Risk Factors Comparison 2024-02-27 to 2023-02-28 Form: 10-K

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Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report on Form 10- K, including our financial statements and the related notes and the section titled " Management' s Discussion and Analysis of Financial Condition and Results of Operations, " and in our other public filings, in evaluating our business. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations, and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations and the market price of our common stock. Summary of Risk Factors Our business is subject to numerous risks and uncertainties that you should consider before investing in our company, as more fully described below. The principal factors and uncertainties that make investing in our company risky include, among others: • We are in **various** ~~the clinical~~ stages of drug development and have a limited operating history and no products approved for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability. • We have incurred significant net losses in each year since our inception and anticipate that we will continue to incur net losses for the foreseeable future. • Drug development is a highly uncertain undertaking and involves a substantial degree of risk. • We will need to obtain substantial additional financing to complete the development and any commercialization of our product candidates, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce, or terminate our commercialization efforts, product development, or other operations. • Due to the significant resources required for the development of our ~~programs~~ **product candidates**, and depending on our ability to access capital, we must prioritize development of certain product candidates. Moreover, we may expend our limited resources on programs that do not yield a successful product candidate or fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success. • Research and development of biopharmaceutical products is inherently risky **. Our** ~~, and our~~ business is heavily dependent on the successful development of our product candidates, which are in **various stages of** preclinical and clinical development **. We** ~~, so we~~ cannot give any assurance that any of our product candidates will receive regulatory, including marketing, approval, which is necessary before they ~~can~~ **may** be commercialized. • We may not be successful in our efforts to continue to create a pipeline of product candidates from our research and drug discovery platform or to develop commercially successful products. If we fail to successfully identify and develop additional product candidates from our research and drug discovery platform, our commercial opportunity may be limited. • We may not be successful in our efforts to carry out our obligations under our collaborations for our product development and research programs; for instance, without limitation, ~~failure to~~ **we may not** complete in a timely manner or at all our contractual obligations to GSK and AbbVie. • We may not be successful in our efforts to **obtain approval for additional or** ~~expand~~ **expanded** indications for ~~approved~~ **any** product candidates **that receive approval for a given indication**. • We have concentrated a substantial portion of our research and development efforts on the treatment of neurodegenerative diseases, a field that has seen both limited success in drug development and evolving standards for regulatory approval. Further, our product candidates are based on new approaches and novel technology, and we must identify and develop new biomarkers that are signs of a disease or condition and that can measure ~~the~~ impact ~~of our product candidates~~ on disease progression **of our product candidates**, which makes it difficult to predict the time and cost of product candidate development and ~~subsequently~~ -- **subsequent** ~~obtaining~~ regulatory approval. • We may encounter substantial delays in our clinical trials ~~,~~ or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all. • Our clinical trials may reveal significant adverse events, toxicities, or other side effects and may fail to demonstrate substantial evidence of the safety and efficacy of our product candidates, which would prevent, delay, or limit the scope of regulatory approval and commercialization **. • Our operations and financial results could be adversely impacted by the effects of worldwide economic conditions, including macroeconomic downturns stemming from increased inflation, supply chain and other economic impacts of the COVID- 19 pandemic and geopolitical events**. • We are highly dependent on our key personnel, and if we are not successful in attracting, motivating, and retaining highly qualified personnel, **including as a result of layoffs and furloughs, pausing of recruiting efforts, or regrettable employee attrition,** we may not be able to successfully implement our business strategy ~~. • Our operations and financial results could continue to be adversely impacted by the COVID- 19 pandemic, including the effects of subsequent variants, in the United States and the rest of the world, including potential supply chain issues and concerns~~. • The market price of our common stock may continue to ~~experience~~ **be volatility volatile** ~~or decline~~, which could result in substantial losses for investors and could negatively impact our ability to conduct additional fundraising in the public markets. Risks Related to Our Business, Financial Condition, and Capital Requirements We are ~~in various stages of drug development and have a limited operating history and no products approved for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability. We are~~ a clinical stage ~~biopharmaceutical~~ **biotechnology** company with a limited operating history, focused primarily on developing therapeutics for neurodegenerative diseases, including FTD, Alzheimer' s disease, Parkinson' s disease, and ALS ~~, as well as oncology therapeutics that focus on innate immune biology~~. We commenced operations in May 2013. To date, we have financed our operations primarily through the sale of equity securities and upfront payments received in connection with our collaboration arrangements with AbbVie and GSK. We have no products approved for commercial sale and have not generated any revenue from product sales. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We are in Phase 2 and Phase 3 clinical trials for one product

candidate, latozinemab ~~,~~ **;** **we** are in **a** Phase 2 clinical trial for one product candidate, AL002 ~~,~~ **;** and we ~~have completed~~ **are in** a **Phase 2 clinical trial for AL101. In the third quarter of 2023, we inactivated the IND for AL101 in FTD, given that we and GSK plan to develop AL101 for the potential treatment of larger indications, including Alzheimer' s disease and Parkinson' s disease. We previously decided to close the** Phase 1 clinical trial for ~~AL101. We decided to close the Phase 1 clinical trial for~~ our AL044 product candidate based on initial PK and tolerability data. **We inactivated the IND for AL044 in the third quarter of 2023.** In addition, **in 2022,** AbbVie decided to terminate ~~the~~ **our** CD33 collaboration program, after **we and** AbbVie **concluded that further development of** ~~and Alector collaboratively reviewed next steps for~~ AL003, the asset being developed under that program, ~~and concluded that further development of AL003~~ was not warranted. To date, we have not completed a pivotal clinical trial, obtained marketing approval for any product candidates, manufactured a commercial scale product, or arranged for a third party to do so on our behalf, or conducted sales and marketing activities necessary for successful product commercialization. Our limited operating history as a company makes any assessment of our future success and viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by clinical- stage ~~biopharmaceutical~~ **biotechnology** companies in rapidly evolving fields, and we have not yet demonstrated an ability to successfully overcome such risks and difficulties. If we do not address these risks and difficulties successfully, our business will suffer. We have incurred net losses in almost every reporting period since our inception. We incurred net losses of $ **130. 4 million, $** 133. 3 million, **and** $ 36. 3 ~~million, and $ 190. 2~~ million for the years ended December 31, **2023,** 2022, **and** 2021 ~~, and 2020~~, respectively. As of December 31, ~~2022~~ **2023**, we had an accumulated deficit of $ ~~579~~ **710** . ~~7~~ **1** million. We have invested significant financial resources in research and development activities, including for our preclinical and clinical product candidates. We do not expect to generate revenue from product sales for several years, if at all. The revenue we currently generate from our collaboration arrangements with AbbVie and GSK is variable and limited in amount. For our collaborations with AbbVie and GSK, we recognize collaboration revenue by measuring the progress towards complete satisfaction of the performance of obligation measured as the program costs are incurred. The amount of our future net losses will depend, in part, on the level of our future expenditures and revenue. Moreover, our net losses may fluctuate significantly from quarter to quarter and year to year, such that a period- to- period comparison of our results of operations may not be a good indication of our future performance. On July 1, 2021, we entered into an agreement with GSK to collaborate on the global development and commercialization of progranulin- elevating monoclonal antibodies, including latozinemab and AL101. Under the terms of the GSK Agreement, we received $ 700 million in upfront payments, of which $ 500 million was received in August 2021 and $ 200 million was received in January 2022. In addition, we will be eligible to receive up to an additional $ 1. 5 billion in clinical development, regulatory, and commercial launch- related milestone payments for latozinemab and AL101. Developing our product candidates is expensive, and we expect to continue to spend substantial amounts as we fund our early- stage research projects and continue to advance our programs through preclinical and clinical development. Even if we are successful in developing our product candidates ~~,~~ **and** obtaining regulatory approvals ~~and ,~~ launching and commercializing any product candidate will require substantial additional funding. We expect to continue to incur significant expenses and increasingly higher operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we: • continue our research and discovery activities; • advance our research and drug discovery platform, including our target, patient, and biomarker selections; • progress our current and any future product candidates through preclinical and clinical development; • initiate and conduct additional preclinical, clinical, or other studies for our product candidates; • work with our ~~contract development and manufacturing organizations (~~CDMOs ~~)~~ to scale up the manufacturing processes for our product candidates or, in the future, establish and operate a manufacturing facility; • change or add contract manufacturers or suppliers; • seek regulatory approvals and marketing authorizations for our product candidates; • establish sales, marketing, and distribution infrastructure to commercialize any products for which we obtain approval; • make milestone, royalty, or other payments due under any license or collaboration agreements; • take steps to seek protection of our intellectual property and defend our intellectual property against challenges from third parties; • obtain, maintain, protect, and enforce our intellectual property portfolio, including intellectual property obtained through license and collaboration agreements; • attract, hire, and retain qualified personnel, especially in light of a competitive hiring and compensation environment; • provide additional internal infrastructure to support our continued research and development operations and any planned commercialization efforts in the future; • implement additional internal systems and infrastructure related to cybersecurity; • meet the requirements and demands of being a public company; • withstand periods of rising rates of inflation; and • defend against any product liability claims or other lawsuits related to our products. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline. We have no products approved for commercial sale. To obtain revenues from the sales of our product candidates that are significant or large enough to achieve profitability, we must succeed, either alone or with third parties, in developing, obtaining regulatory approval for, manufacturing, and marketing therapies with significant commercial success. Our ability to generate revenue and achieve profitability depends on many factors, including: • completing research and preclinical and clinical development of our product candidates; • ~~addressing impacts on our clinical trials resulting from factors related to the effects of the COVID- 19 pandemic and subsequent variants; •~~ obtaining regulatory approvals and marketing authorizations for product candidates for which we successfully complete clinical development and clinical trials; • developing a sustainable and scalable manufacturing process for our product candidates **; •** ~~, as well as~~ establishing and maintaining commercially viable supply relationships with third parties that can provide adequate products and services to support clinical activities and commercial demand of our product candidates; • identifying, assessing, acquiring, and / or developing new product candidates; • negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter; • launching and successfully commercializing product candidates for which we obtain regulatory and marketing approval, ~~either~~ **whether** ~~by~~ **alone or in** ~~collaborating~~

collaboration with a partner ~~or~~ , **including the** ~~if launched independently, by establishing~~ **establishment** ~~a~~ **of any necessary** sales, marketing, and distribution infrastructure; • obtaining and maintaining an adequate price for our product candidates, both in the United States and in foreign countries where our products are commercialized; • obtaining adequate reimbursement for our product candidates from payors; • obtaining market acceptance of our product candidates as viable treatment options; • addressing any competing technological and market developments; • receiving milestones and other payments under our current and any future collaboration arrangements; • **addressing impacts on our clinical trials resulting from factors related to the effects of worldwide economic conditions, including macroeconomic downturns stemming from increased inflation, supply chain and other economic impacts of the COVID- 19 pandemic and geopolitical events; •** maintaining, protecting, expanding, and enforcing our portfolio of intellectual property rights, including patents, trade secrets, and know- how; and • attracting, hiring, and retaining qualified personnel ~~, especially~~ in ~~light of~~ a ~~recent very~~ competitive compensation environment. To date, clinical development of two of our product candidates has been terminated. AbbVie decided to terminate ~~the~~ **our** CD33 collaboration program, after **we and** AbbVie **concluded that further development of** ~~and Alector collaboratively reviewed next steps for~~ AL003, the asset being developed under that program, ~~and concluded that further development of AL003~~ was not warranted. Additionally, we decided to close the Phase 1 clinical trial for our AL044 product candidate based on initial PK and tolerability data. Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of our expenses, or when we will be able to generate any meaningful revenue or achieve or maintain profitability, if ever. In addition, our expenses could increase beyond our current expectations if we are required by the FDA or foreign regulatory agencies ~~,~~ to perform studies in addition to those that we currently anticipate, or if there are any delays in any of our or our current or future collaborators' clinical trials or the development of any of our product candidates. Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs associated with launching and commercializing any approved product candidate and ongoing compliance efforts. Our operations have required substantial amounts of cash since inception, and we expect our expenses to increase significantly in the foreseeable future. To date, we have financed our operations primarily through the sale of equity securities and upfront payments received in connection with our collaboration arrangements with AbbVie and GSK. Developing our product candidates and conducting clinical trials for the treatment of neurodegenerative diseases, including FTD, Alzheimer' s disease, ALS, and Parkinson' s disease, ~~and in oncology,~~ will require substantial amounts of capital. We will also require a significant amount of capital for the further development of our product candidates, and if any of such product candidates are approved, to commercialize any approved products. As of December 31, ~~2022~~ **2023** , we had cash, cash equivalents, and marketable securities of $ ~~712~~ **548** . 9 million. **In January 2024** ~~Based on our current operating plan~~ , we ~~believe that our existing~~ **announced the closing of an underwritten public offering and the net proceeds from the offering were approximately $ 71. 1 million. Our** cash, cash equivalents ~~,~~ and marketable securities **as of December 31** , ~~will be sufficient to fund our projected operations~~ **2023 plus the net proceeds from the offering total $ 620. 0 million, which we anticipate provides runway** through ~~2025~~ **2026** . Our estimate as to how long we expect our existing cash, cash equivalents, and marketable securities to be available to fund our operations is based on assumptions that may **prove to** be ~~proved~~ inaccurate, and we could use our available capital resources sooner than we currently expect. In addition, changing circumstances, including periods of ~~a~~ rising ~~rate of~~ inflation, may cause us to increase our spending significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We may need to raise additional funds sooner than we anticipate if we choose to ~~expand~~ **grow** more rapidly than we presently anticipate. Global markets recently have experienced volatility and instability in connection with macroeconomic downturns stemming from increased inflation, supply chain and other economic impacts of the COVID- 19 pandemic and geopolitical events, including the **ongoing conflict between** ~~Russian~~ - **Russia and** ~~invasion of~~ Ukraine **, and associated sanctions targeting Russia, and the ongoing conflict between Israel and Hamas** , among other matters. In addition, the public market for and stock prices of biotechnology companies have experienced a significant downturn over the last few years. Our ability to raise money in the public markets may be severely impacted for the foreseeable future due to these factors. Additional capital may not be available when we need it, on terms acceptable to us **,** or at all. If adequate capital is not available to us on a timely basis, we may be required to significantly delay, scale back, or discontinue our research and development programs or the commercialization of any product candidates, if approved, or be unable to continue or expand our operations, or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition, results of operations, and growth prospects and cause the price of our common stock to decline. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect ~~your~~ **the** rights ~~as~~ **of** a common stockholder. Debt financing, if available, may be **on** unfavorable terms, including interest rates **,** and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends. If we raise additional funds through collaborations, strategic alliances, or licensing **or other transactions** ~~arrangements with pharmaceutical partners~~ , 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. ~~Due to the significant resources required for the development of our product candidates, and depending on our ability to access capital, we must prioritize development of certain product candidates. Moreover, we may expend our limited resources on programs that do not yield a successful product candidate or fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.~~ We have identified over 100 **potential** immune system targets. Three of our product candidates, latozinemab, AL002, and AL101 ~~,~~ are in clinical development, and we continue to develop our research pipeline ~~. The development of one of our product candidates, AL003, was terminated in June 2022~~ . Together, the development of these programs and product candidates requires significant capital investment. Due to the significant resources required for the development of our programs and product candidates, we must focus our programs and

