotechnology, pharmaceutical and oligonucleotide therapeutics fields. While we believe that our SNA technology, its associated intellectual property and our scientific and technical know-how give us a competitive advantage in this space, competition from many sources remains. Our competitors include larger and better-funded pharmaceutical, biotechnology and oligonucleotide therapeutics companies. Moreover, we also compete with current and future therapeutics developed at universities and other research institutions. We are aware of several companies that are developing oligonucleotide delivery platforms and oligonucleotide-based therapeutics. These competitors include Ionis Pharmaceuticals, Inc., Alnylam Pharmaceuticals, Inc., Dicerna Pharmaceuticals, Inc., Arbutus Biopharma Corp., Wave Life Sciences Ltd., Arrowhead Pharmaceuticals, Inc., ProQR Therapeutics N.V., Stoke Therapeutics, Inc., Neubase Therapeutics, Inc., Idera Pharmaceuticals, Inc., Avidity Biosciences, Dyne Therapeutics, Inc., Atalanta Therapeutics, Inc., PepGen, Inc. and others. These and other competitors compete with us in recruiting scientific and managerial talent, and for funding from pharmaceutical companies. Our success will partially depend on our ability to develop and protect therapeutics that are safer and more effective than competing therapeutics. Our commercial opportunity and success will be reduced or eliminated if competing therapeutics are safer, more effective, or less expensive than the therapeutics we develop. If our therapeutic candidates are approved for the indications we are currently pursuing, they will compete with a range of therapeutic treatments that are either in development or currently marketed. With respect to immunogenic cancers such as melanoma, the most common treatments are chemotherapeutic compounds, radiation therapy and now immunotherapeutic antibodies such as ipilimumab, atezolizumab, pembrolizumab and others. Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we do. If we successfully obtain approval for any therapeutic candidate, we will face competition based on many different factors, including the safety and effectiveness of our therapeutics, the ease with which our therapeutics can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these therapeutics, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing therapeutics could present superior treatment alternatives, including by being more effective, safer, less expensive or marketed and sold more effectively than any therapeutics we may develop. Competitive therapeutics may make any therapeutics we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our therapeutic candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan. The market may not be receptive to our therapeutic candidates based on a novel therapeutic modality, and we may not generate any future revenue from the sale or licensing of therapeutic candidates. Even if approval is obtained for a therapeutic candidate, we may not generate or sustain revenue from sales of the product due to factors such as whether the product can be sold at a competitive cost and otherwise accepted in the market. The therapeutic candidates that we are developing are based on our SNA technology. Market participants with significant influence over acceptance of new treatments, such as physicians and third-party payors, may not adopt a treatment based on SNA technology, and we may not be able to convince the medical community and third-party payors to accept and use, or to provide favorable reimbursement for any therapeutic candidates developed by us or any current or future collaborators. Market acceptance of our therapeutic candidates will depend on, among other factors: • the timing of our receipt of any marketing and commercialization approvals; • the terms of any approvals and the countries in which approvals are obtained; • the safety and efficacy of our therapeutic candidates; • the prevalence and severity of any adverse side effects associated with our therapeutic candidates; • limitations or warnings contained in any labeling approved by the FDA or other regulatory authority; • relative convenience and ease of administration of our therapeutic candidates; • the willingness of patients to accept any new methods of administration; • the success of our physician education programs; • the availability of adequate government and third-party payor reimbursement; • the pricing of our products, particularly as compared to alternative treatments; and • availability of alternative effective treatments for indications our therapeutic candidates are intended to treat and the relative risks, benefits and costs of those treatments. With our focus on SNAs, these risks may increase to the extent the space becomes more competitive or less favored in the commercial marketplace. Additional risks apply in relation to any disease indications we may pursue which are classified as rare diseases and allow for orphan drug designation by regulatory agencies in major commercial markets, such as the U.S., Europe and Japan. Because of the small patient population for a rare disease, if pricing is not approved or accepted in the market at an

appropriate level for an approved product with orphan drug designation, such therapeutic may not generate enough revenue to offset costs of development, manufacturing, marketing and commercialization despite any benefits received from the orphan drug designation, such as market exclusivity, assistance in clinical trial design or a reduction in user fees or tax credits related to development expense. Market size is also a variable in disease indications not classified as rare. Our estimates regarding potential market size for any indication may be materially different from what we discover to exist at the time we commence commercialization, if any, for a therapeutic, which could result in significant changes in our business plan and have a material adverse effect on our business, financial condition, results of operations and prospects. If a therapeutic candidate that has orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the therapeutic candidate is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same therapeutic candidate for the same indication, except in very limited circumstances, for seven years. Orphan drug exclusivity, however, could also block the approval of one of our therapeutic candidates for seven years if a competitor obtains approval of the same therapeutic candidate as defined by the FDA or if our therapeutic candidate is determined to be contained within the competitor' s therapeutic candidate for the same indication or disease. As in the U. S., we may apply for designation of a therapeutic candidate as an orphan drug for the treatment of a specific indication in the European Union before the application for marketing authorization is made. Sponsors of orphan drugs in the European Union can enjoy economic and marketing benefits, including up to ten years of market exclusivity for the approved indication. During such period, marketing applications for similar medicinal products will not be accepted, unless certain exceptions apply. In the EU, a " similar medicinal product " is a medicinal product containing a similar active substance or substances as contained in a currently authorized orphan medicinal product, and which is intended for the same therapeutic indication. Any inability to attract and retain qualified key management and technical personnel would impair our ability to implement our business plan. Our success largely depends on the continued service of key management and other specialized personnel, including Matthias G. Schroff, Ph. D., our Chief Executive Officer. In connection with the management changes resulting from our December 2021 restructuring activities, David A. Giljohann, Ph. D., our former Chief Technology Officer (and previously our Chief Executive Officer) and Douglas E. Feltner, M. D., our former Chief Medical Officer, are no longer employees of the Company. The loss of one or more members of our management team or other key employees or advisors could delay our research and development programs or clinical trials and materially harm our business, financial condition, results of operations and prospects. The relationships that our key managers have cultivated within our industry make us particularly dependent upon their continued employment with us. We are dependent on the continued service of our technical personnel because of the highly technical nature of our therapeutic candidates and our technology and the specialized nature of the regulatory approval process. Because our management team and key employees are not obligated to provide us with continued service, they could terminate their employment with us at any time without penalty. We do not maintain key person life insurance policies on any of our management team members or key employees. Our future success will depend in large part on our continued ability to attract and retain highly qualified scientific, technical and management personnel, as well as personnel with expertise in clinical testing, manufacturing, governmental regulation and commercialization. We face competition for personnel from other companies, universities, public and private research institutions, government entities and other organizations. We may increase the size of our organization, and we may experience difficulties in managing growth. As of December 31, 2021, we had 47 employees. As our development and commercialization plans and strategies develop, and as we further develop as a public company, we may need additional managerial, operational, financial and other personnel, including personnel to support our product development and planned future commercialization efforts. Future growth will impose significant added responsibilities on members of management, including: • identifying, recruiting, integrating, maintaining and motivating additional employees; • managing our internal development efforts effectively, including the clinical, FDA and EMA review processes for our product candidates; and • improving our operational, financial and management controls, reporting systems and procedures. Our future financial performance and our ability to commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day- to- day activities in order to devote a substantial amount of time to managing these growth activities. If we are not able to effectively expand our organization by hiring new employees, we may not be able to successfully implement the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals. If any of our therapeutic candidates are approved for marketing and commercialization and we are unable to develop sales, marketing and distribution capabilities on our own or enter into agreements with third parties to perform these functions on acceptable terms, we will be unable to successfully commercialize any such future therapeutics. We currently have no sales, marketing or distribution capabilities or experience. If any of our therapeutic candidates is approved, we will need to develop internal sales, marketing and distribution capabilities to appropriately commercialize such therapeutics, which would be expensive and time- consuming, or enter into collaborations with third parties to perform these services. If we decide to market our approved therapeutics directly, we will need to commit significant financial and managerial resources to develop a marketing and sales force with technical expertise and supporting distribution, administration and compliance capabilities. If we rely on third parties with such capabilities to market our approved therapeutics or decide to co- promote therapeutics with collaborators, we will need to establish and maintain compliant marketing and distribution arrangements with third parties, and there can be no assurance that we will be able to enter into such arrangements on acceptable terms or at all. In entering into third- party marketing or distribution arrangements, any revenue we receive will depend upon the efforts of the third parties and there can be no assurance that such third parties will establish adequate sales and distribution capabilities or be successful in gaining market acceptance of any approved therapeutic. If we are not successful in commercializing any therapeutic approved in the future, either on our own or through third parties, our business, financial condition, results of operations and prospects could be materially and adversely affected. If we fail to comply with U. S. or foreign regulatory