product candidates on specific diseases and disease pathways and decide which product candidates to pursue and advance and the amount of resources to allocate to each. Our drug development strategy is to clinically test and seek regulatory approval for our product candidates in indications in which we believe there is the most evidence that we will be able to quickly generate proof- of- concept data. We then intend to expand to clinical testing and seek regulatory approvals in other neurodegenerative indications based on genetic and mechanistic overlap with the primary indication. However, even if our product candidates are able to gain regulatory approval in one indication, there is no guarantee that we will be able to obtain approval in other indications, and we may expend significant resources in seeking such approvals. ~~In addition, we may focus resources on pursuing indications outside of neurodegeneration based on the same genetic and mechanistic rationale we utilize in determining on which of our discovery programs to focus.~~ Our decisions concerning the allocation of research, development, collaboration, management, and financial resources toward particular product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities ~~. For example, Innovent will not be continuing development of AL008, and we intend to re- acquire the rights we granted to Innovent for the development and commercialization of AL008. Innovent submitted an IND with the Chinese regulatory authorities, and Alector is in the process of obtaining relevant materials and information from Innovent. Alector plans to evaluate data and documentation from that IND application to potentially support an IND submission in the U. S~~ . Similarly, our potential decisions to delay, terminate, or collaborate with third parties in respect of certain programs may subsequently also prove to be suboptimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the viability or market potential of any of our programs or product candidates or misread trends in the biopharmaceutical industry, in particular for neurodegenerative diseases, such events could have a material adverse effect on our business, financial condition, and results of operations. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases and disease pathways that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing, or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights. Our reliance on genetic screening and use of biomarkers to align patient risk profiles with targeted intervention may eventually require us to develop and use companion diagnostics, which could impact product development costs and timelines depending on the specific diagnostic **test** and any applicable regulatory requirements that would need to be met to enable its use. Risks Related to the Discovery, Development, and Commercialization of Our Product Candidates Research and development of biopharmaceutical products is inherently risky. Our business is heavily dependent on the successful development of our product candidates, which are in various stages of preclinical and clinical development. We cannot give any assurance that any of our product candidates will receive regulatory, including marketing, approval, which is necessary before they can be commercialized. We are in the clinical stages of development of many of the product candidates currently in our programs. To date, we have invested substantially in our efforts and financial resources to identify, procure intellectual property for, and develop our programs and product candidates, and provide general and administrative support for these operations. Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize our product candidates, and we may fail to do so for many reasons, including the following: • our product candidates may not successfully complete preclinical studies or clinical trials; • a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria; • our competitors may develop therapeutics that render our product candidates obsolete or less attractive; • the product candidates that we develop may not be sufficiently covered by intellectual property for which we hold exclusive rights; • the product candidates that we develop may be covered by third parties' patents or other intellectual property or exclusive rights; • the market for a product candidate may change so that the continued development of that product candidate is no longer reasonable or commercially attractive; • a product candidate may not be capable of being produced in sufficient quantities for development or commercialization at an acceptable cost, or at all; • if a product candidate obtains regulatory approval, we may be unable to establish sales and marketing capabilities, or successfully market such approved product candidate, to gain market acceptance; and • a product candidate may not be accepted as safe and effective by patients, the medical community **,** or third- party payors, if applicable. If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations ~~. For example, after completing the Phase 1 trial for AL003 and reviewing the collaboration program with us, AbbVie decided to terminate the CD33 collaboration program, under which AL003 was being developed~~ . We may not be successful in our efforts to further develop our current product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. Most of our product candidates are in the early stages of development **,** and all will require significant additional clinical development, management of preclinical, clinical, and manufacturing activities, regulatory approval, adequate manufacturing supply, a commercial organization, and significant marketing efforts before we generate any revenue from product sales, if at all. We have never completed a clinical development program. We are in Phase 2 and Phase 3 clinical trials for one product candidate, latozinemab, **we** are in Phase 2 clinical development for one product candidate, AL002, ~~and~~ we ~~have completed~~ **are in** a Phase ~~1~~ **2** clinical trial for **one product candidate,** AL101. Further, we cannot be certain that any of our product candidates will be successful in clinical trials. For any product candidates ~~we~~ **that** have advanced into clinical trials, we may terminate such trials or the clinical program prior to their completion. If any of our product candidates successfully complete clinical trials, we generally plan to seek regulatory approval to market our product candidates in the United States, the European Union, and in additional foreign countries where we believe there is a viable commercial opportunity. We have never commenced, compiled **,** or submitted an application seeking regulatory approval to market any product candidate. We may

never receive regulatory approval to market any product candidates even if such product candidates successfully complete clinical trials, which would adversely affect our viability. To obtain regulatory approval in countries outside the United States, we must comply with numerous and varying regulatory requirements of such ~~other~~ countries regarding safety, efficacy, manufacturing and controls, clinical trials, commercial sales, pricing, and distribution of our product candidates. We may also rely on our collaborators or partners to conduct the required activities to support an application for regulatory approval, and to seek approval, for one or more of our product candidates. We cannot be sure that our collaborators or partners will conduct these activities or do so within the timeframe we desire. Even if we (or our collaborators or partners) are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other ~~jurisdictions~~ **jurisdiction**. If we are unable to obtain approval for our product candidates in multiple jurisdictions, our business, financial condition, results of operations, and our growth prospects could be negatively affected. Even if we receive regulatory approval to market any of our product candidates, whether for the treatment of neurodegenerative diseases or other diseases, we cannot be assured that any such product candidate will be successfully commercialized, widely accepted in the marketplace **,** or more effective than other commercially available alternatives. Investment in biopharmaceutical product development involves significant risk that any product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval, and become commercially viable. We cannot provide any assurance that we will be able to successfully advance any of our product candidates through the development process or, if approved, successfully commercialize any of our product candidates. One of our strategies is to identify and pursue clinical development of additional product candidates. Identifying, developing, obtaining regulatory approval, and commercializing additional product candidates for the treatment of neurodegenerative and other diseases will require substantial additional funding and is prone to the risks of failure inherent in drug development. We cannot provide any assurance that we will be able to successfully identify or acquire additional product candidates, advance any of these additional product candidates through the development process, successfully commercialize any such additional product candidates, if approved, or assemble sufficient resources to identify, acquire, develop, or, if approved, commercialize additional product candidates. If we are unable to successfully identify, acquire, develop, and commercialize additional product candidates, our commercial opportunity may be limited. We may not be successful in our efforts to obtain approval for additional or expanded indications for our approved product candidates. Our drug development strategy is to clinically test and seek regulatory approval for our product candidates in indications in which we believe there is the most evidence that we will be able to quickly generate proof- of- concept data. We then intend to expand to clinical testing and seek regulatory approvals in other neurodegenerative indications based on genetic and mechanistic overlap with the primary indication. Conducting clinical trials for additional indications for our product candidates requires substantial technical, financial, and human capital resources and is prone to the risks of failure inherent in drug development. We cannot provide any assurance that we will be successful in our effort to obtain regulatory approval for our product candidates for additional indications even if we obtain approval for an initial indication. We ~~do not have any products approved for commercial sale and have not generated any revenue from product sales. We~~ have concentrated a substantial portion of our research and development efforts on the treatment of neurodegenerative diseases, a field that has seen limited success in drug development. Further, our product candidates are based on new approaches and novel technology, and we must identify and develop new biomarkers that are signs of a disease or condition and that can measure impact on disease progression of our product candidates, which makes it difficult to predict the time and cost of product candidate development and **to** subsequently ~~obtaining~~ **obtain** regulatory approval. We **are focusing** ~~have focused a substantial portion of~~ our research and development efforts on addressing neurodegenerative diseases. Collectively, efforts by biopharmaceutical companies in the field of neurodegenerative diseases have seen limited success in drug development. There are limited currently approved therapeutic options available for patients with FTD, Alzheimer' s disease, Parkinson' s disease, ALS, and other neurodegenerative diseases. Our future success is highly dependent on the successful development of our product candidates for treating neurodegenerative diseases. Developing product candidates and, if approved, commercializing our products for treatment of neurodegenerative diseases subjects us to a number of challenges, including obtaining disease modifying activity and efficacious dose in target tissue and obtaining regulatory approval from the FDA and other regulatory authorities who have only a limited set of precedents to rely on. Our approach to the treatment of neurodegenerative diseases aims to identify and select targets enriched in microglia and other myeloid immune cells which are genetically associated with neurodegenerative diseases. We identify and develop product candidates that are designed to cross the blood brain barrier in sufficient quantity and potency to enable efficacious dosing in the brain and engage the intended target, and we must be able to identify and develop biomarkers and biomarker assays that can accurately identify signs of a disease or condition, assist us in selecting the right patient population, ~~and~~ demonstrate target **and** ~~engagement,~~ pathway engagement, and measure the impact on disease progression of our product candidates. This strategy may not prove to be successful. We cannot be sure that our approach will yield satisfactory therapeutic products that are safe and effective, scalable, or profitable ~~. We may encounter substantial delays in our clinical trials or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all~~. Clinical testing is expensive, time consuming, and subject to uncertainty. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. We cannot be sure that submission of an IND or a clinical trial application (CTA) will result in the FDA or EMA, as applicable, allowing clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could suspend or terminate such clinical trials. A failure of one or more clinical trials can occur at any stage of testing, and our future clinical trials may not be successful. Events that may prevent successful or timely initiation or completion of clinical trials include: • inability to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of clinical trials; • delays in confirming target engagement, patient selection, or other relevant biomarkers to be utilized in preclinical and clinical product candidate development; • delays in reaching a consensus with regulatory agencies on study design; • delays in reaching agreement on acceptable terms with prospective contract research organizations (CROs) and clinical trial sites, the terms of which can be subject to extensive

negotiation and may vary significantly among different CROs and clinical trial sites; • delays in identifying, recruiting, and training suitable clinical investigators; • delays in obtaining required IRB / EC approval at each clinical trial site; • imposition of delays to clinical trials, including as a result of temporary or permanent clinical hold by regulatory agencies for a number of reasons (see for example our discussions of ARIA in other risks described in this " Risk Factors " section), including: • after review of an IND or amendment, CTA or amendment, or equivalent application or amendment; • as a result of a new safety finding that presents unreasonable risk to clinical trial participants; • as a result of modifications to clinical trial protocols or related documentation; • a negative finding from an inspection of our clinical trial operations or study sites; or • the finding that the investigational protocol or plan is clearly deficient to meet its stated objectives; • delays in identifying, recruiting, and enrolling suitable patients to participate in our clinical trials, and delays caused by patients withdrawing from clinical trials, or failing to return for post- treatment follow- up; • difficulty collaborating with patient groups and investigators; • failure by our CROs, other third parties, or us to adhere to clinical trial **protocols and other** requirements; • failure to perform in accordance with the FDA' s or any other regulatory authority' s current good clinical practices (cGCPs) requirements, or applicable EMA or other regulatory guidelines in other countries; • occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits; • changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; • changes in the standard of care on which a clinical development plan was based, which may require new or additional trials; • the cost of clinical trials of our product candidates being greater than we anticipate; • clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon product development programs; and • delays in manufacturing, testing, releasing, validating, or importing / exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing. Any inability to successfully initiate or complete clinical trials could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, we may be required to or we may elect to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which our products have patent protection and may allow our competitors to bring products to market before we do **or sooner than anticipated** , which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. For example, we had been developing AL003 with AbbVie to treat patients with Alzheimer' s disease but on June 30, 2022, AbbVie provided written notice to us formalizing the decision to terminate the CD33 collaboration program ~~,~~ under which AL003 was being developed. ~~Additionally~~ **AbbVie** , ~~Innovent will not be continuing development of AL008, and we intend to re- acquire the rights we granted to Innovent for~~ - **or** ~~the development and commercialization of AL008. Innovent submitted an~~ **any** ~~IND with the~~ **other** ~~Chinese regulatory authorities~~ **collaboration partner may** , ~~and Alector is~~ in the **future** ~~process of obtaining relevant materials and information from Innovent. Alector plans to evaluate data and documentation from that IND application to potentially support an IND submission in the U. S. Furthermore, we decided~~ - **decide** to ~~close~~ **terminate collaboration programs based on, among** ~~the~~ **other** ~~Phase 1~~ **things, our** clinical trial ~~for our AL044 product candidate based on initial PK and tolerability~~ data. We could also encounter delays if a clinical trial is suspended or terminated by us, by the data safety monitoring board for such trial or by the FDA, EMA, or any other regulatory authority, or if the IRBs of the institutions in which such trials are being conducted suspend or terminate the participation of their clinical investigators and sites subject to their review. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA, or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions, lack of adequate funding to continue the clinical trial, **and** impacts of **worldwide economic conditions, including** the COVID- 19 pandemic and ~~subsequent variants~~ **other geopolitical events** . We may in the future advance product candidates into clinical trials and terminate such trials prior to their completion, which could adversely affect our business. Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process and delay, or potentially jeopardize our ability to commence product sales and generate revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. We may encounter difficulties enrolling patients in our clinical trials, and our clinical development activities could thereby be delayed or otherwise adversely affected. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. We ~~continue to pursue~~ **pursued** measures to enroll our Phase 3 INFRONT- 3 and Phase 2 INVOKE- 2 trials ~~. For~~ **, for** example, **by** ~~we are~~ opening additional clinical trial sites and expanding recruitment efforts to enroll the INFRONT- 3 trial. **We completed enrollment in those trials in the second half of 2023. Target enrollment of our Phase 3 INFRONT- 3 trial was based on feedback from the FDA and EMA.** However, we may experience difficulties in patient enrollment in ~~our~~ **other** clinical trials for a variety of reasons, including: • the size and nature of the patient population; • the patient eligibility criteria defined in the protocol, including biomarker- driven identification and / or certain highly- specific criteria related to stage of disease progression, which may limit the patient populations eligible for our clinical trials to a greater extent than competing clinical trials for the same indication that do not have biomarker- driven patient eligibility criteria; • the size of the study population required for analysis of the trial' s primary endpoints; • the proximity of patients to a trial site; • the design of the trial; • our ability to recruit clinical trial investigators with the appropriate competencies and experience; • delays in enrolling patients in our clinical trials caused by ~~the effects of~~ **worldwide economic conditions, including** the COVID- 19 pandemic and ~~subsequent variants~~ **other geopolitical events** ; • competing clinical trials for similar therapies or targeting patient populations meeting our patient eligibility criteria; • **availability of approved products that target the patient populations that we are seeking to enroll; •** clinicians' and

patients' perceptions as to the potential advantages and side effects of the product candidate being studied in relation to other available therapies and product candidates; • our ability to obtain and maintain patient consents; and • the risk that patients enrolled in clinical trials will not complete such trials or that we may not be able to collect data from such patients for any reason. Enrollment of patients in our clinical trials and maintaining patients in our ongoing clinical trials have been, and may continue to be, delayed or limited due to the effects of **worldwide economic conditions, including** the COVID- 19 pandemic and ~~subsequent variants. In addition, if additional COVID- 19 concerns or restrictions arise, including as a result of any new COVID- 19 variants, patients may not be able or willing to visit clinical trial sites for dosing or data collection purposes due to additional limitations on travel new physical distancing imposed or recommended by federal or state governments or patients' reluctance to visit the~~ **other geopolitical events** ~~clinical trial sites during the pandemic~~ . While the impact of the COVID- 19 pandemic is lessening, the effects resulting from the COVID- 19 pandemic ~~and subsequent variants~~ **or other public health concerns** could continue to delay or prevent the anticipated readouts from our clinical trials **. On May 11, 2023, the federal government ended the COVID- 19 public health emergency which ended a number of temporary changes made to federally funded programs while others continue to be in effect. The full impact of this termination of the national emergency and such policy changes on FDA and other regulatory policies and operations remain unclear. We or our partners may encounter difficulties or delays in enrollment of our clinical trials, due to the availability of newly approved therapies and competing products. For example, lecanemab has received FDA approval for the treatment of Alzheimer' s disease, and donanemab, an investigative drug for the treatment of Alzheimer' s disease, may receive FDA approval in 2024. As a result, our or our partners' ability to enroll participants in clinical trials for Alzheimer' s disease may be hampered if potential participants choose to instead avail themselves of approved therapies** . Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex, and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for use in each target indication. For those product candidates that are subject to regulation as biological drug products, we will need to demonstrate that they are safe, pure, and potent for use in their target indications. Each product candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies of our product candidates may not be predictive of the results of early- stage or later- stage clinical trials, and results of early **- stage** clinical trials of our product candidates may not be predictive of the results of later- stage clinical trials. The results of clinical trials in healthy volunteers or one set of patients or disease indications may not be predictive of those obtained in another. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen ~~,~~ and other clinical trial protocol elements **,** and the rate of dropout among clinical trial participants. Open- label or long- term extension studies may also extend the timing and cost of a clinical program substantially. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. This is particularly true in neurodegenerative diseases, where failure rates historically have been higher than in many other disease areas. Most product candidates that begin clinical trials are never approved by regulatory authorities for commercialization. For example, in our ongoing INVOKE- 2 Phase 2 clinical trial in Alzheimer' s disease, ~~cases of~~ **treatment- emergent MRI findings resembling** ARIA have been observed. ARIA are MRI findings ~~suggestive of~~ **that may include** vasogenic edema **, sulcal effusions, microhemorrhages and /** or ~~hemosiderin deposits~~ **superficial siderosis** . The incidence of ARIA has been shown to increase in ~~AD~~ **Alzheimer' s disease** patients with the administration of certain Alzheimer **'** s disease therapeutics, namely anti- β- amyloid antibodies. **We do not yet know whether the biological mechanism (s) causing these MRI changes are the same as that associated with the ARIA that has been described with anti- amyloid beta antibodies.** In our INVOKE- 2 Phase 2 clinical trial, most **cases resembling** ARIA ~~cases~~ were asymptomatic and non- serious. However, a small number of ARIA- related serious adverse events occurred ~~almost exclusively~~ **early in the trial** in patients with the APOE e4 / e4 genotype, as previously reported. To mitigate risks associated with ARIA, **at that time** we voluntarily discontinued dosing and enrollment of APOE e4 / e4 participants in our INVOKE- 2 Phase 2 clinical trial. Following these changes, a small number of ARIA- related serious adverse events occurred in patients who are non- homozygous for the APOE e4 allele. We continue to implement earlier MRI monitoring, ~~consistent with~~ **and are following** recently published guidelines for ARIA monitoring and management. We are conducting this study under the guidance of an IDMC, which is allowed to review unblinded data and to make trial recommendations **. If these measures are not successful in managing the ARIA in our trials, then the FDA, EMA or other regulatory authority may suspend clinical trials, delay or deny approval, or require a more restrictive label or box warning on an approved product** . We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. We cannot be certain that our current clinical trials or any other future clinical trials will be successful. Additionally, any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications, which could have a material adverse effect on our business, financial condition, and results of operations. In addition, even if such clinical trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates. Even if regulatory approval is secured for any of our product candidates, the terms

of such approval may limit the scope and use of our product candidates, which may also limit its commercial potential. **Further, even if regulatory approval is secured for any of our product candidates, we cannot be assured that a federal court will not modify, invalidate, or revoke such approval.** Our operations and financial results could be adversely impacted by the effects of the COVID- 19 pandemic ~~and subsequent variants~~ **or other global health concerns** in the United States and the rest of the world. **On May 11, 2023, the federal government ended the COVID- 19 public health emergency, which ended a number of temporary changes made to federally funded programs while some continue to be in effect.** The **full impact of this termination of the national emergency and the wind- down of the public health emergency on the FDA and other regulatory policies and operations is unclear. To the extent the** COVID- 19 pandemic **or other disease outbreaks continue to pose a threat to our ability to conduct our business operations as planned** , ~~including recent variants~~ **there can be no assurance** that **we will be able to avoid a material** ~~spread throughout the world, has adversely impacted global commercial activity. While the~~ impact **on our business from the pandemic or its consequences. Additionally, a resurgence** of the COVID- 19 pandemic **or other public health concerns could** ~~is lessening, such events have contributed to significant volatility and instability in financial markets, including a rising rate of inflation. The COVID- 19 pandemic and government responses created disruption in global supply chains and~~ adversely ~~impacted many industries. The pandemic could have a continued material adverse~~ impact ~~on~~ economic and market conditions ~~, including a continued rapid increase in inflation rates,~~ and lead to **an** ~~a further~~ extended period of **rapid inflation and** global economic slowdown. **In** ~~We continue to monitor the impact of the COVID- 19 pandemic closely. The extent to which the COVID- 19 pandemic will impact our operations or financial results is uncertain. The COVID- 19 pandemic and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, such as worker shortages; supply chain issues and disruptions; facilities and production suspensions; increases in inflation rates; and spikes in demand for certain goods and services, such as medical services and supplies. While the extent of the impact of the effects of the COVID- 19 pandemic on our business and financial results is uncertain, a continued and prolonged public health crisis such as the COVID- 19 pandemic could have a material adverse effect on our business, financial condition and results of operations. If as a result of the global COVID- 19 pandemic and any new variants that may later arise, we may experience disruptions, especially supply chain disruptions, that could have severe impacts on our business and clinical trials, such as: • the size and nature of the patient populations for our clinical trials; • delays or difficulties in recruiting, enrolling, and maintaining patients in our clinical trials; • delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff; • diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of clinical trials; • interruption of key clinical trial activities, such as clinical trial site monitoring, due to new limitations on travel imposed or recommended by federal or state governments, employers and others; • limitations in resources that would otherwise be focused on the conduct of our business or our clinical trials, including because of sickness or the desire to avoid contact with large groups of people or as a result of government- imposed " shelter in place " or similar working restrictions; • 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 used in our clinical trials; • changes in regulations as part of a response to the COVID- 19 pandemic which may require us to change the ways in which our clinical trials are conducted, or to discontinue the clinical trials altogether, or which may result in unexpected costs; • delays in necessary interactions with regulators, IRBs / ECs and other important agencies and contractors due to limitations in employee resources or forced furlough of government or contractor personnel; and • refusal of the FDA to accept data from clinical trials in affected geographies outside the United States. We may be required to develop, implement, and maintain additional clinical trial policies and procedures designed to help protect subjects from the COVID- 19 virus, which may delay our anticipated timelines for clinical studies and regulatory approval and increase our costs for clinical studies. For example, in March~~ 2020 **and 2021** , the FDA issued a ~~guidance, which the FDA subsequently updated, on conducting clinical trials during the pandemic, which describes a~~ number of ~~considerations for sponsors of clinical trials impacted by the pandemic. In 2020 and 2021, the FDA issued guidance on good manufacturing practice considerations for responding to COVID- 19 infection in employees in drug and biological products manufacturing, remote interactive evaluations of drug manufacturing and bioresearch monitoring facilities; and manufacturing, supply chain, and drug and biological product inspections, among others. In light of the spread of COVID- 19 variants, the FDA, EMA, and comparable foreign regulators may issue additional guidance and policies that may materially impact our business and clinical development timelines. Further changes to existing policies and regulations could increase our compliance costs or delay our clinical plans. To the extent our clinical studies are delayed or data from our clinical studies become compromised due to~~ COVID- 19 related ~~factors~~ **guidance documents for manufacturers and clinical trial sponsors** , ~~we may~~ **many of** ~~be required to expend additional resources to conduct additional studies and / or enroll more participants,~~ which **have expired** ~~could adversely affect our~~ **or were withdrawn with the expiration of the** ~~business operations and delay regulatory approval. The~~ COVID- 19 **public health emergency declaration** ~~pandemic continues to evolve, and the extent to which may impact our business, preclinical studies, and clinical trials will depend~~ on ~~future developments~~ **May 11** , **2023** ~~which are highly uncertain and cannot be predicted with confidence~~ , **although some** ~~such as the duration of the pandemic, travel restrictions, social distancing in the United States and other countries, business closures or business disruptions, the effectiveness of actions taken in the United States and other countries to contain and treat the disease, and the possibility of new variants. We may also suffer from any of the foregoing disruptions if the~~ COVID- 19 **related guidance documents** ~~virus and subsequent variants~~ continue ~~to develop and experience a resurgence~~ in ~~any particular country~~ **effect. Should the FDA issue additional guidance that mandates material changes to** ~~or~~ **our** ~~region~~ **clinical trials** in **response to a pandemic or** ~~the~~ **other** ~~future~~ **public health outbreak, the costs of such clinical trials may increase** . The spread of COVID- 19 and ~~its~~ subsequent variants has caused us to modify our business practices including by employing more