requirements, regulatory authorities could withhold marketing or commercialization approvals, limit or withdraw any marketing or commercialization approvals we may receive and subject us to other penalties that could materially harm our business. We and our therapeutic candidates, as well as our suppliers, contract manufacturers, distributors, and contract testing laboratories are subject to extensive regulation by governmental authorities in the European Union, the U. S., and other countries, with the regulations differing from country to country. If we or current or future collaborators, manufacturers or service providers fail to comply with applicable requirements, these regulatory authorities could refuse to issue necessary approvals for marketing and commercialization. Even if we receive marketing and commercialization approval of a therapeutic candidate, we and our third-party service providers will be subject to continuing regulatory requirements, including a broad array of regulations related to establishment registration and product listing, manufacturing processes, risk management measures, quality and pharmacovigilance systems, pre- and post- approval clinical data, labeling, advertising and promotional activities for such therapeutic, record keeping, distribution, and import and export of therapeutics for any therapeutic for which we obtain marketing approval. We are required to submit safety and other post market information and reports and are subject to continuing regulatory review, including in relation to adverse patient experiences with the therapeutic and clinical results that are reported after a therapeutic is made commercially available, both in the U. S. and any foreign jurisdiction in which we seek regulatory approval. The FDA and certain foreign regulatory authorities, such as the EMA, have significant post- market authority, including the authority to require labeling changes based on new safety information and to require post- market studies or clinical trials to evaluate safety risks related to the use of a therapeutic or to require withdrawal of the therapeutic from the market. The FDA also has the authority to require a Risk Evaluation and Mitigation Strategies, or REMS, plan either before or after approval, which may impose further requirements or restrictions on the distribution or use of an approved therapeutic. The EMA now routinely requires risk management plans, or RMPs, as part of the marketing authorization application process, and such plans must be continually modified and updated throughout the lifetime of the product as new information becomes available. In addition, for nationally authorized medicinal products, the relevant governmental authority of any European Union member state can request an RMP whenever there is a concern about the risk / benefit balance of the product. The manufacturer and manufacturing facilities we use to make a future therapeutic, if any, will also be subject to periodic review and inspection by the FDA and other regulatory agencies, including for continued compliance with cGMP requirements. The discovery of any new or previously unknown problems with our third- party manufacturers, manufacturing processes or facilities may result in restrictions on the therapeutic, manufacturer or facility, including withdrawal of the therapeutic from the market. If we rely on third- party manufacturers, we will not have control over compliance with applicable rules and regulations by such manufacturers. Any product promotion and advertising will also be subject to regulatory requirements and continuing regulatory review. Although a physician may prescribe products for off- label use since the FDA and other regulatory agencies do not regulate a physician' s choice of drug treatment made in the physician' s independent medical judgment, they do restrict promotional communications from companies or their sales force with respect to off- label uses of products for which marketing clearance has not been issued. Companies may only share truthful and not misleading information that is otherwise consistent with a product' s FDA approved labeling. If we or our future collaborators, manufacturers or service providers fail to comply with applicable continuing regulatory requirements in the U. S. or foreign jurisdictions in which we seek to market our therapeutics, we or they may be subject to, among other things, fines, warning and untitled letters, clinical holds, delay or refusal by the FDA or foreign regulatory authorities to approve pending applications or supplements to approved applications, suspension, refusal to renew or withdrawal of regulatory approval, recalls, seizures or administrative detention of products, refusal to permit the import or export of therapeutics, operating restrictions, inability to participate in government programs including Medicare and Medicaid, and total or partial suspension of production or distribution, injunction, restitution, disgorgement, debarment, civil and criminal penalties and criminal prosecution. Price controls imposed in foreign markets may adversely affect our future profitability. In some countries, particularly member states of the European Union, the pricing of prescription drugs is subject to governmental control at the national level, and in some cases also at the regional level. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a therapeutic. 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 and reimbursement 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. In some countries, we or current or future collaborators may be required to conduct a clinical trial or other studies that compare the cost- effectiveness of our SNA therapeutic candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third- party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any therapeutic candidate approved for marketing is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, financial condition, results of operations or prospects could be adversely affected. Our business entails a significant risk of product liability and our inability to obtain sufficient insurance coverage could have a material adverse effect on our business, financial condition, results of operations or prospects. Our business exposes us to significant product liability risks inherent in the development, testing, manufacturing and marketing of therapeutic treatments. Product liability claims could delay or prevent completion of our development programs. If we succeed in marketing therapeutics, such claims could result in an investigation by certain regulatory authorities, such as the FDA or foreign regulatory authorities, of the safety and effectiveness of our therapeutics, our manufacturing processes and facilities or our marketing programs and potentially a recall of our therapeutics or more serious enforcement action, limitations on the approved indications for which they may be used or suspension or withdrawal of approvals. Regardless of the merits or eventual outcome, liability claims may also result in decreased demand for our therapeutics, injury to our reputation, costs to defend the

related litigation, a diversion of management' s time and our resources, substantial monetary awards to trial participants or patients and a decline in our stock price. We currently have product liability insurance that we believe is appropriate for our stage of development and may need to obtain higher levels of product liability insurance prior to marketing any of our therapeutic candidates. Any insurance we have or may obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could have a material adverse effect on our business. Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements which could have an adverse effect on our business. We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include, but is not limited to, intentional failures to comply with FDA, the Centers for Medicare & Medicaid Services, or CMS, the Department of Health and Human Services, or HHS, Office of Inspector General, or OIG, or other agency regulations, applicable laws, regulations, guidance or codes of conduct set by foreign governmental authorities or self- regulatory industry organizations, or provide accurate information to any governmental authorities, such as the FDA, comply with manufacturing standards we may establish, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. For example, on November 9, 2021, the Audit Committee of our Board of Directors was notified of a claim made by a former Company senior researcher regarding alleged improprieties that researcher claims to have committed with respect to our XCUR- FXN preclinical program for the treatment of Friedreich' s ataxia. The Audit Committee retained external counsel to conduct an internal investigation of the claim. Based on the results of outside counsel' s investigation, the Audit Committee of our Board of Directors and we concluded that the subject matters under investigation did not have a material adverse impact on our financial condition or results of operations and did not require any change in our financial statements. Following our report of the results of the investigation, a securities class action lawsuit was filed against us and our former officers. In addition, a derivative lawsuit was filed against us as a nominal defendant, and certain of our current and former officers and directors. These and any future investigations or lawsuits may adversely affect our business, financial condition, results of operations and cash flows. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws, regulations, guidance and codes of conduct intended to prevent fraud, kickbacks, self- dealing and other abusive practices. These laws, regulations, guidance and codes of conduct may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions, including, fines, debarment, or disqualification of those employees from participation in certain government- regulated activities, and serious harm to our reputation. This could include violations of the U. S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, other U. S. federal and state law, and requirements of non- U. S. jurisdictions, including the European Union Data Protection Directive. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, regulations, guidance or codes of conduct. For example, a derivative lawsuit was filed against us and certain of our current and former officers and directors due to a claim made by a former Company senior researcher regarding alleged improprieties as discuss above. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including exclusion from participation in the U. S. federal healthcare programs, the imposition of significant fines or other sanctions. Compliance with governmental regulations regarding the treatment of animals used in research could increase our operating costs, which would adversely affect the commercialization of our technology. The Animal Welfare Act, or AWA, is the federal law that covers the treatment of certain animals used in research. Currently, the AWA imposes a wide variety of specific regulations that govern the humane handling, care, treatment and transportation of certain animals by producers and users of research animals, most notably relating to personnel, facilities, sanitation, cage size, and feeding, watering and shipping conditions. Third parties with whom we contract are subject to registration, inspections and reporting requirements under the AWA. Furthermore, some states have their own regulations, including general anti- cruelty legislation, which establish certain standards in handling animals. Comparable rules, regulations, and or obligations exist in many foreign jurisdictions. If we or our contractors fail to comply with regulations concerning the treatment of animals used in research, we may be subject to fines and penalties and adverse publicity, and our operations could be adversely affected. Our internal computer systems, or those of our CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our therapeutic development programs. Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such events could cause interruptions of our operations. For instance , the loss of preclinical study or clinical trial data involving our therapeutic candidates could result in delays in our development and regulatory filing efforts and significantly increase our costs. In addition , theft or other exposure of data may interfere with our ability to protect our intellectual property, trade secrets, and other information critical to our operations. We can provide no assurances that certain sensitive and proprietary information relating to one or more of our therapeutic candidates has not been, or will not in the future be, compromised. Although we have invested resources to enhance the security of our computer systems, there can be no assurances we will not experience additional unauthorized intrusions into our computer systems, or those of our CROs and other contractors and consultants, that we will successfully detect future unauthorized intrusions in a timely manner, or that future unauthorized intrusions will not result in material adverse effects on our financial condition, reputation, or business prospects. Payments related to the elimination of ransomware may materially affect our financial condition and results of

operations. Certain data breaches must also be reported to affected individuals and the government, and in some cases to the media, under provisions of HIPAA, as amended by HITECH, other U. S. federal and state law, and requirements of non- U. S. jurisdictions, including the European Union Data Protection Directive. Financial penalties may also apply in some data breaches where noncompliance with the applicable law is identified. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the development of our therapeutic candidates could be delayed ~~. If we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected. Our research, development and manufacturing involve the use of hazardous materials and various chemicals. We maintain quantities of various flammable and toxic chemicals in our facilities in Chicago, Illinois that are required for our research, development and manufacturing activities. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. We believe our procedures for storing, handling and disposing these materials in our Chicago facilities comply with the relevant guidelines of Chicago, the state of Illinois, and the Occupational Safety and Health Administration of the U. S. Department of Labor. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards mandated by applicable regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood- borne pathogens and the handling of animals and biohazardous materials. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of these materials, 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 connection with our storage or disposal of biological or hazardous materials. Additional federal, state and local laws and regulations affecting our operations may be adopted in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate, any of these laws or regulations~~ . Our information technology systems could face serious disruptions that could adversely affect our business. Our information technology and other internal infrastructure systems, including corporate firewalls, servers, documents storage systems, backup systems, leased lines and connection to the Internet, face the risk of systemic failure that could disrupt our operations. A significant disruption in the availability of our information technology and other internal infrastructure systems could cause interruptions and delays in our **operations** ~~research and development work~~ . Our business and operations could suffer in the event of system failures or unauthorized or inappropriate use of or access to our information technology systems. We are increasingly dependent on our information technology systems and infrastructure for our business. We collect, store and transmit sensitive information including intellectual property, proprietary business information and personal information in connection with business operations. The secure maintenance of this information is critical to our operations and business strategy. Some of this information could be an attractive target of criminal attack or unauthorized access and use by third parties with a wide range of motives and expertise, including organized criminal groups, " hacktivists, " patient groups, disgruntled current or former employees and others. Cyber-attacks are of ever- increasing levels of sophistication, and despite our security measures, our information technology systems and infrastructure may be vulnerable to such attacks or may be breached, including due to employee error or malfeasance. The pervasiveness of cybersecurity incidents in general and the risks of cyber- crime are complex and continue to evolve. Although we are making significant efforts to maintain the security and integrity of our information systems and are exploring various measures to manage the risk of a security breach or disruption, there can be no assurance that our security efforts and measures will be effective or that attempted security breaches or disruptions would not be successful or damaging. Despite the implementation of security measures, our internal computer systems and those of our employees, contractors and consultants are vulnerable to damage or interruption from computer viruses, unauthorized or inappropriate access or use, natural disasters, pandemics (including COVID- 19), terrorism, war, and telecommunication and electrical failures. Such events could cause interruption of our operations. For example, the loss or compromise of ~~pre- clinical~~ **preclinical** data for our therapeutic candidates could result in delays in our regulatory filings and development efforts, as well as delays in the commercialization of our products, and significantly increase our costs. To the extent that any disruption, security breach or unauthorized or inappropriate use or access to our systems were to result in a loss of or damage to our data, or inappropriate disclosure of confidential or proprietary information, including but not limited to patient, employee or vendor information, we could incur notification obligations to affected individuals and government agencies, liability, including potential lawsuits from patients, collaborators, employees, stockholders or other third parties and liability under foreign, federal and state laws that protect the privacy and security of personal information, and the development and potential commercialization of our therapeutic candidates could be delayed. Existing insurance arrangements may not provide protection for the costs that may arise from such loss or damage. Any long- term disruption in our ability to access our information technology systems could have a material adverse effect on our operations, our business, results of operations and stock price. Increasing scrutiny and changing expectations from customers, regulators, investors, and other stakeholders with respect to our environmental, social and governance practices may impose additional costs on us or expose us to new or additional risks. Companies are facing increasing scrutiny from customers, regulators, investors, and other stakeholders related to their environmental, social and governance practices. Investor advocacy groups, investment funds and influential investors are also increasingly focused on these practices, especially as they relate to the environment, health and safety, supply chain management, diversity and human rights. Failure to adapt to or comply with regulatory requirements or investor or stakeholder expectations and standards could negatively impact our reputation and the price of our ordinary shares. Any of the factors mentioned above, or the perception that we or our suppliers, or contract manufacturers or collaborators have not responded appropriately to the growing concern for such issues, regardless of whether we are legally required to do so, may damage our reputation and have a material adverse effect on