remote workers and operating under **a** hybrid work model. In addition, we may take actions as required by government authorities and regulations or that we determine are in the best interests of our employees, customers, partners, and suppliers. **We continue to maintain both a remote and hybrid work force, with** ~~Many~~ **many** ~~of our~~ employees ~~continue~~ **continuing** to work remotely ~~. Our ability to perform critical functions could be harmed. We may incur incremental expenses in connection with travel for remote employees, which we will continue to monitor; such expenses could adversely impact our results of operations. Additionally, certain third parties with whom we engage, including our collaborators, contract organizations, third party manufacturers, suppliers, clinical trial sites, regulators and other third parties with whom we conduct business have similarly adjusted their operations and assessed their capacity in light of the COVID- 19 pandemic and the impact of subsequent variants. If these third parties experience shutdowns or business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively impacted. For example, certain of our clinical trial sites experienced clinical trial visit delays, and we are aware that for a period of time, some participants in our then ongoing trials did not receive scheduled doses or assessments on time. These events could negatively impact the integrity, reliability, or robustness of the data from our clinical trials. We and our CROs made certain adjustments to the operation of such trials in an effort to ensure the monitoring and safety of patients and minimize risks to trial integrity during the pandemic in accordance with the guidance issued by the FDA, and we may be required to make further adjustments in the future due to any resurgence of COVID- 19~~ . To the extent the ongoing COVID- 19 pandemic or other ~~disease outbreaks~~ **public health concerns** adversely affect our operations and financial results, it may also have the effect of heightening many of the other risks described in this " Risk Factors " section. We face significant competition in an environment of rapid technological and scientific change **. Some competitors have achieved** , and there is a possibility that ~~our~~ **other** competitors ~~may~~ **will** achieve regulatory approval before us ~~or develop~~ **. Our competitors'** therapies ~~that are~~ **may be** safer, more advanced, or more effective than ours, which may negatively impact our ability to successfully market or commercialize any product candidates we may develop and ultimately harm our financial condition. The development and commercialization of new drug products is highly competitive. Moreover, the neurodegenerative field is characterized by strong and increasing competition, and a strong emphasis on intellectual property. We may face competition with respect to any of our product candidates that we seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization. There are a number of large pharmaceutical and biotechnology companies that are currently pursuing the development of products for the treatment of neurodegenerative diseases, including FTD, Alzheimer' s disease, Parkinson' s disease, and ALS ~~, as well as for the treatment of cancer~~ . Many of these current or potential competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. For example, in January 2023, FDA **granted accelerated** ~~approved~~ **approval , and in July 2023, FDA granted full approval to** lecanemab, an anti- amyloid beta protofibril antibody for the treatment of ~~Alzeimer~~ **Alzheimer** ' s disease developed by Eisai Co., Ltd. (Eisai) and Biogen Inc. (Biogen). Eisai has also filed marketing authorization applications **for lecanemab** in Japan and Europe **. Eisai further announced that they expect to initiate a Phase 1 clinical trial with a TREM2 agonist in Alzheimer' s disease in 2024** . Additionally, in July 2022, Biogen announced that the FDA accepted ~~a~~ **an** NDA for tofersen, ~~an~~ **a** drug for ALS associated with mutations in superoxide dismutase 1 (SOD1), and in September 2022, Amylyx Pharmaceuticals, Inc. announced that the FDA approved RELYVRIO ™ (sodium phenylbutyrate and taurursodiol) for the treatment of adults with ALS **. The FDA granted accelerated approval to tofersen in April 2023, to be marketed as QALSODY ™. In seeking accelerated approval, Biogen pointed to biomarker data and the slowing of disease progression in a longer- term follow- up in their study. In addition, companies such as Prevail Therapeutics, Inc. (Prevail) and Passage Bio, Inc. (Passage Bio) have developed gene therapy based products (PR006 and PBFT02, respectively) for the treatment of FTD- GRN. Vigil Therapeutics has developed small molecule (VG- 3927) and antibody (iluzanebart) candidates targeting TREM2. There are also pharmaceutical and biotechnology companies, such as Denali Therapeutics, Inc. (Denali), F. Hoffman La Roche Ltd. (Roche), and Aliada Therapeutics, Inc. (Aliada), that are developing technologies for the transport of products across the blood- brain barrier** . Other competitors are pursuing product candidates that act on the same targets or through comparable mechanisms of action. Furthermore, mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early- stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient enrollment in clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop. Furthermore, currently approved products could be discovered to have application for treatment of neurodegenerative disease indications, which could give such products significant regulatory and market timing advantages over any of our product candidates. Our competitors also may obtain FDA, EMA, or other regulatory approval for their products more rapidly than we may obtain approval for ours **, including through fast track designation, priority review, accelerated approval or breakthrough therapy designation,** and may obtain orphan drug exclusivity from the FDA for indications our product candidates are targeting, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, products or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors. In addition,

we could face litigation or other proceedings with respect to the scope, ownership, validity, and / or enforceability of our patents relating to our competitors' products **,** and our competitors may allege that our products infringe, misappropriate, or otherwise violate their intellectual property. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize. The manufacture of our product candidates is complex, and we may encounter difficulties in production. If we or any of our third- party manufacturers encounter such difficulties, or fail to meet rigorously enforced regulatory standards, our ability to provide supply of our product candidates for clinical trials or our products **, if approved,** for patients ~~, if approved~~ , could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure. The processes involved in manufacturing our product candidates are complex, expensive, highly- regulated, and subject to multiple risks. Further, as product candidates are developed through preclinical studies to late- stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials. In order to conduct clinical trials of our product candidates, or supply commercial products, if approved, we will need to manufacture them in large quantities. Our CDMOs may be unable to successfully **produce or** increase the manufacturing **scale or** capacity for any of our product candidates in a timely or cost- effective manner, or at all. In addition, quality issues may arise during scale- up activities. If **any** ~~our CDMOs are unable to successfully scale up the manufacture~~ of **the foregoing occurs** ~~our product candidates in sufficient quality and quantity~~ , the development, testing, and clinical trials of that product candidate may be delayed or become infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained **in any or all jurisdictions in which such approval or launch is intended** , which could significantly harm our business. The same risk would apply to our internal manufacturing facilities, should we in the future decide to build internal manufacturing capacity. In addition, building internal manufacturing capacity would carry significant risks in terms of being able to plan, design, and execute on a complex project to build manufacturing facilities in a timely and cost- efficient manner. In addition, the manufacturing process for any products that we may develop is subject to FDA, EMA, and foreign regulatory authority approval processes, and continuous oversight, and we will need to contract with manufacturers who can meet all applicable FDA, EMA, and foreign regulatory authority requirements, including complying with current good manufacturing practices (cGMPs) on an ongoing basis. If we or our third- party manufacturers are unable to reliably produce products to specifications acceptable to the FDA, EMA, or other regulatory authorities, ~~including recent FDA guidance on good manufacturing practice considerations for responding to COVID- 19 infection in employees in drug and biological products manufacturing, as well as any future guidance and regulations,~~ we may not obtain or maintain the approvals we need to commercialize such products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our CDMOs will be able to manufacture the approved product to specifications acceptable to the FDA, EMA, or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates, impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, financial condition, results of operations, and growth prospects. If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any product candidates we may develop, we may not be successful in commercializing those product candidates if and when they are approved. We do not have a sales or marketing infrastructure and have no experience in the sale, marketing, or distribution of pharmaceutical products. To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing, and commercial support infrastructure to sell, or participate in commercial activities with our collaborators for, some of our product candidates if and when they are approved. There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists ~~is~~ **are** expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel. Factors that may inhibit our efforts to commercialize any approved product on our own include: • our inability to recruit and retain adequate numbers of effective sales, marketing, reimbursement, customer service, medical affairs, and other support personnel; • the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future approved products; • our inability to negotiate arrangements for formulary access, reimbursement, and other acceptance by payors; • the inability to price our products at a sufficient price point to ensure an adequate and attractive level of profitability ~~;~~ **,** and our ability to recognize revenue from such prices; • restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population; • the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and • unforeseen costs and expenses associated with creating an independent commercialization organization. If we enter into arrangements with third parties to perform sales, marketing, commercial support, and distribution services, our product revenue or the profitability of product revenue may be lower than if we were to market and sell any products we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize our product candidates or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not

establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates if approved. Even if any product candidates we develop receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors, and others in the medical community necessary for commercial success. The commercial success of any of our products will depend upon its degree of market acceptance by physicians, patients, third- party payors, and others in the medical community. Even if any product candidates we may develop receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors, and others in the medical community. The degree of market acceptance of any product candidates we may develop, if approved for commercial sale, will depend on a number of factors, including: • the efficacy and safety as demonstrated in clinical trials and published in peer- reviewed journals; • the potential and perceived advantages compared to alternative treatments; • the ability to offer our products for sale at competitive prices; • sufficient third-party coverage or reimbursement; • the ability to offer appropriate patient access programs, such as co- pay assistance; • the extent to which physicians recommend our products to their patients; • convenience and ease of dosing and administration compared to alternative treatments; • the clinical indications for which the product candidate is approved by FDA, EMA, or other regulatory agencies; • product labeling or product insert requirements of the FDA, EMA, or other comparable foreign regulatory authorities, including any limitations, contraindications, or warnings contained in a product' s approved labeling; • restrictions on how the product is distributed; • the timing of market introduction of competitive products; • publicity concerning our products or competing products and treatments; • the strength of marketing and distribution support; and • the prevalence and severity of any side effects. If any product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenue, and we may not become profitable. Any products we commercialize may become subject to unfavorable pricing regulations, third- party reimbursement practices, or healthcare reform initiatives, which would harm our business. The regulations that govern marketing approvals, pricing, and reimbursement for new drugs vary widely from country to country. In the United States, recently enacted or potential future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to ~~continuing~~ **continued** governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay **or render commercially inviable** our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval. Our ability to successfully commercialize any products that we may develop also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and third- party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U. S. healthcare industry and elsewhere is cost containment. Government authorities and third- party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Government authorities currently impose mandatory discounts for certain patient groups, such as Medicare, Medicaid, and Veterans Affairs hospitals, and may seek to increase such discounts at any time. Future regulation may negatively impact the price of our products, if approved. Increasingly, third- party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. In order to get reimbursement, physicians may need to show that patients have superior treatment outcomes with our products compared to standard of care drugs, including lower- priced generic versions of standard of care drugs. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval. In the United States, no uniform policy of coverage and reimbursement for products exists among third- party payors **,** and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the medicine is approved by the FDA, EMA, or other comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third- party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government- funded and private payors for any approved products we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize product candidates, and our overall financial condition. Current and future CMS coverage

restrictions on classes of drugs that encompass our product candidates, including our candidates for treating Alzheimer' s disease, could have a material adverse impact on our ability to commercialize our product candidates, if approved, generate revenue and attain profitability. It is unclear how future CMS coverage decisions and policies will impact our business. Our product candidates for which we intend to seek approval may face biosimilar competition sooner than anticipated. Even if we are successful in achieving regulatory approval to commercialize a product candidate ahead of our competitors, our product candidates may face competition from biosimilar products. In the United States, our product candidates are regulated by the FDA as biologic products and we intend to seek approval for these product candidates pursuant to the BLA pathway. The Biologics Price Competition and Innovation Act of 2009 (BPCIA) created an abbreviated pathway for the approval of biosimilar and interchangeable biologic products. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as " interchangeable " based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our product candidates. We believe that any of our product candidates approved as a biologic product under a BLA should qualify for the 12- year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to Congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products ~~for competing products~~ **entitled to the 12- year period of exclusivity** , potentially creating the opportunity for competition sooner than anticipated. Moreover, the extent to which a biosimilar product, once approved, will be substituted for any one of our reference products in a way that is analogous to traditional generic substitution for non- biologic products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. In addition, a competitor could decide to forego the biosimilar approval path and submit a full BLA after completing its own preclinical studies and clinical trials. In such cases, any exclusivity to which we may be eligible under the BPCIA would not prevent the competitor from marketing its product as soon as it is approved. In Europe, the European Commission has granted marketing authorizations for several biosimilar products pursuant to a set of general and product class- specific guidelines for biosimilar approvals issued over the past few years. In Europe, a competitor may reference data supporting approval of an innovative biological product, but will not be able to get it on the market until 10 years after the time of approval of the innovative product. This 10- year marketing exclusivity period will be extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. In addition, companies may be developing biosimilar products in other countries that could compete with our products, if approved. If competitors are able to obtain marketing approval for biosimilars referencing our product candidates, if approved, such ~~products~~ **product candidates** may become subject to competition from such biosimilars, with the attendant competitive pressure and potential adverse consequences. Such competitive products may be able to immediately compete with us in each indication for which our product candidates may have received approval. Any legal proceedings or claims involving or against us could be costly and time- consuming to defend and could harm our reputation regardless of the outcome. We may ~~in the future~~ become subject to legal proceedings and claims that arise in the ordinary course of business, including intellectual property, data privacy, product liability, employment, class action or derivative, whistleblower and other litigation claims, and governmental and other regulatory investigations and proceedings. Such matters can be time- consuming, divert management' s attention and resources, cause us to incur significant expenses or liability, or require us to change our business practices. In addition, the expense of litigation and the timing of this expense from period to period are difficult to estimate, subject to change, and could adversely affect our financial condition and results of operations. Because of the potential risks, expenses, and uncertainties of litigation, we may, from time to time, settle disputes, even where we have meritorious claims or defenses, by agreeing to settlement agreements. Any of the foregoing could adversely affect our business, financial condition, and results of operations. If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates. We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk when and if we commercialize any products. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing, or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, or a breach of warranties. Claims could also be asserted under state consumer protection acts **or in countries outside the United States under the applicable legal regimes** . If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit testing and commercialization of our product candidates. Even successful defense **or negotiations of a settlement** would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in: • decreased or interrupted demand for our products; • injury to our reputation; • withdrawal of clinical trial participants and inability to continue clinical trials; • initiation of investigations by regulators; • costs to defend the related litigation; • a diversion of management' s time and our resources; • substantial monetary awards to trial participants or patients; • product recalls, withdrawals or labeling, marketing, or promotional restrictions; • loss of revenue; • exhaustion of any available insurance and our capital resources; and • the inability to commercialize any product candidate. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with collaborators. Our insurance policies may have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay

such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise. Risks Related to Regulatory Approval and Other Legal Compliance Matters The regulatory approval processes of the FDA, EMA, and comparable foreign regulatory authorities are lengthy, time consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be substantially harmed. The time required to obtain approval by the FDA, EMA, and comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials, and depends upon numerous factors, including the type, complexity, and novelty of the product candidates involved. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate' s clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical, or other studies. We have not submitted **an application** for ~~,~~ or obtained regulatory approval for any product candidate, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval. Further, development of our product candidates and / or regulatory approval may be delayed for reasons beyond our control. For example, the U. S. federal government has experienced and may in the future experience shutdown or budget sequestration, which could result in significant reductions to the FDA' s budget, employees, and operations, which may lead to slower response times and longer review periods, potentially affecting our ability to progress development of our product candidates or obtain regulatory approval for our product candidates. To the extent FDA and other regulatory authorities experience any delays or limited resources in reviewing our regulatory applications or requests for meetings and / or guidance, and inspection of manufacturing facilities prior to regulatory approval **, e. g.,** due to the effects of **worldwide economic conditions, including** the COVID- 19 pandemic or other **geopolitical events, or other** reasons, we may experience significant delays in our anticipated timelines for our clinical studies and / or **for** seeking regulatory approvals, which could adversely affect our business. Applications for our product candidates could fail to receive regulatory approval in an initial or subsequent indication for many reasons, including but not limited to the following: • the FDA, EMA, or comparable foreign regulatory authorities may disagree with the design, implementation, or the interpretation of the results of our clinical trials; • the FDA, EMA, or comparable foreign regulatory authorities may determine that our product candidates are not safe and effective, only moderately or insufficiently effective or have undesirable or unintended side effects, toxicities, or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use; • the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval **;** • the FDA, EMA, or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials; • the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA, BLA, or other submission or to obtain regulatory approval in the United States or elsewhere; • we may be unable to demonstrate to the FDA, EMA **,** or comparable foreign regulatory authorities that a product candidate' s risk- benefit ratio, on its own or when compared to the standard of care, is acceptable; • the FDA, EMA, or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures, and specifications, or facilities of third- party manufacturers with which we contract for clinical and commercial supplies; and • the approval policies or regulations of the FDA, EMA, or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval or resulting in delays in our regulatory approval, including, for example, in connection with the FDA' s approval of Biogen' s Aduhelm in Alzheimer' s disease amid questions regarding the underlying data, as well as the ~~ongoing~~ government investigation of the FDA' s approval process for Aduhelm. This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations, and growth prospects **. In addition, the FDA and other regulatory authorities may change their policies, issue additional regulations or revise existing regulations, any of which could delay our ability to obtain approvals, increase the costs of compliance or restrict our ability to maintain any regulatory approvals we may have obtained. If the Supreme Court reverses or curtails the Chevron doctrine, which gives deference to regulatory agencies such as FDA to interpret relevant statutes, more companies may bring lawsuits against FDA to challenge longstanding FDA decisions and policies which could undermine FDA' s authority, lead to uncertainties in the industry, and disrupt FDA' s normal operations, which could delay FDA' s review of our regulatory submissions** . Our product candidates may cause undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences. Adverse events or other undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay, or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, EMA, or other comparable foreign regulatory authorities. Drug- related side effects could affect patient recruitment, the ability of enrolled patients to complete the study, and / or result in potential product liability claims. We are required to maintain product liability insurance pursuant to certain of our development and commercialization agreements. We may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. A successful product liability claim or series of claims brought against us could adversely affect our results of operations, business, and reputation. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, withdrawal of clinical trial participants, costs due to related litigation, distraction of management' s attention from our primary business, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our product candidates, and decreased demand for our product candidates, if approved for commercial sale. **Treatment- emergent MRI findings resembling** ARIA have been observed **.** in our ~~ongoing~~ INVOKE- 2 Phase 2 clinical trial

~~in AD~~. ARIA are MRI findings ~~suggestive of~~ **that may include** vasogenic edema **, sulcal effusions, microhemorrhages and /** or ~~hemosiderin deposits~~ **superficial siderosis** . The incidence of ARIA has been shown to increase in ~~AD~~ **Alzheimer' s disease** patients with the administration of certain Alzheimer ~~'~~ **’** s disease therapeutics, namely anti- β- amyloid antibodies. **We do not yet know whether the biological mechanism (s) causing the MRI changes in INVOKE- 2 are the same as that associated with the ARIA that has been described with anti- amyloid beta antibodies.** In **INVOKE- 2, most cases resembling ARIA were asymptomatic and non- serious. However, a small number of ARIA- related serious adverse events occurred early in the trial in patients with the APOE e4 / e4 genotype, as previously reported. To mitigate risks associated with ARIA, at that time we voluntarily discontinued dosing and enrollment of APOE e4 / e4 participants in** our INVOKE- 2 Phase 2 clinical trial ~~, most ARIA cases were asymptomatic and non- serious~~. ~~However~~ **Following these changes** , a small number of ARIA- related serious adverse events occurred ~~almost exclusively in patients with the APOE e4 / e4 genotype, as previously reported. To mitigate risks associated with ARIA, we voluntarily discontinued dosing and enrollment of APOE e4 / e4 participants in our INVOKE- 2 Phase 2 clinical trial. Following these changes, a small number of ARIA- related serious adverse events occurred~~ in patients who are non- homozygous for the APOE e4 allele. We continue to implement earlier MRI monitoring, ~~consistent with~~ **and are following** recently published guidelines for ARIA monitoring and management. We are conducting this study under the guidance of an IDMC, which is allowed to review unblinded data and to make trial recommendations. Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects or adverse events caused by such products, a number of potentially significant negative consequences could result, including but not limited to: • regulatory authorities may withdraw approvals of such product and cause us to recall our products; • regulatory authorities may require additional warnings on the label; • we may be required to change the way the product is administered, monitor patients over the course of treatment, or conduct additional clinical trials or post- approval studies; • we may be required to create a Risk Evaluation and Mitigation Strategy plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers, ~~requiring~~ pre- prescription screening or ongoing monitoring for ARIA and / or other adverse events, and / or other elements, such as boxed warning on the packaging **(for example, as required for lecanemab)** , to assure safe use; • we could be sued and held liable for harm caused to patients; and • our reputation may suffer. Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, financial condition, results of operations, and growth prospects. We currently are and may continue in the future to conduct clinical trials for our product candidates outside the United States, and the FDA, EMA, and applicable foreign regulatory authorities may not accept data from such trials. We currently are and may continue in the future choose to conduct one or more of our clinical trials outside the United States, including in Europe, Latin America, Asia **,** or Australia. The acceptance of study data from clinical trials conducted outside the United States or another jurisdiction by the FDA, EMA, or applicable foreign regulatory authority may be subject to certain conditions. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to cGCP regulations. Additionally, the FDA’ s clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, EMA, or any applicable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction, as regulatory authorities in different jurisdictions may impose different requirements for approval, including requirements with respect to trial design or trial diversity. If the FDA, EMA, or any applicable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time- consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction. Our reliance on genetic screening and use of biomarkers to align patient risk profiles with targeted intervention may eventually require us to develop and use companion diagnostics, which could result in additional regulatory requirements that would need to be met to enable its use. Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions. Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA or EMA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing, and promotion of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the United States, including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to regulatory approval. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties, and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any partner we work with ~~fail~~ **fails** to comply with the regulatory requirements in international markets or ~~fail~~ **fails** to receive applicable marketing approvals, our target market will be reduced, and our ability to realize the full market potential of our product candidates will be harmed. Even if we obtain regulatory approval for a product candidate, our products will remain subject to extensive post- marketing requirements and regulatory scrutiny. If any of our product candidates are approved, they will be subject to ongoing

regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record- keeping, conduct of post- marketing studies, and submission of safety, efficacy, and other post- market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities. Manufacturers and manufacturers' facilities are required to comply with extensive requirements imposed by the FDA, EMA, and comparable foreign regulatory authorities, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA, BLA, or marketing authorization application (MAA). Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control. Any regulatory approvals that we receive for our product candidates will be subject to limitations on the approved indicated uses for which the product may be marketed and promoted or to the conditions of approval (including any requirement to implement a Risk Evaluation and Mitigation Strategy), or contain requirements for potentially costly post- marketing testing. We will be required to report certain adverse reactions and production problems, if any, to the FDA, EMA, and comparable foreign regulatory authorities. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to ~~assure~~ **ensure** compliance. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post- approval marketing and promotion of products to ensure that they are manufactured, marketed, and distributed only for the approved indications and in accordance with the provisions of the approved labeling. We will have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product' s approved label. As such, we may not promote our products for indications or uses for which they do not have approval. The holder of an approved NDA, BLA, or MAA must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process. We could also be asked to conduct post- marketing clinical trials to verify the safety and efficacy of our products in general or in specific patient subsets. If original marketing approval was obtained via the accelerated approval pathway, we could be required to conduct a successful post- marketing clinical trial to confirm clinical benefit for our products. An unsuccessful post- marketing study or failure to complete such a study could result in the withdrawal of marketing approval. If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things: • issue warning letters that would result in adverse publicity; • impose civil or criminal penalties; • suspend or withdraw regulatory approvals; • suspend any of our ongoing clinical trials; • refuse to approve pending applications or supplements to approved applications submitted by us; • impose restrictions on our operations, including closing our contract manufacturers' facilities; • seize or detain products; or • require a product recall. Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected. We have ~~received~~ orphan drug designation from the FDA for latozinemab ~~and AL101~~ for treatment of FTD and may seek orphan drug designation for some of our other product candidates, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug status, including market exclusivity, which may cause our revenue, if any, to be reduced. Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200, 000 in the United States, or a patient population greater than 200, 000 in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting an NDA or BLA. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user- fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. While ~~we have obtained~~ **latozinemab has (and AL101 previously had)** orphan drug designation ~~from the FDA for latozinemab and AL101~~ for treatment of FTD, we may be unable to reap the benefits associated with orphan drug status. In addition, we ~~plan to seek orphan drug designations for some of our other product candidates in the future but~~ may be unable to obtain ~~an~~ orphan drug designation for any additional product candidates **, if we seek such designation** . If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan drug exclusivity. This means that the FDA may not approve any other NDA or BLA application to market the same drug or biologic for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan exclusivity, if FDA revokes the orphan drug designation, or if FDA finds that the holder of the orphan exclusivity has not assured the availability of sufficient quantities of the orphan product to meet the needs of patients with the disease or condition for which the drug was designated. Even though the FDA has approved orphan drug status for latozinemab ~~and AL101~~ for treatment of FTD, the FDA can still approve other drugs that have a different active ingredient for use in treating FTD. Furthermore, orphan drug exclusivity does not prevent the FDA from approving another marketing application for the same drug product for a different indication before the expiration of the orphan exclusivity period. As discussed above, in litigation in 2021, a court disagreed with the FDA' s longstanding position that orphan drug exclusivity only applies to the approved use or

indication within an eligible disease, and not to all uses or indications within the entire designated disease or condition. This appellate court decision created uncertainty in the application of orphan drug exclusivity. In January ~~,~~ 2023, the FDA published a notice in the Federal Register to clarify that while the agency complies with the applicable court ruling ~~. The~~ **, the** FDA intends to continue tying the scope of orphan- drug exclusivity to the uses or indications for which a drug is approved, which permits other sponsors to obtain approval of a drug for new uses or indications within the same orphan designated disease or condition that has not yet been approved. It is unclear how future litigation, legislation, agency decisions, and administrative actions will impact the scope of orphan drug exclusivity. We have ~~received~~ **obtained** Fast Track designation **and Breakthrough Therapy designation** from the FDA **,** for latozinemab ~~and AL101~~ for the treatment of patients with FTD carrying specific genetic mutation in the granulin gene, but we may be unable to obtain or maintain the benefits associated with the Fast Track designation. Fast Track designation is designed to facilitate the development and expedite the review of therapies which treat serious conditions and fill an unmet medical need. Programs with Fast Track designation may benefit from early and frequent communications with the FDA, potential priority review, and the ability to submit a rolling application for regulatory review. Fast Track designation applies to both the product and the specific indication for which it is being studied. In December 2019, the FDA granted Fast Track designation for latozinemab **,** and in January 2020, the FDA granted Fast Track designation for AL101, each for the treatment of patients with FTD carrying specific genetic mutations in the granulin gene. If our clinical development program does not continue to meet the criteria for Fast Track designation, or if our clinical trials are suspended or terminated, or put on clinical hold due to unexpected adverse events or issues with clinical supply, we may not realize all the benefits associated with the Fast Track program **. For example, we inactivated the AL101 IND for FTD in the third quarter of 2023, and therefore Fast Track designation no longer applies** . Furthermore, Fast Track designation does not change the standards for approval. Fast Track designation alone does not guarantee qualification for the FDA' s priority review procedures **. In February 2024, the FDA granted Breakthrough Therapy Designation to latozinemab for the treatment of FTD- GRN. The benefits of Breakthrough Therapy designation include the same benefits as Fast Track designation, plus intensive guidance from the FDA to ensure an efficient drug development program** . Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations. Third- party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could impact our ability to sell our products profitably. In particular, in 2010, the Patient Protection and Affordable Care Act, or Affordable Care Act (ACA) was enacted, which, among other things, subjected biologic products to potential competition by lower- cost biosimilars, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjected manufacturers to new annual fees and taxes for certain branded prescription drugs, and provided incentives to programs that increase the federal government' s comparative effectiveness research. In June 2021, the United States Supreme Court held that Texas and other challengers had no legal standing to challenge the ACA, dismissing the case without specifically ruling on the constitutionality of the ACA. Accordingly, the ACA remains in effect in its current form. It is unclear how this Supreme Court decision, future litigation, or healthcare measures promulgated by ~~the Biden administration~~ **administrative or legislative action** will impact our business, financial condition, and results of operations. Complying with any new legislation or changes in healthcare regulation could be time- intensive and expensive, resulting in a material adverse effect on our business. Under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than they receive on the sale of approved products, which could have a material impact on our business. In August 2022, Congress passed the Inflation Reduction Act of 2022, which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high- priced single source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out- of- pocket prescription drug costs for beneficiaries, among other changes. **In March 2023, the CMS published its first guidance on how negotiations will be conducted, starting in 2026 for high expenditure drugs as determined and selected by Health and Human Services. In June 2023, CMS issued a revised guidance for the Medicare Drug Price Negotiation Program under the Inflation Reduction Act. Various industry stakeholders, including pharmaceutical companies, the U. S. Chamber of Commerce, the National Infusion Center Association, the Global Colon Cancer Association, and the Pharmaceutical Research and Manufacturers of America, have initiated lawsuits against the federal government asserting that the price negotiation provisions of the Inflation Reduction Act are unconstitutional. The impact of these judicial challenges as well as future legislative, executive, and administrative actions and agency rules implemented by the government on us and the pharmaceutical industry as a whole is unclear.** The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved. Many states have proposed or enacted legislation that seeks to indirectly or directly regulate pharmaceutical drug pricing, such as by requiring biopharmaceutical manufacturers to publicly report proprietary pricing information or to place a maximum price ceiling on pharmaceutical products purchased by state agencies. For example, a number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our