our business, financial condition, results of operations cash flows and / or ordinary share price. Natural disasters or other unexpected events may disrupt our operations, adversely affect our results of operations and financial condition, and may not be covered by insurance. The occurrence of one or more unexpected events, including fires, tornadoes, tsunamis, hurricanes, earthquakes, floods, and other forms of severe hazards in the United States or in other countries in which we or our suppliers or manufacturers operate or are located could adversely affect our operations and financial performance. These types of unexpected events could result in physical damage to and complete or partial closure of one or more of the manufacturing facilities operated by our contract manufacturers, or the temporary or long- term disruption in the supply of products, and / or disruption of our ability to deliver products to customers. Further, the long- term effects of climate change on general economic conditions and the pharmaceutical manufacturing and distribution industry in particular are unclear, and changes in the supply, demand or available sources of energy and the regulatory and other costs associated with energy production and delivery may affect the availability or cost of goods and services, including natural resources, necessary to run our businesses. Existing insurance arrangements may not provide protection for the costs that may arise from such events, particularly if such events are catastrophic in nature or occur in combination. Any long- term disruption in our ability to service our customers from one or more distribution centers or outsourcing facilities could have a material adverse effect on our operations, our business, results of operations and stock price. Our current operations are concentrated in one location and any events affecting this location may have material adverse consequences. Our current operations are located in our facilities situated in Chicago, Illinois. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, power shortage, telecommunication failure or other natural or man- made accidents or incidents that result in us being unable to fully utilize the facilities, may have a material adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our therapeutic candidates or interruption of our business operations. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption may have a material adverse effect on our business, financial position, results of operations and prospects. The investment of our cash, cash equivalents and fixed income marketable securities is subject to risks which may cause losses and affect the liquidity of these investments. As of December 31, ~~2021~~ **2022**, we had $ ~~43~~ **9**. 8 million in cash, cash equivalents, and restricted cash ~~and $ 4. 5 million in short- term investments~~. We ~~historically have invested~~ -- **invest our** excess cash in ~~certificates of deposit~~ **U. S. government** or **U. S. government agency** ~~money market mutual funds that invest in~~ securities ~~issued or guaranteed by the U. S. government or U. S. government agencies~~, floating rate and variable rate demand notes of U. S. and foreign corporations, and commercial paper. ~~During the fourth quarter of 2019, we have made direct purchases, and expect to continue to make direct purchases of, U. S. government or U. S. government agency securities, floating rate and variable rate demand notes of U. S. and foreign corporations, and commercial paper.~~ These investments are subject to general credit, liquidity, market and interest rate risks, including potential future impacts ~~similar to the impact of U~~ **from economic, capital market or bank instability**. ~~S. sub- prime mortgage defaults~~ **We may from time to time have balances in bank accounts** that **are in excess** ~~have affected various sectors~~ of ~~the financial markets~~ **insured deposit limits,** and ~~caused credit and liquidity issues~~ **could be subject to risks of bank failures**. We may realize losses in the fair value of these investments, an inability to access cash in these investments for a potentially meaningful period, or a complete loss of these investments, which would have a negative effect on our financial statements. In addition, should our investments cease paying or reduce the amount of interest paid to us, our interest income would suffer. The market risks associated with our investment portfolio may have an adverse effect on our results of operations, liquidity and financial condition. We have incurred significant losses since our..... and development programs and commercialization efforts. If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired. We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, the Sarbanes- Oxley Act of 2002, or Sarbanes- Oxley Act, and the rules and regulations of The Nasdaq Capital Market. Pursuant to Section 404 of the Sarbanes- Oxley Act, or Section 404, we are ~~now~~ required to perform system and process evaluation and testing of our internal control over financial reporting to allow our management to report on the effectiveness of our internal control over financial reporting. However, while we remain **a non- accelerated filer or** an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. Further, we may in the future discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Moreover, our internal controls over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system' s objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected. Moreover, we are aware that the remote working arrangements implemented in connection with the COVID- 19 pandemic potentially present new areas of risk, and we continue to carefully monitor any impact to our internal controls and procedures. **Our limited resources and recent reductions in force, as well as the turnover in our board of directors and the potential for future management changes, present significant continuity risk and could impact our ability to maintain effective internal control over financial reporting.** If we are unable to assert that our internal control over financial reporting is effective, investors could lose confidence in the reliability of our financial statements, the market price of our stock could

decline and we could be subject to sanctions or investigations by The Nasdaq Capital Market, the SEC or other regulatory authorities. Risks Related to Intellectual Property ~~If we are not able to obtain and enforce patent protection for our technology or therapeutic candidates, development and commercialization of our therapeutic candidates may be adversely affected. Our success depends in part on our ability to obtain and maintain patents and other forms of intellectual property rights, including in-licenses of intellectual property rights of others, for our therapeutic candidates, methods used to manufacture our therapeutic candidates and methods for treating patients using our therapeutic candidates, as well as our ability to preserve our trade secrets, to prevent third parties from infringing upon our proprietary rights and to operate without infringing upon the proprietary rights of others. As of December 31, 2021, our patent portfolio consists of over 90 issued patents and allowed patent applications and over 100 pending patent applications. We may not be able to apply for patents on certain aspects of our therapeutic candidates in a timely fashion or at all. Our existing issued and granted patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing therapeutics and technology. There is no guarantee that any of our pending patent applications will result in issued or granted patents, that any of our issued or granted patents will not later be found to be invalid or unenforceable or that any issued or granted patents will include claims that are sufficiently broad to cover our therapeutic candidates or to provide meaningful protection from our competitors. Moreover, the patent position of pharmaceutical and biotechnology companies can be highly uncertain because it involves complex legal and factual questions. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our current and future proprietary technology and therapeutic candidates are covered by valid and enforceable patents or are effectively maintained as trade secrets. If third parties disclose or misappropriate our proprietary rights, it may materially and adversely impact our position in the market. The U. S. Patent and Trademark Office, or USPTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case. The standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and pharmaceutical patents. As such, we do not know the degree of future protection that we will have on our proprietary therapeutics and technology. While we will endeavor to try to protect our therapeutic candidates with intellectual property rights such as patents, as appropriate, the process of obtaining patents is time- consuming, expensive and sometimes unpredictable. In addition, there are numerous recent changes to the patent laws and proposed changes to the rules of the USPTO, which may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, the Leahy- Smith America Invents Act enacted in 2011 involves significant changes in patent legislation. The U. S. Supreme Court has ruled on several patent cases in recent years, some of which cases either narrow the scope of patent protection available in certain circumstances or weaken the rights of patent owners in certain situations. The 2013 decision by the Supreme Court in Association for Molecular Pathology v. Myriad Genetics, Inc. precludes a claim to a nucleic acid having a stated nucleotide sequence that is identical to a sequence found in nature and unmodified. We currently are not aware of an immediate impact of this decision on our patents or patent applications because we are developing oligonucleotide therapeutics which contain modifications that we believe are not found in nature. However, this decision has yet to be clearly interpreted by courts and by the USPTO. We cannot assure you that the interpretations of this decision or subsequent rulings will not adversely impact our patents or patent applications. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U. S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that may weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. Once granted, patents may remain open to opposition, interference, re- examination, post- grant review, inter partes review, nullification or derivation action in court or before patent offices or similar proceedings for a given period after allowance or grant, during which time third parties can raise objections against such initial grant. In the course of such proceedings, which may continue for a protracted period of time, the patent owner may be compelled to limit the scope of the allowed or granted claims thus attacked, or may lose the allowed or granted claims altogether. In addition, there can be no assurance that: • Others will not or may not be able to make, use or sell compounds that are the same as or similar to our therapeutic candidates but that are not covered by the claims of the patents that we own or license. • We or our licensors, or any current or future collaborators, are the first to make the inventions covered by each of our issued patents and pending patent applications that we own or license. • We or our licensors, or any current or future collaborators, are the first to file patent applications covering certain aspects of our inventions. • Others will not independently develop similar or alternative technologies or duplicate any of our technology without infringing our intellectual property rights. • A third- party will not challenge our patents and, if challenged, a court may not hold that our patents are valid, enforceable and infringed. • Any issued patents that we own or have licensed will provide us with any competitive advantages, or will not be challenged by third parties. • We will develop additional proprietary technologies that are patentable. • The patents of others will not have an adverse effect on our business. • Our competitors will not conduct research and development activities in countries where we lack enforceable patent rights and then use the information learned from such activities to develop competitive therapeutics for sale in our major commercial markets. Patent term may be inadequate to protect our competitive position on our future therapeutics for an adequate amount of time. Given the amount of time required for the development, testing and regulatory review of new therapeutic candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. We expect to seek extensions of patent terms in the U. S. and, if available, in other countries where we have patents covering our product candidates. In the U. S., the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years as compensation for patent term lost~~

~~during product development and the FDA regulatory review process. However, the patent term extension or restoration cannot extend the remaining term of a patent beyond a total of 14 years from the approval date of the product candidate. Only one patent applicable to an approved product candidate is eligible for the extension and the application for extension must be made prior to expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restorations of patent term for some of our currently owned or licensed patents to add patent life beyond their current expiration dates. However, the applicable authorities, including the FDA and the USPTO in the U. S., and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.~~ We currently license patent rights from Northwestern University ~~and may in the future license patent rights from other third- party owners or licensees~~ . If Northwestern University **does** ~~or such other owners or licensees do~~ not properly or successfully obtain, maintain or enforce the patents underlying such licenses, or if they retain or license to others any competing rights, our competitive position and business prospects may be adversely affected. We ~~do, and will continue to,~~ rely on intellectual property rights licensed from third parties to protect our technology. We are a party to a number of licenses that give us rights to third-party intellectual property that is necessary or useful for our business. In particular, we have a license from Northwestern University, which provides us the exclusive worldwide right under certain patents and patent applications owned by Northwestern University to exploit therapeutics and processes using nanoparticles, nanotechnology, microtechnology and nanomaterial- based constructs as therapeutics or accompanying therapeutics as a means of administration **. To the extent we are successful in selling, licensing or otherwise generating value from our historical assets, it would depend significantly on the value of the rights licenses from Northwestern** . We may also license additional third- party intellectual property in the future. Our success will depend in part on the ability of our licensors to obtain, maintain and enforce patent protection for our licensed intellectual property, and in particular, for those patents to which we have secured exclusive rights. Our licensors may not successfully prosecute the patent applications licensed to us. Even if patents issue or are granted, our licensors may fail to maintain these patents, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue litigation less aggressively than we would. Further, we may not obtain exclusive rights, which would allow for third parties to develop competing therapeutics. Without protection for, or exclusive rights to, the intellectual property we license, other companies might be able to offer substantially identical therapeutics for sale, which could adversely affect our competitive business position and harm our business prospects. ~~In addition, the U. S. government has certain rights to the inventions covered by the patent rights licensed to us by third parties and Northwestern University, as an academic research and medical center, has reserved the right to practice the patent rights it has licensed to us (i) for research, teaching and / or other educationally related purposes (including the right to distribute materials for such purposes) and (ii) for use in the field of diagnostics (including theradiagnostics) and in any field other than the field of use licensed to us. We currently have Collaboration, Option and License Agreements with Ipsen and AbbVie, and may in the future have additional Collaboration, Option and License Agreements with other third- parties. If Ipsen or AbbVie, or such other licensees do not properly or successfully collaborate to research and develop SNAs, our competitive position and business prospects may be adversely affected. We do, and will continue to, rely on collaboration with third parties to develop our technology. We are a party to a number of licenses that provide rights to a third-party that is necessary or useful for our business. In particular, we have a Collaboration, Option and License Agreement with Ipsen, to collaborate together to research and develop SNAs. We also have a Collaboration, Option and License Agreement with AbbVie, to collaborate together to research, develop, and manufacture new nucleic acid therapeutics focusing on certain hair loss disorders. We may also collaborate with additional third- parties in the future. Our success will depend in part on the ability of our licensees to research and develop SNAs based on our existing intellectual property. Without successful collaboration to research and develop SNAs, other companies might be able to offer substantially identical therapeutics for sale, which could adversely affect our competitive business position and harm our business prospects. Other companies or organizations may challenge our or our licensors' patent rights or may assert patent rights that prevent us from developing and commercializing our therapeutic candidates. Oligonucleotide and SNA- based therapeutics are a relatively new scientific field. We have obtained grants and issuances of SNA therapeutic patents and have licensed many of these patents from a third- party on an exclusive basis for therapeutics applications. The issued patents and pending patent applications in the U. S. and in key markets around the world that we own or license claim many different methods, compositions and processes relating to the discovery, development, manufacture and commercialization of SNA therapeutics. Specifically, we own and have licensed a portfolio of patents, patent applications and other intellectual property covering SNA compositions of matter as well as their methods of use. As the field of SNA therapeutics matures, patent applications are being processed by national patent offices around the world. There is uncertainty about which patents will issue, and, if they do, as to when, to whom, and with what claims. In addition, third parties may attempt to invalidate our intellectual property rights. Even if our rights are not directly challenged, disputes could lead to the weakening of our intellectual property rights. Our defense against any attempt by third parties to circumvent or invalidate our intellectual property rights could be costly to us, could require significant time and attention of our management and could have a material adverse effect on our business and our ability to successfully compete. There are many issued and pending patents that claim aspects of oligonucleotide chemistry and modifications that we may need to apply to our SNA therapeutic candidates. There are also many issued patents that claim targeting genes or portions of genes that may be relevant for SNA therapeutics we wish to develop. Thus, it is possible that one or more organizations will hold patent rights to which we will need a license. If those organizations refuse to grant us a license to such patent rights on reasonable terms, we may not be able to market therapeutics or perform research and development or other activities covered by these patents. We may be unable to protect our intellectual property rights throughout the world. Obtaining a valid and enforceable issued or granted patent covering our~~

~~technology in the U. S. and worldwide can be extremely costly. In jurisdictions where we have not obtained patent protection, competitors may use our technology to develop their own therapeutics and, further, may export otherwise infringing therapeutics to territories where we have patent protection, but where it is more difficult to enforce a patent as compared to the U. S. Competitor therapeutics may compete with our future therapeutics in jurisdictions where we do not have issued or granted patents or where our issued or granted patent claims or other intellectual property rights are not sufficient to prevent competitor activities in these jurisdictions. The legal systems of certain countries, particularly certain developing countries, make it difficult to enforce patents and such countries may not recognize other types of intellectual property protection, particularly that relating to biotechnology and pharmaceuticals. This could make it difficult for us to prevent the infringement of our patents or marketing of competing therapeutics in violation of our proprietary rights generally in certain jurisdictions. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. We generally file a provisional patent application first, also known as a priority filing, at the USPTO. An international application under the Patent Cooperation Treaty, or PCT, is usually filed within twelve months after the priority filing. Based on the PCT filing, national and regional patent applications may be filed in the U. S., European Union, Japan, Australia and Canada and, depending on the individual case, also in any or all of, inter alia, China, India, South Korea, and Mexico. We have so far not filed for patent protection in all national and regional jurisdictions where such protection may be available. In addition, we may decide to abandon national and regional patent applications before grant or after grant by nonpayment of maintenance fees for the resulting patent. Finally, the grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications might in some jurisdictions be refused by the relevant registration authorities, while granted by others. It is also quite common that depending on the country, various scopes of patent protection may be granted on the same therapeutic candidate or technology. The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws in the U. S., and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. 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 from others in those jurisdictions. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many 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 with respect to any patents relevant to our business, our competitive position in the relevant jurisdiction may be impaired and our business and results of operations may be adversely affected.~~ We or our licensors, or any current or future strategic partners, may become subject to third- party claims or litigation alleging infringement of patents or other proprietary rights or seeking to invalidate patents or other proprietary rights, and we may need to resort to litigation to protect or enforce our patents or other proprietary rights, all of which could be costly, time consuming, delay or prevent the development and commercialization of our therapeutic candidates, or put our patents and other proprietary rights at risk. We or our licensors, or any current or future strategic partners, may be subject to third- party claims for infringement or misappropriation of patent or other proprietary rights. We are generally obligated under our license agreements to indemnify and hold harmless our licensors for damages arising from intellectual property infringement by us. If we or our licensors, or any current or future strategic partners, are found to infringe a third- party patent or other intellectual property rights, we could be required to pay damages, potentially including treble damages, if we are found to have willfully infringed. In addition, we or our licensors, or any current or future strategic partners, may choose to seek, or be required to seek, a license from a third- party, which may not be available on acceptable terms, if at all. Even if a license can be obtained on acceptable terms, the rights may be non- exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. If we fail to obtain a required license, we or any current or future collaborator may be unable to effectively market therapeutic candidates based on our technology, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. In addition, we may find it necessary to pursue claims or initiate lawsuits to protect or enforce our patent or other intellectual property rights. The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation would divert our management' s attention. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations. If we were to initiate legal proceedings against a third- party to enforce a patent covering one of our therapeutics or our technology, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the U. S., defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one or more of our therapeutics or certain aspects of our technology. Such a loss of patent protection could have a material adverse impact on our business. Patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without legally infringing our patents or other intellectual property rights. It is also possible that we have failed to identify relevant third- party patents or applications. For example, U. S. applications filed before November 29, 2000 and certain U. S. applications filed after that date

that will not be filed outside the U. S. remain confidential until patents issue. Patent applications in the U. S. and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our therapeutics or technology could have been filed by others without our knowledge. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our SNA technology, our therapeutics or the use of our therapeutics. Third- party intellectual property right holders may also actively bring infringement claims against us. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we are unable to successfully settle future claims on terms acceptable to us, we may be required to engage in or continue costly, unpredictable and time- consuming litigation and may be prevented from or experience substantial delays in marketing our therapeutics. If we fail in any such dispute, in addition to being forced to pay damages, we may be temporarily or permanently prohibited from commercializing any of our therapeutic candidates that are held to be infringing. We might, if possible, also be forced to redesign therapeutic candidates so that we no longer infringe the third- party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business. We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property. We may also be subject to claims that former employees or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distraction to management and other employees. If we fail to comply with our obligations under any license, collaboration or other agreements, we may be required to pay damages and could lose intellectual property rights that are necessary for developing and protecting our therapeutic candidates or we could lose certain rights to grant sublicenses. Our current licenses impose, and any future licenses we enter into are likely to impose, various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement, and other obligations on us. If we breach any of these obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and the licensor may have the right to terminate the license, which could result in us being unable to develop, manufacture and sell therapeutics that are covered by the licensed technology or could enable a competitor to gain access to the licensed technology. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor' s rights in such unlicensed intellectual property. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future therapeutics, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in therapeutics that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize therapeutics, we may be unable to achieve or maintain profitability. ~~If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. In addition to seeking patent protection for certain aspects of our therapeutic candidates, we also consider trade secrets, including confidential and unpatented know- how important to the maintenance of our competitive position. We protect trade secrets and confidential and unpatented know- how, in part, by entering into non- disclosure and confidentiality agreements with parties who have access to such knowledge, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants that obligate them to maintain confidentiality and assign their inventions to us. 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 in the U. S. and certain foreign jurisdictions 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 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. Under the terms of the Northwestern University License Agreements, Northwestern University could publish research findings relating to the patent rights licensed to us by Northwestern University, which could have a material adverse effect on our business. We are also subject both in the U. S. and outside the U. S. to various regulatory schemes regarding requests for the information we provide to regulatory authorities, which may include, in whole or in part, trade secrets or confidential commercial information. While we are likely to be notified in advance of any disclosure of such information and would likely object to such disclosure, there can be no assurance that our challenge to the request would be successful. We may be subject to claims that we or our employees or consultants have wrongfully used or disclosed alleged trade secrets of our employees' or consultants' former employers or their clients. These claims may be costly to defend and if we do not successfully do so, we may be required to pay monetary damages and may lose valuable intellectual property rights or personnel. Many of our employees were previously employed at universities or pharmaceutical or biotechnology companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could hamper our ability to commercialize, or prevent us from commercializing, our therapeutic candidates, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to~~