products candidates. Such initiatives and legislation may affect the prices we may obtain or demand for any of our product candidates for which we may obtain regulatory approval. Further, in April 2022, CMS released a national policy for coverage of aducanumab and any future monoclonal antibodies directed against amyloid approved by the FDA with an indication for use in treating Alzheimer' s disease. CMS reiterated this policy in January 2023 in connection with the **accelerated** approval of lecanemab. According to the two- part National Coverage Determination (NCD), Medicare will cover monoclonal antibodies that target amyloid (or plaque) for the treatment of Alzheimer' s disease that receive traditional approval from the FDA ~~when furnished in accordance with the coverage criteria specified below~~ under coverage with evidence development. **Following full approval of lecanemab in July 2023,** CMS **reiterated that it would broadly** ~~will also provide enhanced access and coverage ---~~ **cover the medication while continuing to gather** ~~for Medicare patients participating in CMS- approved studies, such as a~~ data ~~collection through routine clinical practice or registries~~ . Additionally, for drugs that FDA has not determined to have shown a clinical benefit or that received an accelerated approval, Medicare will provide coverage in FDA or National Institutes of Health approved clinical trials **. In February 2023, CMS again reiterated these policies in rejecting a petition from the Alzheimer' s Association to provide wider coverage for lecanemab. In June 2023, CMS announced that Medicare will cover new Alzheimer' s drugs with traditional FDA approval when a physician and clinical team participate in CMS' registry to collect evidence on how these drugs work in the real world** . Current and future CMS coverage restrictions on classes of drugs that encompass our product candidates could have a material adverse impact on our ability to commercialize our product candidates, if approved, generate revenue and attain profitability. It is unclear how future CMS coverage decisions and policies will impact our business. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. A number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance ~~burdens~~ **requirements** and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our products. **Further, FDA recently authorized the state of Florida to import certain prescription drugs from Canada for a period of two years to help reduce drug costs, provided that Florida' s Agency for Health Care Administration meets the requirements set forth by the FDA. Other states may follow Florida.** We are unable to predict the future course of federal or state healthcare legislation in the United States directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. These and any further changes in the law or regulatory framework that reduce our revenue or increase our costs could also have a material and adverse effect on our business, financial condition and results of operations. The continuing efforts of the government, insurance companies, managed care organizations, and other payors of healthcare services to contain or reduce costs of healthcare and / or impose price controls may adversely affect: • the demand for our product ~~,~~ if we obtain regulatory approval; • our ability to receive or set a price that we believe is fair for our products; • our ability to generate revenue and achieve or maintain profitability; • the level of taxes that we are required to pay; and • the availability of capital. We expect that the above healthcare reform measures and others that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, lower reimbursement, and new payment methodologies. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. This could lower the price that we receive for any approved product. ~~The~~ **There** ~~Biden administration and the states~~ may ~~pass~~ **be** further **federal and state** legislation and regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures. Any denial in coverage or reduction in reimbursement from Medicare or other government- funded programs may result in a similar denial or reduction in payments from private payors, which may prevent us from being able to generate sufficient revenue, attain profitability, or commercialize our product candidates, if approved. In addition, increased scrutiny by the U. S. Congress of the FDA' s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post- marketing testing and other requirements. Our employees, independent contractors, consultants, commercial partners, and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements. We are exposed to the risk of fraud, misconduct, or other illegal activity by our employees, independent contractors, consultants, commercial partners, and vendors. Misconduct by these parties could include intentional, reckless, and negligent conduct that fails to: • comply with the laws of the FDA, EMA, and other comparable foreign regulatory authorities; • provide true, complete, and accurate information to the FDA, EMA, and other comparable foreign regulatory authorities; • comply with clinical or manufacturing standards; • comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws; or • report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. In particular, research, sales, marketing, education, and other business arrangements in the healthcare industry are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, educating, marketing and promotion, sales and commission, certain customer incentive programs, and other business arrangements generally. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our

business, including the imposition of significant fines or other sanctions. If we fail to comply with healthcare laws, we could face substantial penalties and our business, operations, and financial conditions could be adversely affected. If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations will be subject to various federal and state fraud and abuse laws. The laws that may impact our operations include the following: • Among other things the federal Anti- Kickback Statute, prohibits, persons from knowingly and willfully soliciting, receiving, offering, or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order, or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. 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. In addition, the government may assert that a claim including items or 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 civil and criminal false claims laws and civil monetary penalty laws, including the False Claims Act, impose criminal and civil penalties, including through civil " qui tam " or " whistleblower " actions, against individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other third- party payors that are false or fraudulent or knowingly making a false statement to improperly avoid, decrease, or conceal an obligation to pay money to the federal government. Similar to the federal Anti- Kickback Statute, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation. • The federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e. g., public or private) and knowingly and willfully falsifying, concealing, or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. • HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH) and their respective implementing regulations, impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security, and transmission of individually identifiable health information without appropriate authorization. • The federal Physician Payment Sunshine Act, created under the ACA, and its implementing regulations, require applicable manufacturers of drugs, devices, biologicals, and medical supplies for which payment is available under Medicare, Medicaid, or the Children' s Health Insurance Program to report annually to the U. S. Department of Health and Human Services under the Open Payments Program, information related to payments and other transfers of value made to covered recipients, including physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non- physician healthcare professionals (such as nurse practitioners and physician assistants, among others) and teaching hospitals, and information regarding ownership and investment interests held by physicians (as defined by law) and their immediate family members. • Federal consumer protection and unfair competition laws broadly regulate marketplace activities and activities that potentially harm consumers. • Analogous state and foreign laws and regulations, such as state and foreign anti- kickback, false claims, consumer protection, and unfair competition laws may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales, and marketing arrangements, as well as submitting claims involving healthcare items or services reimbursed by any third- party payer, including commercial insurers. • 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 that otherwise restricts payments that may be made to healthcare providers and other potential referral sources. • State laws also require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration, and items of value provided to healthcare professionals and entities. • State and foreign laws also govern the privacy and security of health information in certain circumstances, ~~many of~~ **such as Washington' s My Health, My Data Act,** which **, among other things, provides for a private right of action. Many of these laws** differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could, despite our efforts to comply, be subject to challenge under one or more of such laws. Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal, and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid, and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our product candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws. If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business. We and any contract manufacturers and suppliers we engage are subject to numerous federal, state, and local environmental, health, and safety laws, regulations, and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the

emission and discharge of hazardous materials into the ground, air, and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third- party facilities. We also could incur significant costs associated with civil or criminal fines and penalties. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research, product development, and manufacturing efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty, and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Our business is subject to complex and evolving U. S. and foreign laws and regulations relating to security, privacy and data protection. These laws and regulations are subject to change and uncertain interpretation, and could result in claims, changes to our business practices, or monetary penalties, and otherwise may harm our business. A wide variety of state, national, and international laws and regulations apply to security and cybersecurity requirements and the collection, use, retention, protection, disclosure, transfer, and other processing of personal data **, including the data obtained in our clinical trials. These laws and regulations include the General Data Protection Regulation (GDPR) in the European Union and similar requirements in other jurisdictions, as well as state privacy laws within the United States** . These security and data protection and privacy- related laws and regulations are evolving and may result in ever- increasing regulatory and public scrutiny and escalating levels of enforcement and sanctions. We are continually working to comply with these laws, and we **have devoted, and** anticipate needing **to continue** to devote significant additional resources to our compliance efforts. It is possible that ~~the~~ new legislation **or regulations** may impose new obligations and requirements on similarly situated companies, and these laws **or regulations** may be interpreted and applied in a manner that is inconsistent from jurisdiction to jurisdiction **, that can result in new** or **modified compliance obligation or that may be** inconsistent with our ~~current~~ policies and practices. Our actual or perceived failure to adequately comply with applicable laws and regulations relating to security, privacy **,** and data protection, or to protect our systems, personal data **,** and other data we process or maintain, could result in regulatory fines, investigations and enforcement actions, penalties and other liabilities, claims for damages by affected individuals, and damage to our reputation, **and could impact our ability to use, process, disclose, or transfer data obtained in our clinical trials,** any of which could materially affect our business, financial condition, results of operations **,** and prospects. Inadequate funding for the FDA and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business. The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. In the past, the U. S. government has experienced budgetary shutdowns and certain regulatory agencies, such as the FDA, have had to furlough critical FDA and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations. Our business activities may be subject to the Foreign Corrupt Practices Act (FCPA), similar anti- bribery and anti- corruption laws, and other regulations. Our business activities may be subject to the FCPA and similar anti- bribery or anti- corruption laws, regulations, or rules of other countries in which we operate, including the U. K. Bribery Act. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non- U. S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non- U. S. governments. Additionally, in many other countries, the healthcare providers who engage in our clinical trials or prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these investigators, prescribers and purchasers are subject to regulation under the FCPA. Recently the SEC and Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of

these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of our facilities, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition. Risks Related to Our Reliance on Third Parties We expect to depend on collaborations with third parties for the research, development, and commercialization of certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates. We currently use and expect to continue to use third- party collaborators for the research, development, and commercialization of certain of the product candidates we may develop, including our arrangements with AbbVie, GSK, and Adimab. **As discussed previously, GSK can terminate its GSK Agreement with us, subject to certain notice provisions, in its entirety and for convenience at any time. Similarly, AbbVie can terminate the AbbVie Agreement for convenience at any point during the term of the agreement, including the research, development, and clinical trial process. Adimab can terminate its agreements with us in the event of uncured materials breaches, and subject to certain notice requirements. In the event that one of our current third- party collaborators discontinues its collaboration with us, we may not be able to find a suitable alternative collaboration partner or partners, or we may need to obtain and expend additional and unanticipated capital to maintain our current development programs.** Our likely collaborators for any other collaboration arrangements include large and mid- sized pharmaceutical companies, regional and national pharmaceutical companies, biotechnology companies, and academic institutions. Such arrangements with any third parties, generally provide us with shared or limited control over the amount and timing of resources that our collaborators dedicate to the development or potential commercialization of any product candidates we may seek to develop with them. Our ability to generate revenue from these arrangements with commercial entities will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of our current collaborations or any collaboration that we may enter into. Collaborations involving our research programs, or any product candidates we may develop, pose risks to us **,** including the following: • collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations; • collaborators may decide to not pursue development and commercialization of any product candidates we develop or may elect not to continue or renew development or commercialization programs **, for example,** based on clinical trial results, changes in the collaborator' s strategic focus or available funding **, the collaborator' s assessment regarding the commercial viability of the product candidate,** or external factors such as an acquisition that diverts resources or creates competing priorities or collaborators may elect to fund or commercialize a competing product; • collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, provide insufficient quantities of materials for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing; • collaborations may be terminated in their entirety or with respect to certain product candidates or technologies and, if so terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates or technologies; • collaborators may not properly obtain, maintain, enforce, or defend intellectual property or proprietary rights relating to our product candidates or research programs or may use our proprietary information in such a way as to expose us to potential litigation or other intellectual property related proceedings, including proceedings challenging the scope, ownership, validity, and enforceability of our intellectual property; • collaborators may own or co- own intellectual property covering our product candidates or research and development programs that results from our collaboration with them, and in such cases, we may not have the exclusive right to commercialize such intellectual property or such product candidates or research programs; • we may need the cooperation of our collaborators to enforce or defend any intellectual property we contribute to or that arises out of our collaborations, which may not be provided to us; • collaborators may control certain interactions with regulatory authorities, which may impact our ability to obtain and maintain regulatory approval of our product candidates; • disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of our product candidates or research programs or that result in costly litigation or arbitration that diverts management attention and resources; • collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates or research programs if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours; • collaborators may restrict us from researching, developing, or commercializing certain products or technologies without their involvement; • collaborators with manufacturing, marketing, or distribution rights to one or more product candidates may not commit sufficient resources to the manufacture, marketing, or distribution of such product candidates; • we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control; • collaborators may grant sublicenses to our technology or product candidates or undergo a change of control, and the sublicensees or new owners may decide to take the collaboration in a direction which is not in our best interest; • collaborators may become bankrupt, which may significantly delay our research or development programs, or may cause us to lose access to valuable technology, know- how, or intellectual property of the collaborator relating to our products, product candidates, or research programs; • key personnel at our collaborators may leave, which could negatively impact our ability to productively work with our collaborators; • collaborations may require us to incur short and long- term expenditures, issue securities that dilute our stockholders, or disrupt our management and business; • if our collaborators do not satisfy their obligations under our agreements with them, if they terminate our collaborations with them, or if we fail to satisfy our obligations to our collaborators, we may not be able to develop or commercialize product candidates as planned; • **the terms of a collaboration agreement may be amended in a manner that could negatively impact us; •** collaborations may require us to share in development and commercialization costs pursuant to budgets that we do not fully