management. If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected. Third parties may independently develop similar or superior technology. There can be no assurance that others will not independently develop, or have not already developed, similar or more advanced technologies than our technology; or that others will not design around, or have not already designed around, aspects of our technology and / or our trade secrets developed therefrom. If third parties develop technology similar or superior to our technology, or they successfully design around our current or future technology, our competitive position, business prospects, and results of operations could be materially and adversely affected. The intellectual property which we have licensed from Northwestern University was discovered through government funded programs and thus may be subject to federal regulations such as " march- in " rights, certain reporting requirements, and a preference for U. S. industry. Compliance with such regulations may limit our exclusive rights, subject us to expenditure of resources with respect to reporting requirements, and limit our ability to contract with non- U. S. manufacturers. We have licensed certain intellectual property from Northwestern University pursuant to the Northwestern University License Agreements. The Northwestern University License Agreements indicate that the rights licensed to us by Northwestern University are subject to the obligations to and the rights of the U. S. government, including those set forth in the Bayh- Dole Act of 1980, or Bayh- Dole Act. As a result, the U. S. government may have certain rights to intellectual property embodied in our current or future therapeutics based on the licensed Northwestern University intellectual property. These U. S. government rights in certain inventions developed under a government- funded program include a non- exclusive, non- transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U. S. government has the right to require us to grant exclusive, partially exclusive, or nonexclusive licenses to any of these inventions to a third- party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations, also referred to as " march- in rights. " While the U. S. government has sparingly used, and to our knowledge never successfully exercised, such march- in rights, any exercise of the march- in rights by the U. S. government could harm our competitive position, business, financial condition, results of operations, and prospects. If the U. S. government exercises such march- in rights, we may receive compensation that is deemed reasonable by the U. S. government in its sole discretion, which may be less than what we might be able to obtain in the open market. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the U. S. government requires that any therapeutics embodying any invention generated through the use of U. S. government funding be manufactured substantially in the U. S. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U. S. manufacturers may limit our ability to contract with non- U. S. therapeutic manufacturers for therapeutics covered by such intellectual property. Risks Related to Government Regulation We may be unable to obtain U. S. or foreign regulatory approval and, as a result, unable to commercialize our therapeutic candidates. Our therapeutic candidates are subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, packaging, advertising and promotion, pricing, marketing, sampling, and distribution of therapeutics. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process are required to be successfully completed in the U. S. and in many foreign jurisdictions before a new therapeutic can be marketed. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. It is possible that none of the therapeutic candidates we may develop will obtain the regulatory approvals necessary for us or any current or future collaborators to begin selling them. We have very limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA as well as foreign regulatory authorities, such as the EMA and European Union national competent authorities. The time required to obtain FDA and foreign regulatory approvals is unpredictable but typically takes many years following the commencement of clinical trials, depending upon the type, complexity and novelty of the therapeutic candidate. The standards that the FDA and its foreign counterparts use when regulating us are not always applied predictably or uniformly and can change. Any analysis we perform of data from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations, for example, from future legislation or administrative action, or from changes in the policy of the FDA or foreign regulatory authorities during the period of therapeutic development, clinical trials and regulatory review by the FDA or foreign regulatory authorities. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign laws, regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be. In addition, unfavorable changes in our industry or the global economy, including as a result of the COVID- 19 pandemic, could contribute to some of the events listed above and further impact our ability to progress our clinical trials, submit for marketing approval or commercialize our product candidates, if approved, as planned. Because the therapeutics we are developing may represent a new class of therapeutic, the FDA and its foreign counterparts have not yet established any definitive policies, practices or guidelines in relation to these therapeutics. While we believe the therapeutic candidates that we are currently developing are regulated as new drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, the FDA could decide to regulate them or other therapeutics we may develop as biologics under the Public Health

Service Act. The lack of policies, practices or guidelines may hinder or slow review by the FDA or foreign regulatory authorities of any regulatory filings that we may submit. Moreover, the FDA may respond to these submissions by defining requirements we may not have anticipated. Such responses could lead to significant delays in the clinical development of our therapeutic candidates. Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues from the particular therapeutic candidate for which we are seeking approval. Furthermore, any regulatory approval to market a therapeutic may be subject to limitations on the approved uses for which we may market the therapeutic or the labeling or other restrictions. Regulatory authorities also may impose requirements for costly post- marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the therapeutic. In addition, the FDA has the authority to require a REMS plan as part of a NDA or a Biologics License Application, or BLA, or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug or biologic, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe- use criteria and requiring treated patients to enroll in a registry. These limitations and restrictions may limit the size of the market for the therapeutic and affect coverage and reimbursement by third- party payors. We are also subject to numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third- party reimbursement. The foreign regulatory approval process varies among countries and may include all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities outside the U. S. and vice versa. Certain of our therapeutic candidates may require companion diagnostics in certain indications. Failure to successfully develop, validate and obtain regulatory clearance or approval for such tests could harm our product development strategy or prevent us from realizing the full commercial potential of our therapeutic candidates. Certain of our therapeutic candidates may require companion diagnostics to identify appropriate patients for those therapeutic candidates in certain indications. Companion diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities as a medical device and may require separate regulatory authorization prior to commercialization. We may rely on third parties for the design, development, testing and manufacturing of these companion diagnostics, the application for and receipt of any required regulatory authorization, and the commercial supply of these companion diagnostics. If these parties are unable to successfully develop companion diagnostics for these therapeutic candidates, or experience delays in doing so, the development of our therapeutic candidates may be adversely affected and we may not be able to obtain marketing authorization for these therapeutic candidates. Furthermore, our ability to market and sell, as well as the commercial success, of any of our therapeutic candidates that require a companion diagnostic will be tied to, and dependent upon, the receipt of required regulatory authorization and the continued ability of such third parties to make the companion diagnostic commercially available on reasonable terms in the relevant geographies. Any failure to develop, validate, obtain and maintain marketing authorization for a companion diagnostic and supply such companion diagnostic will harm our business, results of operations and financial condition. If we or current or future collaborators, manufacturers or service providers fail to comply with healthcare laws and regulations, we or they could be subject to enforcement actions, which could affect our ability to develop, market and sell our therapeutics and may harm our reputation. Although we do not currently have any products on the market, our current and future business operations may subject us to additional healthcare statutory and regulatory requirements and enforcement by the federal, state and foreign governments of the jurisdictions in which we conduct our business. Healthcare providers, including physicians and third- party payors play a primary role in the recommendation and prescription of any therapeutic candidates for which we obtain marketing approval. Our arrangements with third- party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research, market, sell or distribute our therapeutic candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include, but are not limited to, the following: • the U. S. federal Anti- Kickback Statute, which prohibits, among other things, persons and entities from soliciting, receiving, offering or providing remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, to induce either the referral of an individual for a healthcare item or service, or the purchasing or ordering of an item or service, for which payment may be made, in whole or in part, under a federal healthcare program, such as Medicare or Medicaid. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers, among others, on the other. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation; • the U. S. federal False Claims Act, which imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. For example, pharmaceutical companies have been prosecuted under the False Claims Act in connection with their alleged off- label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes, and allegedly providing free product to customers with the expectation that the customers would bill federal health care programs for the product. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act; • federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; • federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and / or discounts on approved products; • HIPAA includes a fraud and abuse provision sometimes referred to as the HIPAA All- Payor Fraud Law, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program (i. e., not just

federal healthcare programs), or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; similar to the federal Anti- Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation; • HIPAA, as amended by the HITECH, and its implementing regulations, which impose obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses and their business associates that perform certain services involving the use or disclosure of individually identifiable health information as well as their covered subcontractors, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions; • the federal Physician Payments Sunshine Act and the implementing regulations, also referred to as " Open Payments, " issued under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, which require that certain manufacturers of pharmaceutical and biological drugs reimbursable under Medicare, Medicaid, or the Children' s Health Insurance Program report to CMS all consulting fees, travel reimbursements, research grants, and other payments, transfers of value or gifts made to U. S.- licensed physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such a physician assistants and nurse practitioners), and U. S. teaching hospitals with limited exceptions, as well as ownership and investment interests held by physicians and their immediate family members; and • analogous state laws and regulations, such as, state anti- kickback and false claims laws potentially applicable to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non- governmental third- party payors, including private insurers; and some state laws require pharmaceutical companies to comply with the pharmaceutical industry' s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures, state and local laws that require the registration of pharmaceutical sales representatives, and state laws governing the privacy and security of personal data (including personal health information) in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and state transparency laws that require the reporting of certain pricing information; among other state laws. Ensuring that our future business arrangements with third- parties comply with applicable healthcare laws and regulations could involve substantial costs. If our operations are found to be in violation of any such requirements, we may be subject to penalties, including significant administrative, civil and / or criminal penalties, monetary damages, disgorgement, fines, imprisonment, additional integrity reporting requirements and regulatory oversight, the curtailment or restructuring of our operations, or exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, any of which could adversely affect our financial results. Although an effective compliance program can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management' s attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources. If we or current or future collaborators, manufacturers or service providers fail to comply with applicable federal, state or foreign laws or regulations, we could be subject to significant penalties and enforcement actions, which could affect our ability to develop, market and sell our therapeutics successfully and could harm our reputation and lead to reduced acceptance of our therapeutics by the market. These penalties and enforcement actions include, among others: • adverse regulatory inspection findings; • warning or untitled letters; • voluntary product recalls or public notification or medical product safety alerts to healthcare professionals; • restrictions on, or prohibitions against, marketing our therapeutics; • restrictions on, or prohibitions against, importation or exportation of our therapeutics; • suspension of review or refusal to approve pending applications or supplements to approved applications; • exclusion from participation in government- funded healthcare programs; • exclusion from eligibility for the award of government contracts for our therapeutics; • integrity oversight and reporting obligations; • FDA debarment; • suspension or withdrawal of therapeutic approvals; • seizures or administrative detention of therapeutics; • injunctions; and • civil and criminal penalties and fines. Any therapeutics we develop may become subject to unfavorable pricing regulations, third- party coverage and reimbursement practices or healthcare reform initiatives, thereby harming our business. The regulations that govern marketing approvals, pricing and reimbursement for new therapeutics vary widely from country to country. Some countries require approval of the sale price of a therapeutic before it can be marketed. In many countries, the pricing review period begins after marketing or therapeutic licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. Although we intend to monitor these regulations, our programs are currently in the early stages of development and we will not be able to assess the impact of price regulations for a number of years. As a result, we might obtain regulatory approval for a therapeutic in a particular country, but then be subject to price regulations that delay our commercial launch of the therapeutic and negatively impact the revenues we are able to generate from the sale of the therapeutic in that country. Patients who are prescribed therapeutics for the treatment of their conditions generally rely on third- party payors to reimburse all or part of the costs associated with their prescription drugs. There is significant uncertainty related to third- party payor coverage and reimbursement of newly approved therapeutics. Our ability to commercialize any therapeutics successfully also will depend in part on the extent to which coverage and reimbursement for these therapeutics and related treatments will be available from government health administration authorities, private health insurers and other organizations. However, there may be significant