control, and our failure to share in such costs could have a detrimental impact on the collaboration or our ability to share in revenue generated under the collaboration ~~and~~ ; • collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all ~~. If~~ **; and • if** a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our development or commercialization program under such collaboration could be delayed, diminished, or terminated. For example, AbbVie, after reviewing the CD33 collaboration program with us, decided to terminate the CD33 collaboration program, under which AL003 was being developed. Additionally, **GSK is** ~~Innovent will not be~~ conducting the **PROGRESS** ~~AL008 first in human studies in China, Innovent will not be continuing development of AL008, and we intend to re-~~ **AD Phase 2 trial** ~~acquire the rights we granted to Innovent for the development and commercialization of AL008. Innovent submitted an IND~~ with **AL101 / GSK4527226** ~~the Chinese regulatory authorities~~ , and Alector is **responsible for up to $ 140** ~~in the process of obtaining relevant materials and information from Innovent~~ . **5 million of the costs of such study. As such, the timing at which such costs are incurred, and the day- to- day operations of conducting such study are not within** Alector **' s control** ~~plans to evaluate data and documentation from that IND application to potentially support an IND submission in the U. S~~ . We may face significant competition in seeking appropriate collaborations. For example **,** business combinations among biotechnology and pharmaceutical companies have resulted in a reduced number of potential collaborators. In addition, the negotiation process is time- consuming and complex, and we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue. We may not realize the benefit of collaborations if we or our collaborator elects not to exercise the rights granted under the agreement or if we or our collaborator are unable to successfully integrate a product candidate into existing operations and company culture **. For example, AbbVie may decide not to exercise its exclusive option to develop and commercialize our TREM2 program, and in that case, we would not receive a $ 250. 0 million milestone payment for such opt- in or any future payments, and all rights to the TREM2 program would revert back to us** . In addition, if our agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator' s technology or intellectual property or require us to stop development of those product candidates completely. We may also find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. Many of the risks relating to product development, regulatory approval, and commercialization described in this " Risk Factors " section also apply to the activities of our collaborators and any negative impact on our collaborators may adversely affect us. We expect to rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research, or testing. We currently rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators, to conduct some aspects of our research and preclinical testing and our clinical trials. Any of these third parties may terminate their engagements with us or be unable to fulfill their contractual obligations. If we need to enter into alternative arrangements, it would delay our product development activities. Our reliance on these third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. **For example, if our CROs or clinical sites deviate from the clinical protocol or cGCPs, then such deviations could have serious negative impacts on our trials, including exclusion of patients or sites from our trials, which could put patients at risk or make assessment of the clinical endpoints infeasible or inconclusive.** Moreover, the FDA requires us to comply with cGCPs for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible, reproducible, and accurate and that the rights, integrity, and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on ~~a~~ government- sponsored databases within certain timeframes. We may also be exposed to additional liabilities if our contracted third parties engage in activities associated with improper use of information obtained in the course of patient recruitment for our clinical trials, cGCP noncompliance or noncompliance under applicable privacy laws, which could result in regulatory sanctions and cause serious harm to our reputation and business operations. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, **clinical data to advance development of any of our product candidates or to achieve** marketing approvals for any **of our** product candidates ~~we may develop~~ and **we** will not be able to, or may be delayed in our efforts to, successfully commercialize our medicines. We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors, including with the shipment of any drug supplies, could delay clinical development or marketing approval of any product candidates we may develop or commercialization of our medicines, producing additional losses and depriving us of potential product revenue. We contract with third parties for the manufacture of materials for our research programs, preclinical studies, clinical trials, and for commercialization of any product candidates that we may develop. Additionally, GSK, and AbbVie, have certain product manufacturing rights under their respective agreements. This reliance on third parties carries and may increase the risk that we

will not have sufficient quantities of such materials, product candidates, or any medicines that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts. We do not have any manufacturing facilities. We currently rely on CDMOs for the manufacture of our materials for preclinical studies and clinical trials and expect to continue to do so for preclinical studies, clinical trials, and for commercial supply of any product candidates that we may develop. We currently have established relationships with several CDMOs ~~,~~ for the manufacture of each of our product candidates, as well as with GSK ~~, and AbbVie,~~ for latozinemab and AL101, and **with AbbVie** for AL002 ~~, respectively~~ . We may be unable to establish any further agreements with CDMOs or to do so on acceptable terms. Even if we are able to establish agreements with third- party manufacturers, reliance on CDMOs entails additional risks, including: • the possible breach of the manufacturing agreement by the third party; • the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; • reliance on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting; and • the inability to produce required volume in a timely manner and to quality standards. Third- party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our CDMOs or collaboration partners **,** to comply with applicable regulations could result in clinical holds on our trials, sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures, or recalls of product candidates or medicines, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business, financial condition, results of operations, and prospects. Any medicines that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future third- party manufacturers could delay clinical development or marketing approval. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer and may incur added costs and delays in identifying and qualifying any such replacement. Furthermore, securing and reserving production capacity with contract manufacturers may result in significant costs. Our current and anticipated future dependence upon others for the manufacture of any product candidates we may develop ~~or medicines~~ may adversely affect our future profit margins and our ability to commercialize any medicines that receive marketing approval on a timely and competitive basis. We, and the CDMO partners on which we rely, depend on third- party suppliers for key raw materials used in our manufacturing processes, and the loss of these third- party suppliers or their inability to supply us with adequate raw materials, ~~whether due to the effects of the COVID- 19 pandemic or otherwise,~~ could harm our business. We and the CDMO partners on which we rely depend on third- party suppliers for the supply of the raw materials required for the production of our product candidates, and we expect to continue to depend on third-party manufacturers for the commercial supply of any of our product candidates for which we obtain marketing approval. ~~The~~ **Their** dependence on these third- party suppliers and the challenges faced in obtaining adequate supplies of raw materials involve several risks, including supply chain issues caused by the effects of **worldwide economic conditions, including** the COVID- 19 pandemic, **national security concerns, export or import restrictions, trade tariffs, or other geopolitical events,** limited control over pricing, the availability of such materials, the quality of such materials, and delivery schedules **. To the extent our business relies on customers, vendors, or suppliers in countries where the U. S. government has imposed any of these or other trade restrictions, our business may experience a material adverse effect** . As a small company, our negotiation leverage is limited, and we are likely to get lower priority than our competitors who are larger than we are. We do not have long- term supply agreements, and we purchase our required drug product on a development manufacturing services agreement or purchase order basis. We cannot be certain that ~~the~~ suppliers will continue to provide the quantities of these raw materials that are required or satisfy the anticipated specifications and quality requirements. Any supply interruption in limited or sole sourced raw materials, including those caused by the effects of **worldwide economic conditions including** the COVID-19 pandemic ~~and subsequent variants~~ **or other geopolitical events,** could materially harm our ability to manufacture our product candidates until a new source of supply, if any, can be identified and qualified. In such an event, we may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Any performance failure on the part of the suppliers could delay the development and potential commercialization of our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business. Risks Related to Our Intellectual Property If we are unable to obtain and maintain patent protection for any product candidates we develop, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize any product candidates we may develop may be adversely affected. Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary product candidates and other technologies we may develop. We seek to protect our proprietary position by filing patent applications in the United States and abroad relating to our core programs and product candidates, as well as other technologies that are important to our business. As our product candidates enter and progress through clinical development, we continue to pursue intellectual property protection with respect to certain aspects of those product candidates. For example, we have filed or intend to file patent applications on aspects of our technology and core product candidates; however, there can be no assurance that any such patent applications will issue as granted patents. Furthermore, in cases in which we have only filed provisional patent applications on certain aspects of our technology and product candidates, each of those provisional patent applications is not eligible to become an issued patent until, among other things, we file a non- provisional patent application within 12 months of the filing date of the applicable provisional patent application. Any failure to file a non- provisional patent application within this timeline could cause us to lose the ability to obtain patent protection for the inventions disclosed in the associated provisional patent applications. Furthermore, in some cases, we may not be able to obtain issued claims covering compositions relating to our core programs and product candidates, as well as other technologies that are important to our

business, and instead may need to rely on filing patent applications with claims covering a method of use and / or method of manufacture for protection of such core programs, product candidates, and other technologies. There can be no assurance that any such patent applications will issue as granted patents, and even if they do issue, such patent claims may be insufficient to prevent third parties, such as our competitors, from utilizing our technology. Any failure to obtain or maintain patent protection with respect to our core programs and product candidates could have a material adverse effect on our business, financial condition, results of operations, and prospects. If any of our patent applications, or those of our collaborators, do not issue as patents in any jurisdiction, we may not be able to compete effectively. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our patents or those of our collaborators with respect to our product candidates. With respect to both our intellectual property and that of our collaborators related to our product candidates, we cannot predict whether the patent applications we and our collaborators are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors or other third parties. The patent prosecution process is expensive, time- consuming, and complex, and we or our collaborators may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into nondisclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, CDMOs, consultants, advisors, and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we or our collaborators were first to file for patent protection of such inventions. If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical technology and product candidates would be adversely affected. The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Our or our collaborators' pending and future patent applications may not result in patents being issued which protect our product candidates or other technologies or which effectively prevent others from commercializing competitive technologies and product candidates. Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we or our collaborators license or own currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents to which we or our collaborators have rights may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether product candidates or other technologies will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non- infringing manner which could materially adversely affect our business, financial condition, results of operations and prospects. The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. We or our collaborators may be subject to a third- party pre- issuance submission of prior art to the United States Patent and Trademark Office (USPTO) or foreign patent offices or become involved in opposition, derivation, revocation, reexamination, post- grant and inter partes review, inventorship dispute, or interference proceedings or other similar proceedings challenging our or our collaborators' patent rights. An adverse determination in any such submission, proceeding, or litigation could reduce the scope of, or invalidate or render unenforceable, such patent rights, allow third parties to commercialize our product candidates or other technologies and compete directly with us, without payment to us. Moreover, we, or any one of our collaborators, may have to participate in post- grant challenge proceedings, such as oppositions in a foreign patent office, in which a third party challenges the features of patentability with respect to our or our collaborators' patents and patent applications. Such challenges may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection for our product candidates and other technologies. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. If we or our collaborators are unsuccessful in any such proceeding or other inventorship dispute, we may be required to obtain and maintain licenses from third parties. Such licenses may not be available on commercially reasonable terms or at all, or may be non-exclusive. If we are unable to obtain and maintain such licenses, we may need to cease the development, manufacture, and commercialization of one or more of the product candidates we may develop. The loss of exclusivity or the narrowing of our owned and licensed patent claims could limit our ability to stop others from using or commercializing similar or identical technology and products. In addition, given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our intellectual property may not provide us with rights to exclude others for sufficient period of time from commercializing products similar or identical to ours. Some of our patents and patent applications may be co-owned with third parties. In addition, collaborators or future licensors may co- own their patents and patent applications with

other third parties with whom we do not have a direct relationship. Our rights to certain of these patents and patent applications may be dependent, in part, on inter- institutional or other operating agreements between the joint owners of such patents and patent applications, who are not parties to our license agreements. If our collaborators or future licensors do not have exclusive control of the grant of licenses under any such third- party co- owners' interest in such patents or patent applications or we are otherwise unable to secure such exclusive rights, such co- owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology to the extent such products and technology are not also covered by our intellectual property. In addition, we may need the cooperation of any such co- owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects. Our rights to develop and commercialize are subject, in part, to the terms and conditions of agreements with others, including terms and conditions regarding intellectual property rights. We rely on certain patent rights and proprietary technology from third parties that are important or necessary to the development of our product candidates, and development and commercialization of our product candidates are subject to the terms and conditions of certain collaboration agreements with third parties. For example, in 2014 we entered into the Adimab Collaboration Agreement with Adimab. Under the 2014 Adimab Collaboration Agreement, we are developing antibodies discovered by Adimab in our latozinemab and AL101 product candidates, and we are developing an antibody optimized by Adimab in our AL002 product candidate. In August 2019, we entered into a new collaboration agreement with Adimab for development of antibodies for use in future programs. In 2021, we entered into another collaboration agreement with Adimab, which ~~grants~~ **granted** us an exclusive option to obtain a specified number of engineered sequences ~~.~~ discovered or optimized by Adimab and directed against targets that we select. Additionally, in October 2017, we entered into an agreement with AbbVie to co- develop and commercialize medicines with AbbVie to treat Alzheimer' s disease and other neurodegenerative diseases. In July 2021, we entered into the GSK Agreement to collaborate on the global development and commercialization of the progranulin- elevating monoclonal antibodies, latozinemab and AL101. Our agreements with Adimab, AbbVie, GSK, and other agreements we enter into in the future may not provide exclusive rights to use certain intellectual property and technology retained by the collaborator in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future. As a result, we may not be able to prevent competitors or other third parties from developing and commercializing competitive products that utilize technology retained by such collaborators to the extent such products are not also covered by our intellectual property. In addition, subject to the terms of any such agreements, we may not have the right to control the preparation, filing, prosecution, and maintenance, and we may not have the right to control the enforcement and defense of certain patents and patent applications relating to or affecting our development candidates. ~~In addition~~ **For example** , the GSK Agreement provides GSK with certain rights with respect to preparation, filing, prosecution, maintenance, enforcement, and defense of certain patents and patent applications. We cannot be certain that patents and patent applications as to which preparation, filing, prosecution, maintenance, enforcement, or defense are controlled by our collaborators will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If our collaborators fail to prosecute, maintain, enforce, and defend such patents, or lose rights to those patents or patent applications, our rights ~~as~~ to such patents may be reduced or eliminated, our right to develop and commercialize any of our product candidates that are **the** subject of such rights could be adversely affected, and we may have a reduced ability to prevent competitors from making, using, and selling competing products. In addition, even where we have the right to control prosecution of patent applications we have licensed to and from collaborators, we may still be adversely affected or prejudiced by actions or inactions of our collaborators that took place prior to the date upon which we assumed control ~~over~~ **of** patent prosecution. Furthermore, our or our collaborators' patents may be subject to a reservation of rights by one or more third parties. For example, we received an award from the National Institute of Health in support of our research into the production and characterization of novel therapeutic antibodies against the neurotrophic factor PGRN degrading receptor SORT1. As a result, the U. S. government may have certain rights to resulting intellectual property. When new technologies are developed with U. S. government funding, the U. S. government generally obtains certain rights in any resulting patents, including a non- exclusive license authorizing the U. S. government to use the invention or to have others use the invention on its behalf. The U. S. government' s rights may also permit it to disclose the funded inventions and technology to third parties and to exercise march- in rights to use or allow third parties to use the technology developed using U. S. government funding. The U. S. government may exercise its march- in rights if it determines that action is necessary because we fail to achieve the practical application of the government funded technology, or because action is necessary to alleviate health or safety needs, to meet requirements ~~of~~ **for public use under** federal regulations, or to give preference to U. S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in facilities in the United States in certain circumstances and if **the U. S. government does not waive** this requirement ~~is not waived~~ . Any exercise by the U. S. government of such rights or by any third party of its reserved rights **could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects. Moreover, the government may implement new policies and guidelines that impose certain risks on our intellectual property. On July 28, 2023, President Biden issued an Executive Order that emphasized a preference for domestic manufacturing for subject inventions under the Bayh Dole Act. On December 7, 2023, the National Institutes of Science and Technology (NIST) published a draft framework for expanding the use of the government' s march- in rights under Bayh Dole. To date, the government has not exercised its march- in rights against any federal funding recipient (assignee or exclusive licensee). However, the framework proposes using the price of pharmaceuticals as a factor in determining whether a federally funded drug is sufficiently accessible to the public and as a basis for the exercise of the government' s march- in rights. If the final framework applies to certain inventions developed with government funding and no waivers or exceptions apply, the U. S. government could exercise its march- in rights for**