delays in obtaining coverage for newly- approved therapeutics. Moreover, eligibility for coverage does not necessarily signify that a therapeutic will be reimbursed in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution costs. Also, interim payments for new therapeutics, if applicable, may be insufficient to cover our costs and may not be made permanent. Thus, even if we succeed in bringing one or more therapeutics to the market, these therapeutics may not be considered cost- effective, and the amount reimbursed for any therapeutics may be insufficient to allow us to sell our therapeutics on a competitive basis. Because our programs are in the early stages of development, we are unable at this time to determine their cost effectiveness or the likely level or method of reimbursement. Increasingly, the third- party payors who reimburse patients or healthcare providers, such as government and private insurance plans, are seeking greater upfront discounts, additional rebates and other concessions to reduce the prices for therapeutics. If the price we are able to charge for any therapeutics we develop, or the reimbursement provided for such therapeutics, is inadequate in light of our development and other costs, our return on investment could be adversely affected. We currently expect that some therapeutics we develop may need to be administered under the supervision of a physician on an outpatient basis. Under currently applicable U. S. law, certain therapeutics that are not usually self- administered (including injectable therapeutics) may be eligible for coverage under Medicare through Medicare Part B. Medicare Part B is part of original Medicare, the federal health care program that provides health care benefits to the aged and disabled, and covers outpatient services and supplies, including certain pharmaceutical products that are medically necessary to treat a beneficiary' s health condition. Specifically, Medicare Part B coverage may be available for eligible beneficiaries when the following, among other requirements, have been satisfied: • the product is reasonable and necessary for the diagnosis or treatment of the illness or injury for which the product is administered according to accepted standards of medical practice; • the product is typically furnished incident to a physician' s services; • the product has been approved by the FDA. Under the Medicaid Drug Rebate Statute, a manufacturer must participate in the Medicaid Drug Rebate Program in order to receive payment for its covered outpatient drugs under Medicare Part B (the Medicare program that generally covers physician- administered, outpatient drugs). In addition, manufacturers who participate in the Medicaid Drug Rebate Program are also required to (1) sign the Pharmaceutical Pricing Agreement and participate in the 340B Drug Pricing Program, and (2) sign the VA Master Agreement for inclusion of the manufacturer' s drugs on the Federal Supply Schedule, or FSS. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of HHS as a condition for states to receive federal matching funds for the manufacturer' s outpatient drugs furnished to Medicaid patients. Under the 340B Drug Pricing Program, the manufacturer must extend discounts to entities eligible to participate in the program. Average 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 therapeutics from countries where they may be sold at lower prices than in the U. S. Self- administered therapeutics are typically reimbursed under Medicare Part D, and therapeutics that are administered in an inpatient hospital setting are typically reimbursed under Medicare Part A under a bundled payment. On March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap for single source and innovator multiple source drugs, beginning January 1, 2024. It is difficult for us to predict how Medicare coverage and reimbursement policies will be applied to our therapeutics in the future and coverage and reimbursement under different federal healthcare programs are not always consistent. Medicare reimbursement rates may also reflect budgetary constraints placed on the Medicare program. Commercial third- party payors often rely upon Medicare coverage policies and payment limitations in setting their own reimbursement rates. Our inability to promptly obtain coverage, and adequate reimbursement from both government- funded and private payors for new therapeutics we develop and for which we obtain regulatory approval could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our financial condition. In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics. Additionally, if any companion diagnostic provider is unable to obtain reimbursement or is inadequately reimbursed, that may limit the availability of such companion diagnostic, which would negatively impact prescriptions for our product candidates, if approved. We believe that the efforts of governments and third- party payors to contain or reduce the cost of healthcare, and specifically, therapeutics, and legislative and regulatory proposals to broaden the availability of healthcare will continue to affect the business and financial condition of pharmaceutical and biotechnology companies. A number of legislative and regulatory changes in the healthcare system in the U. S. and other major healthcare markets have been proposed. These developments could, directly or indirectly, affect our ability to sell our therapeutics, if approved, at a favorable price. For example, in the U. S., in 2010, the U. S. Congress passed the ACA, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of health spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional policy reforms. Provisions of the ACA addressing coverage and reimbursement of pharmaceutical products that may be of importance to our potential therapeutic candidates include the following: • Increases to pharmaceutical manufacturer rebate liability under the Medicaid Drug Rebate Program due to an increase in the minimum basic Medicaid rebate on most branded prescription drugs and the application of Medicaid rebate liability to drugs used in risk- based Medicaid managed care plans. • The expansion of the 340B Drug Pricing Program to require discounts for " covered outpatient drugs " sold to certain children' s hospitals, critical access hospitals, freestanding cancer hospitals, rural referral centers, and sole community hospitals. • Requirements imposed on pharmaceutical companies to offer discounts on brand- name drugs to patients who fall within the Medicare Part D coverage gap, commonly referred to as the " Donut Hole. " In February 2018, Congress passed the Bipartisan Budget Act of 2018, which, effective as of 2019, increased the discount to be paid by pharmaceutical companies from 50 % to 70 % of a brand- name drug' s negotiated price and added biosimilars to the coverage gap discount program. • Requirements

imposed on pharmaceutical companies to pay an annual non- tax- deductible fee to the federal government based on each company' s market share of prior year total sales of branded drugs to certain federal healthcare programs, such as Medicare, Medicaid, Department of Veterans Affairs, and Department of Defense. Since we currently expect our branded pharmaceutical sales to constitute a small portion of the total federal healthcare program pharmaceutical market, we do not currently expect this annual assessment to have a material impact on our financial condition. • For therapeutic candidates classified as biologics, marketing approval for a follow- on biologic therapeutic may not become effective until 12 years after the date on which the reference innovator biologic therapeutic was first licensed by the FDA, with a possible six- month extension for pediatric therapeutics. After this exclusivity ends, it may be possible for biosimilar manufacturers to enter the market, which is likely to reduce the pricing for such therapeutics and could affect our profitability if our therapeutics are classified as biologics. Separately, pursuant to certain health reform legislation and related initiatives, CMS is working with various healthcare providers to develop, refine, and implement Accountable Care Organizations, or ACOs, and other innovative models of care for Medicare and Medicaid beneficiaries, including the Bundled Payments for Care Improvement Initiative, the Financial Alignment Initiative Demonstration, and other models. The continued development and expansion of ACOs and other innovative models of care will have an uncertain impact on any future reimbursement we may receive for approved therapeutics administered by such organizations. There have been judicial, administrative, executive, and legislative challenges to certain aspects of the ACA. For example, on June 17, 2021 the U. S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the " individual mandate " was repealed by Congress. Thus, the ACA will remain in effect in its current form. Further, prior to the U. S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. In addition, Congress is considering additional health reform measures. It is unclear how any such challenges and the healthcare reform measures of the Biden administration will impact the ACA and our business. There has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there have been several recent U. S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that seek to implement several of the administration' s proposals. As a result, the FDA released a final rule and guidance in on September 2020, providing pathways for states to build and submit importation plans for drugs from Canada. On November 20, 2020, CMS issued an interim final rule implementing the Trump administration' s Most Favored Nation, or MFN, executive order, which would tie Medicare Part B payments for certain physician- administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. As a result of litigation challenging the Most Favored Nation model, on December 27, 2021, CMS published a final rule that rescinded the Most Favored Nation model interim final rule. Further, in July 2021, the Biden administration released an executive order that included multiple provisions aimed at prescription drugs. In response to Biden' s executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform. The plan sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. No legislation or administrative actions have been finalized to implement these principles. In addition, individual states have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing. In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our therapeutic candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most European Union member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever- increasing European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our therapeutic candidates, restrict or regulate post- approval activities and affect our ability to commercialize our therapeutic candidates, if approved. In markets outside of the United States and European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. Further, it is possible that additional governmental action is taken in response to the COVID- 19 pandemic. We cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our current or any future

~~therapeutic candidates we may develop may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.~~ We face potential liability related to the privacy and security of health information we obtain from clinical trials sponsored by us. Most healthcare providers, including research institutions from which we **have** ~~obtain~~ **obtained** patient health information, are subject to privacy and security regulations promulgated under HIPAA, as amended by the HITECH. We are not currently classified as a covered entity or business associate under HIPAA and thus are not directly subject to its requirements or penalties. However, any person may be prosecuted under HIPAA' s criminal provisions either directly or under aiding- and- abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial penalties if we receive or use individually identifiable health information from a HIPAA- covered healthcare provider or research institution or business associate that has not satisfied HIPAA' s requirements for disclosure of individually identifiable health information. In addition, we may maintain sensitive personally identifiable information, including health information, that we ~~receive~~ **received** throughout the clinical trial process, in the course of our research collaborations, and directly from individuals (or their healthcare providers) who ~~enroll~~ **enrolled** in our patient assistance programs. As such, we may be subject to state laws requiring notification of affected individuals and state regulators in the event of a breach of personal information, which is a broader class of information than the health information protected by HIPAA. ~~Furthermore, certain health privacy laws, data security laws, data breach notification laws, consumer protection laws and genetic testing laws may apply directly to our operations and / or those of our collaborators and may impose restrictions on our collection, use and dissemination of individuals' health information. Patients about whom we or our collaborators obtain health information, as well as the providers who share this information with us, may have statutory or contractual rights that limit our ability to use and disclose the information. We may be required to expend significant capital and other resources to ensure ongoing compliance with applicable privacy and data security laws. Claims that we have violated individuals' privacy rights or breached our contractual obligations, even if we are not found liable, could be expensive and time- consuming to defend and could result in adverse publicity that could harm our business.~~ If we or ~~third- party manufacturers, CROs or~~ **our** ~~other~~ contractors or consultants fail to comply with applicable federal, state or local regulatory requirements, we could be subject to a range of regulatory actions ~~that could affect our or our contractors' ability to develop and commercialize our therapeutic candidates and could harm or prevent sales of any affected therapeutics that we are able to commercialize, or could substantially increase the costs and expenses of developing, commercializing and marketing our therapeutics~~ . Any threatened or actual government enforcement action could also generate adverse publicity and require that we devote substantial resources that could otherwise be used in other aspects of our business. Increasing use of social media could give rise to liability, breaches of data security or reputational damage. We are subject to European data protection laws, including the European Union' s General Data Protection Regulation 2016 / 679, or GDPR. If we fail to comply with existing or future data protection regulations, our business, financial condition, results of operations and prospects may be materially adversely affected. By virtue of our **prior** clinical trial activities in the United Kingdom and Europe, we are subject to European data protection laws, including the GDPR. The GDPR which came into effect on May 25, 2018, establishes new requirements applicable to the processing of personal data (i. e., data which identifies an individual or from which an individual is identifiable), affords new data protection rights to individuals (e. g., the right to erasure of personal data) and imposes penalties for serious breaches of up to 4 % annual worldwide turnover or € 20 million, whichever is greater. Individuals (e. g., study subjects) also have a right to compensation for financial or non- financial losses (e. g., distress). There may be circumstances under which a failure to comply with the GDPR, or the exercise of individual rights under the GDPR, would limit our ability to utilize clinical trial data collected on certain subjects. The GDPR imposes additional responsibility and liability in relation to our processing of personal data. This may be onerous and we may be unsuccessful in implementing all measures required by data protection authorities or courts in interpretation of the GDPR, which may materially adversely affect our business, financial condition, results of operations and prospects. ~~Our ability to obtain services, reimbursement or funding from the federal government may be impacted by possible reductions in federal spending. U. S. federal government agencies currently face potentially significant spending reductions. The Budget Control Act of 2011, or BCA, established a Joint Select Committee on Deficit Reduction, which was tasked with achieving a reduction in the federal debt level of at least $ 1. 2 trillion. That committee did not draft a proposal by the BCA' s deadline. As a result, automatic cuts, referred to as sequestration, in various federal programs were scheduled to take place. This includes reductions to Medicare payments to providers of 2 % per fiscal year, that began in April 2013, and, due to subsequent legislative amendments, will remain in effect through 2031 unless additional Congressional action is taken. COVID- 19 relief legislation, including the Coronavirus Aid, Relief and Economic Security Act, or CARES Act, which was signed into law in March 2020, among other things, suspended the 2 % Medicare sequester from May 1, 2020 through March 31, 2022. Under current legislation, the actual reduction in Medicare payments will vary from 1 % in 2022 to up to 3 % in the final fiscal year of this sequester. These reductions may also impact the ability of relevant agencies to timely review and approve therapeutic research and development, manufacturing, and marketing activities, which may delay our ability to develop, market, and sell any therapeutics we may develop. If any of our therapeutic candidates receives marketing approval and we or others later identify undesirable side effects caused by the therapeutic candidate, our ability to market and derive revenue from the therapeutic candidates could be compromised. In the event that any of our therapeutic candidates receive regulatory approval and we or others identify undesirable side effects, adverse events or other problems caused by one of our therapeutics, any of the following adverse events could occur, which could result in the loss of significant revenue to us and materially and adversely affect our results of operations and business: • regulatory authorities may withdraw their approval of the therapeutic or seize the therapeutic; • we may need to recall the therapeutic or change the way the therapeutic is administered to patients; • additional restrictions may be imposed on the marketing of the particular therapeutic or the manufacturing processes for the therapeutic or any component thereof; • we may be subject to fines, restitution or disgorgement of profits or revenues, injunctions, or the imposition of civil penalties or criminal prosecution; • regulatory authorities may require the addition of labeling statements, such as a " black box "~~

warning or a contraindication; • regulatory authorities may require us to implement a REMS, or to conduct post- marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the therapeutic; • we may be required to create a medication guide outlining the risks of such side effects for distribution to patients; • we could be sued and held liable for harm caused to patients; • the therapeutic may become less competitive; and • our reputation may suffer. Risks Related to Ownership of Our Common Stock Our stock price does not meet the minimum bid price for continued listing on Nasdaq. Our ability to continue operations or to publicly or privately sell equity securities and the liquidity of our common stock could be adversely affected if do not regain compliance with the minimum bid price requirement and we are delisted from Nasdaq. On December 30, 2021, we received a letter from the staff of The Nasdaq Stock Market LLC, or Nasdaq, notifying us that, for the previous 30 consecutive business days, the bid price for our common stock had closed below the minimum $ 1. 00 per share requirement for continued listing on The Nasdaq Global Select Market under Nasdaq Listing Rule 5550 (a) (2). In accordance with Nasdaq Listing Rule 5810 (c) (3) (A) we have been provided an initial period of 180 calendar days, or until June 28, 2022, to regain compliance with Nasdaq' s bid price requirement. If, at any time before June 28, 2022, the bid price for our common stock closes at $ 1. 00 or more for a minimum of 10 consecutive business days, we will regain compliance with the bid price requirement, unless the Nasdaq staff exercises its discretion to extend this 10- day period pursuant to Nasdaq rules. We have not regained compliance with Nasdaq Listing Rules as of the filing date of this Annual Report. If we do not regain compliance with Nasdaq Listing Rule 5550 (a) (2) by June 28, 2022, we may be eligible for additional time to comply. To qualify, we will be required to meet certain continued listing requirements for market value of publicly held shares and all other initial listing standards for Nasdaq. If we meet these requirements, Nasdaq may grant us an additional 180 calendar days to regain compliance with the bid price requirement. If we do not regain compliance with the bid price requirement and are not eligible for an additional compliance period, our common stock may be delisted. There can be no assurance that, if we receive a delisting notice and appeal the delisting determination by the staff, such appeal would be successful. There can be no assurance that we will maintain compliance with the requirements for listing our common stock on Nasdaq. Delisting could adversely affect our ability to raise additional capital through the public or private sale of equity securities, would significantly affect the ability of investors to trade our securities and would negatively affect the value and liquidity of our common stock. Delisting could also have other negative results, including the potential loss of confidence by employees, the loss of institutional investor interest and fewer business development opportunities. The market price of our common stock has been, and is likely to continue to be, highly volatile, and you may not be able to resell your shares at or above the price you paid for them. Our stock price will continue to be volatile. As a result of this volatility, investors may not be able to sell their common stock at or above the price paid for the shares. The market price for our common stock may be influenced by a variety of factors, including the other risks described in this section titled " Risk Factors " and the following: • the success of competitive therapeutics or technologies; • results of our preclinical studies and clinical trials of our therapeutic candidates, or those of our competitors, or any current or future collaborators; • regulatory or legal developments in the United States and other countries, especially changes in laws or regulations applicable to our therapeutics; • introductions and announcements of new therapeutics by us, our future commercialization partners, or our competitors, and the timing of these introductions or announcements; • actions taken by regulatory agencies with respect to our therapeutics, clinical studies, manufacturing process or sales and marketing terms; • actual or anticipated variations in our financial results or those of companies that are perceived to be similar to us; • the success of our efforts to acquire or in- license additional technologies, therapeutics or therapeutic candidates; • developments concerning any current or future collaborations, including but not limited to those with our sources of manufacturing supply and our commercialization partners; • announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments; • developments or disputes concerning patents or other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our therapeutics; • our ability or inability to raise additional capital and the terms on which we raise it; • the recruitment or departure **development, execution and announcement** of key personnel **any proposed strategic alternative** ; • changes in **investors may react negatively to our controlled company status and** the structure **influence** of healthcare payment systems **our controlling stockholder or our reconstituted board and / or our uncertain business strategy** ; • market conditions **strategic decisions by us or our competitors, such as acquisitions, divestitures, spin- offs, joint ventures, strategic investments or changes** in **business strategy** the pharmaceutical and biotechnology sectors ; • actual **we are unable to achieve the perceived benefits of** or **our Company as rapidly or to the extent** anticipated **by financial** changes in earnings estimates or changes in stock market analyst recommendations regarding our ~ **or** common stock, other comparable companies or our industry generally **analysts** ; • our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market; • fluctuations in the valuation of companies perceived by investors to be comparable to us; • announcement and expectation of additional financing efforts; • speculation in the press or investment community; • trading volume of our common stock and overall fluctuations in U. S. equity markets, including as a result of the COVID- 19 pandemic; • sales of our common stock by us or our stockholders; • the concentrated ownership of our common stock; • changes in accounting principles; • terrorist acts, acts of war or periods of widespread civil unrest; • natural disasters and other calamities; and • general economic, industry, political and market conditions, including, but not limited to, the ongoing impact of the COVID- 19 pandemic. In addition, the stock markets in general, and the markets for pharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that has been often unrelated to the operating performance of the issuer. These broad market and industry factors, such as those related to the COVID- 19 pandemic and Russia' s invasion of Ukraine and retaliatory actions taken by the **United States** U. S., NATO and others, may seriously harm the market price of our common stock, regardless of our operating performance. Raising additional funds by issuing securities may cause dilution to existing stockholders and raising funds through lending and licensing arrangements may restrict our operations or require us to relinquish proprietary rights. Until such time, if ever, as we can generate substantial product revenues, we expect **to attempt** to finance our cash needs

through a combination of equity offerings ~~,~~ **and** debt financings ~~, grants and license and development agreements in connection with any collaborations~~ . ~~We do not have any committed external source~~ **As discussed elsewhere, it may be very challenging to obtain equity or debt financing given the current transitional state** of ~~funds~~ **the Company** . ~~To~~ **However, to** the extent that we raise additional capital through the issuance of shares or other securities convertible into shares, our stockholders will be diluted. Future issuances of our common stock or other equity securities, or the perception that such sales may occur, could adversely affect the prevailing market price of our common stock and impair our ability to raise capital through future offerings of equity or equity- linked securities ~~. For example, on December 23, 2019, we completed the sale of 10, 000, 000 shares of our common stock in the December 2019 Offering and on August 2, 2019 we completed the sale of 31, 625, 000 shares of our common stock in the August 2019 Offering. The issuance of shares in both the December 2019 Offering and August 2019 Offering were pursuant to a shelf registration statement on Form S- 3 that was declared effective by the SEC on July 24, 2019. The shelf registration statement allows us to sell from time- to- time up to $ 125. 0 million of common stock, preferred stock, debt securities, warrants, or units comprised of any combination of these securities, for our own account in one or more offerings; the remaining amount available under this shelf registration after the December 2019 Offering (inclusive of the exercise of the underwriters' option in January 2020 to purchase additional shares at the public offering price in connection with the December 2019 Offering) is approximately $ 31. 3 million. On December 16, 2021, we completed a registered direct offering with certain institutional investors, pursuant to which we issued (i) an aggregate of 13, 006, 614 shares of our common stock, (ii) pre- funded warrants to purchase up to an aggregate of 21, 569, 454 shares of our common stock, and (iii) warrants to purchase up to 17, 288, 034 shares of our common stock. The securities being offered in the December 2021 Offering were pursuant to the effective shelf registration statement on Form S- 3 that was declared effective by the SEC on January 7, 2021. The issuance of the shares pursuant to the December 2019 Offering, the August 2019 Offering and the December 2021 Offering and / or the resale of a substantial number of shares of our common stock in the public market or the sale of any shares of our common stock under the equity distribution agreement could adversely affect the market price for our common stock and make it more difficult for you to sell shares of our common stock at times and prices that you feel are appropriate. Adverse market and price pressures that may result from the December 2019 Offering, the August 2019 Offering or the December 2021 Offering or an offering pursuant to the shelf registration statement may continue for an extended period of time and continued negative pressure on the market price of our common stock could have a material adverse effect on our ability to raise additional equity capital. Debt financing and preferred 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 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 favorable to us. Any debt financing that we enter into may involve covenants that restrict our operations. These restrictive covenants may include limitations on additional borrowing and specific restrictions on the use of our assets as well as prohibitions on our ability to create liens, pay dividends, redeem our stock or make investments. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves~~ . We are an " emerging growth company " and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors. We are an " emerging growth company " as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including (1) not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes- Oxley Act, (2) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and (3) exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. In addition, as an emerging growth company, we are only required to provide two years of audited financial statements and two years of selected financial data. We ~~could be an~~ **expect to lose** emerging growth company ~~for up to five years, although circumstances could cause us to lose that~~ status **at** ~~earlier, including if~~ the **end** ~~market value~~ of **this** ~~our common stock held by non- affiliates exceeds $ 700. 0 million as of any June 30 before that time or if we have total annual gross revenue of $ 1. 07 billion or more during any fiscal~~ year ~~before that time, in which cases we would no longer be an emerging growth company as of the following December 31, or if we issue more than $ 1. 0 billion in non- convertible debt during any three- year period before that time, in which case we would no longer be an emerging growth company immediately~~ . Even after we no longer qualify as an emerging growth company, we may still qualify as a " smaller reporting company **" and / or " non- accelerated filer** " which would allow us to take advantage of many of the same exemptions from disclosure requirements including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes- Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our share price may be more volatile ~~. Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval. Based on the beneficial ownership of our common stock as of December 31, 2021, our executive officers and directors, together with holders of five percent or more of our outstanding common stock and their respective affiliates, will~~

beneficially own approximately 32 % of our outstanding common stock. As a result, these stockholders, if acting together, will continue to have significant influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets and any other significant corporate transaction. The interests of these stockholders may not be the same as or may even conflict with your interests. For example, these stockholders could delay or prevent a change of control of our Company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise . Anti- takeover provisions in our charter documents and under the General Corporation Law of the State of Delaware could make an acquisition of us more difficult and may prevent attempts by our stockholders to replace or remove our management. Provisions in our amended and restated certificate of incorporation and our bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders, and the ability of the Board of Directors of the Company, or the Board, to issue preferred stock without stockholder approval. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or DGCL, which prohibits stockholders owning in excess of 15 % of the outstanding combined organization voting stock from merging or combining with the combined organization. Although we believe these provisions collectively will provide for an opportunity to receive higher bids by requiring potential acquirers to negotiate with our Board, they would apply even if the offer may be considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove then- current management by making it more difficult for stockholders to replace members of the Board, which is responsible for appointing the members of management. Anti- takeover provisions in our charter documents could discourage, delay or prevent a change in control of us and may affect the trading price of our common stock. Our corporate documents and the DGCL contain provisions that may enable our Board to resist a change in control of us even if a change in control were to be considered favorable by our stockholders. These provisions: • stagger the terms of our Board and require 66 and 2 / 3 % stockholder voting to remove directors, who may only be removed for cause; • authorize our Board to issue " blank check " preferred stock and to determine the rights and preferences of those shares, which may be senior to our common stock, without prior stockholder approval; • establish advance notice requirements for nominating directors and proposing matters to be voted on by stockholders at stockholders' meetings; • prohibit our stockholders from calling a special meeting and prohibit stockholders from acting by written consent; • require 66 and 2 / 3 % stockholder voting to effect certain amendments to our certificate of incorporation and bylaws; and • prohibit cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates. These provisions could discourage, delay or prevent a transaction involving a change in control of us. These provisions could also discourage proxy contests and make it more difficult for stockholders to elect directors of their choosing and cause us to take other corporate actions our stockholders desire. Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your 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. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. Our amended and restated certificate of incorporation designates the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees or agents. Our amended and restated certificate of incorporation provides that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any of the following types of actions or proceedings under Delaware statutory or common law: derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or agents to us or our stockholders, any action asserting a claim arising pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws or any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein. This provision would not apply to suits brought to enforce a duty or liability created by the Securities Exchange Act of 1934, as amended, or any other claims for which a court or forum other than the Court of Chancery has exclusive jurisdiction or for which the Court of Chancery does not have subject matter jurisdiction. Furthermore, Section 22 of the Securities Act of 1933, as amended, or the Securities Act, creates concurrent jurisdiction for federal and state courts over all Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. Our amended and restated certificate of incorporation also provides that any person purchasing or otherwise acquiring any interest in any shares of our common stock shall be deemed to have notice of and to have consented to this provision of our amended and restated certificate of incorporation. This choice of forum provision may limit our stockholders' ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, employees or agents, which may discourage such lawsuits against us and our directors, officers, employees and agents even though an action, if successful, might benefit our stockholders. Stockholders who do bring a claim in the Court of Chancery could face additional litigation costs in pursuing any such claim, particularly if they do not reside in or near Delaware. The Court of Chancery may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments or results may be more favorable to us than to our stockholders. If a court were to find this exclusive forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in any action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could have a material adverse effect on our business,

financial condition or results of operations. ~~Changes in tax laws or regulations that are applied adversely to us or our customers may have a material adverse effect on our business, cash flow, financial condition or results of operations. New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, the Biden administration and Congress have proposed various U. S. federal tax law changes, which if enacted could have a material impact on our business, cash flow, financial condition or results of operations. In addition, it is uncertain if and to what extent various states will conform to federal tax laws. Future tax reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one-time charges, and could increase our future U. S. tax expense.~~ Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited. We have incurred substantial losses during our history and do not expect to become profitable in the near future and we may never achieve profitability. Our net operating loss, or NOL, carryforwards generated in tax years beginning on or before December 31, 2017, are only permitted to be carried forward for 20 years under applicable U. S. tax law. Under the Tax **Cuts and Jobs** Act, as modified by the CARES Act, our federal NOLs generated in tax years beginning after December 31, 2017, may be carried forward indefinitely, but the deductibility of such federal NOLs **is** ~~in tax years beginning after December 31, 2020 may~~ be limited ~~. It is uncertain if and~~ to **80 % of taxable income** ~~what extent various states will conform to the Tax Act and the CARES Act~~ . In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an " ownership change, " generally defined as a greater than 50 % change (by value) in its equity ownership over a three- year period, the corporation' s ability to use its pre- change NOL, and other pre- change tax attributes (such as research tax credits) to offset its post- change income or taxes may be limited. We have experienced ownership changes in the past. **We completed a review of our changes in ownership through December 31, 2022 and determined that we experienced an" ownership change" within the meaning of Section 382 (g) during the fourth quarter of 2022. This ownership change has and will continue to subject our net operating loss carryforwards to an annual limitation, which will significantly restrict our ability to use them to offset our taxable income in periods following the ownership change. We determined that at the date of the 2022 ownership change, we had a net unrealized built- in loss (" NUBIL"). The NUBIL was determined based on the difference between the fair market value of our assets and their tax basis at the ownership change date. Because of the NUBIL, certain deductions recognized during the five- year period beginning on the date of the IRC Section 382 ownership change (the" recognition period") are subject to the same limitation as the net operating loss carryforwards or certain other deductions.** In addition, we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which are outside of our control. As a result, if we earn net taxable income, our ability to use our pre- change NOL carryforwards to offset U. S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. General Risk Factors FINRA sales practice requirements may limit a stockholder' s ability to buy and sell our stock due to our low stock price. The Financial Industry Regulatory Authority, or FINRA, has adopted rules requiring that, in recommending an investment to a customer, a broker-dealer must have reasonable grounds for believing that the investment is suitable for that customer. Prior to recommending speculative or low- priced securities to their non- institutional customers, broker- dealers must make reasonable efforts to obtain information about the customer' s financial status, tax status, investment objectives and other information. Under interpretations of these rules, FINRA has indicated its belief that there is a high probability that speculative or low- priced securities will not be suitable for at least some customers. If these FINRA requirements are applicable to us or our securities, which we believe they are, they may make it more difficult for broker- dealers to recommend that at least some of their customers buy our common stock, which may limit the ability of our stockholders to buy and sell our common stock and could have an adverse effect on the market for and price of our common stock. 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 will be influenced by the research and reports that industry or securities analysts publish about us or our business. Our research coverage by securities and industry analysts is currently limited. In addition, because we did not become a reporting company by conducting an underwritten initial public offering of our common stock, security analysts of brokerage firms may not provide wider coverage of our Company. In addition, investment banks may be less likely to agree to underwrite secondary offerings on our behalf than they might if we became a public reporting company by means of an underwritten initial public offering, because they may be less familiar with our Company as a result of more limited coverage by analysts and the media, and because we became public at an early stage in our development. The failure to receive wider research coverage or support in the market for our shares will have an adverse effect on our ability to develop a liquid market for our common stock and the trading price for our stock would be negatively impacted. In the event we obtain wider securities or industry analyst coverage, 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 target studies and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.