these subject inventions under the new framework, which could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects. If we fail to comply with our obligations in the agreements under which we option or license intellectual property rights from our collaborators or future licensors or otherwise experience disruptions to our business relationships with our collaborators or future licensors, we could lose intellectual property rights that are important to our business. We have entered into agreements with our collaborators to option or license certain intellectual property and may need to obtain additional intellectual property rights from others to advance our research or allow commercialization of product candidates we may develop. It is possible that we may be unable to obtain additional intellectual property rights at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third- party patents do not exist which might be enforced against our current technology, manufacturing methods, product candidates, or future methods or products resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and / or other forms of compensation to third parties, which could be significant. In addition, each of our agreements with collaborators do, and we expect our future agreements will, impose various economic, development, diligence, commercialization, and other obligations on us. Certain of our collaboration agreements also require us to meet development timelines, or to exercise commercially reasonable efforts to develop and commercialize licensed products. In spite of our efforts, our collaborators might conclude that we have materially breached our obligations under such agreements and might therefore terminate or seek damages under the agreements, thereby removing or limiting our ability to develop and commercialize products and technology covered by these agreements. If termination of these agreements causes us to lose the rights to certain patents or other intellectual property, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties may have the freedom to seek regulatory approval of, and to market, products similar to or identical to ours and we may be required to cease our development and commercialization of certain of our product candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and growth prospects. Moreover, disputes may arise regarding intellectual property subject to a collaboration agreement, including: • the scope of the option or license rights granted under the agreement and other interpretation- related issues; • the extent to which our technology and processes infringe on intellectual property of the collaborator that is not subject to the option or license rights granted under the agreement; • the sublicensing of patent and other rights under our collaborative development relationships; • our diligence obligations under the agreement and what activities satisfy those diligence obligations; and • the inventorship and ownership of inventions and know- how resulting from the joint creation or use of intellectual property by our collaborators and us and our other partners. In addition, the agreements under which we currently have rights to option or license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and growth prospects. Moreover, if disputes over intellectual property that we have optioned or licensed prevent or impair our ability to maintain our current arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and growth prospects. We may not be able to protect our intellectual property and proprietary rights throughout the world. Filing, prosecuting, and defending patents on our product candidates and other technologies in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in or into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products, and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert counterclaims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. 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 patents. If we, our collaborators **,** or any of our future licensors is forced to grant a license to third parties with respect to any patents relevant to our

business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected. Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. Periodic maintenance fees, renewal fees, annuity fees, and various other government fees on patents and applications will be due to the USPTO and various government patent agencies outside of the United States over the lifetime of our owned or licensed patents and applications. In certain circumstances, we rely on our collaborators or licensing partners to pay these fees due to U. S. and non- U. S. patent agencies. The USPTO and various non- U. S. government agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. We also are dependent on our collaborators or licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non- compliance can result in abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and growth prospects. The ongoing conflict between Russia and Ukraine, including the sanctions targeting Russia, could interfere with filing of patent applications, prosecution of applications, and maintenance of issued patents in Russia, Ukraine, and via the Eurasian Patent Office. For example, the conflict and sanctions could interfere with payment of filing fees, extension fees, and annuities. The conflict and sanctions could also interfere with enforcement or defense of patents issued in Russia, Ukraine, and via the Eurasian Patent Office. ~~The~~ **Similarly, the ongoing** conflict **between Israel and Hamas could interfere with our ability to prosecute, maintain, enforce and defend patents in Israel. These conflicts** and associated sanctions could therefore increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any future issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Changes in U. S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products. Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. For example, under the Leahy- Smith America Invents Act (the America Invents Act), the first inventor to file a patent application in the United States is entitled to the patent on an invention regardless of whether another party was the first to invent the claimed invention. Therefore, a third party that filed a patent application in the USPTO after March 2013, but before us, could be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This possibility requires us to be cognizant of the time from invention to the time of filing a patent application. Because patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we were the first to file any patent application related to our product candidates or other technologies. Certain procedures at the USPTO under the America Invents Act could affect the way patent applications are prosecuted and also may affect patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post- grant proceedings, including post- grant review, inter partes review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. In addition, the patent positions of companies in the development and commercialization of pharmaceuticals are particularly uncertain. Rulings from the U. S. Supreme Court and the U. S. Court of Appeals for the Federal Circuit have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. ~~This combination~~ **For example, in the recent Supreme Court decision, Amgen Inc. v. Sanofi, 143 S. Ct. 1243 (2023), the Court affirmed a Federal Circuit decision and held that patent claims reciting a genus** of ~~events has~~ **antibodies defined by a functional property were invalid because the specification did not provide sufficient teaching to make and use the full scope of the claimed genus. These rulings have** created uncertainty with respect to the validity and enforceability of patents, once obtained **, for example, with respect to written description and enablement requirements** . Depending on future actions by the U. S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future. Issued patents covering our product candidates and other technologies could be found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad. If we initiated legal proceedings against a third party to enforce a patent covering our product candidates or other technologies, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the United States, 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, including lack of novelty, obviousness, written description, or 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. Third parties may raise claims challenging the validity or enforceability of our patents before administrative bodies in the United States or abroad, even outside the context of litigation.

Such mechanisms include re- examination, post- grant review, inter partes review, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e. g., opposition proceedings). Such proceedings could result in the revocation of, cancellation of, or amendment to our patents in such a way that they no longer cover our product candidates or other technologies. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we or our licensing partners and the patent examiner were unaware during prosecution. If a third party 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 our product candidates or other technologies. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations, and growth prospects. If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be materially harmed. Depending upon the timing, duration, and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U. S. patents may be eligible for limited patent term extension under the Hatch- Waxman Act. The Hatch- Waxman Act permits a patent term extension of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar extensions as compensation for patent term lost during regulatory review processes are also available in certain foreign countries and territories, such as in Europe under a Supplementary Protection Certificate. However, we may not be granted an extension in the United States and / or foreign countries and territories because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is shorter than what we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and growth prospects could be materially harmed. We may be subject to claims challenging the inventorship of our patents and other intellectual property. We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents, trade secrets, or other intellectual property as an inventor or co- inventor. For example, we may have inventorship disputes arise from conflicting obligations of employees, consultants, or others who are involved in developing our product candidates or other technologies. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership of our patents, trade secrets, or other intellectual property. If the defense of any such claims fails, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates and other technologies. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and growth prospects. If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. In addition to seeking patents for our product candidates and other technologies, we also rely on trade secrets and confidentiality agreements to protect our unpatented know- how, technology, and other proprietary information and to maintain our competitive position. We consider trade secrets and know- how to be one of our primary sources of intellectual property. Trade secrets and know- how can be difficult to protect. We expect our trade secrets and know- how to over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel from academic to industry scientific positions. We seek to protect these trade secrets and other proprietary technology, in part, by entering into non- disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate and academic collaborators, outside scientific collaborators, CROs, CDMOs, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants, train our employees not to bring or use proprietary information or technology from former employers to us or in their work, and remind former employees when they leave their employment of their confidentiality obligations. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. Despite our 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. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, 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 or other third party, our competitive position would be materially and adversely harmed. We may not be successful in obtaining, through acquisitions or otherwise, necessary rights to our product candidates or other technologies. Many pharmaceutical companies, biotechnology companies, and academic institutions that are competing with us in the field of neurodegeneration therapy may have patents and have filed and are likely filing patent applications potentially relevant to our business. In order to avoid infringing these third- party patents, we may find it necessary or prudent to obtain licenses to such patents from such third- party intellectual property holders. We may also require licenses from third parties for certain technologies for use with future product candidates. In addition, with respect to any patents we co- own with third parties, we may wish to obtain licenses to such co- owners' interest to such patents. However, we may be unable to secure such licenses or otherwise acquire any rights to compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for our future product candidates. The licensing or acquisition of third- party intellectual property rights is a competitive area, and more established companies may pursue strategies to license or acquire third- party intellectual property rights that we may consider attractive or necessary. These established companies may have a

competitive advantage over us due to their size, capital resources, and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third- party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third- party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and growth prospects. We may be subject to claims that our employees, consultants, or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property. Many of our employees, consultants, and advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors and potential competitors. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know- how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual' s current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management. In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and growth prospects. Third-party claims of intellectual property infringement, misappropriation, or other violation against us or our collaborators may prevent or delay the development and commercialization of our product candidates and other technologies. The field of discovering treatments for neurodegenerative diseases is highly competitive and dynamic. Due to the focused research and development that is taking place by various companies, including us and our competitors, in this field, the intellectual property landscape is in flux, and it may remain uncertain in the future. Additionally, the technology used in our product candidates is still in development and no products utilizing similar technology have yet reached the market. As such, there may be significant intellectual property related litigation and proceedings relating to our, and other third party, intellectual property and proprietary rights in the future. Our commercial success depends in part on our and our collaborators' ability to develop, manufacture, market, and sell any product candidates that we develop and to use our proprietary technologies without infringing, misappropriating, and otherwise violating the patents and other intellectual property rights of third parties. There is a substantial amount of complex litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, and we may become subject to, or threatened with, such actions in the future, regardless of their merit. In addition, we may undertake costly administrative proceedings for challenging third party patents, including post- grant, derivation, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. Numerous U. S. and foreign issued patents and pending patent applications owned by third parties exist in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates and other technologies may give rise to claims of infringement of the patent rights of others. We cannot be assured that our product candidates and other technologies that we have developed, are developing, or may develop in the future will not infringe existing or future patents owned by third parties. We may not be aware of patents that have already been issued and that a third party, for example, a competitor in the fields in which we are developing product candidates, and other technologies might assert are infringed by our current or future product candidates or other technologies, including claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover our product candidates or other technologies. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our product candidates or other technologies, could be found to be infringed by our product candidates or other technologies. In addition, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates or other technologies may infringe. Third parties may have patents or obtain patents in the future and claim that the manufacture, use or sale of our product candidates or other technologies infringes upon these patents. In the event that any third -party claims that we infringe their patents or that we are otherwise employing their proprietary technology without authorization and initiates litigation against us, even if we believe such claims are without merit, a court of competent jurisdiction could hold that such patents are valid, enforceable, and infringed by our product candidates or other technologies. In this case, the holders of such patents may be able to block our ability to manufacture or commercialize the applicable product candidate or technology unless we obtain a license under the applicable patents, or until such patents expire or are finally determined to be held invalid or unenforceable. Such a license may not be available on commercially reasonable terms or at all. Even if we are able to obtain a license, the license would likely obligate us to pay license fees or royalties or both, and the rights granted to us might be nonexclusive, which could result in our competitors gaining access to the same intellectual property. If we are unable to obtain a necessary license to a third- party patent on commercially reasonable terms, we may be unable to commercialize our product candidates or other technologies, or such commercialization efforts may be significantly delayed, which could in turn significantly harm our business. Defense of infringement claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and other employee resources from our business, and may impact our reputation. In the event of a successful claim of infringement against us, we may be enjoined from further developing or commercializing our

infringing product candidates or other technologies. In addition, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties, and / or redesign our infringing product candidates or technologies, which may be impossible or require substantial time and monetary expenditure. In that event, we would be unable to further develop and commercialize our product candidates or other technologies, which could harm our business significantly. Engaging in litigation to defend against third parties alleging that we have infringed, misappropriated, or otherwise violated their patents or other intellectual property rights is very expensive, particularly for a company of our size, and time- consuming. Some of our competitors may be able to sustain the costs of litigation or administrative proceedings more effectively than we can because of greater financial resources. Patent litigation and other proceedings may also absorb significant management time. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings against us could impair our ability to compete in the marketplace. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and growth prospects. We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights ~~,~~ or to defend against allegations of patent infringement, which could be expensive, time consuming, and unsuccessful. Competitors may infringe our patents or the patents of our licensing partners, or we may be required to defend against claims of infringement. In addition, our patents or the patents of our licensing partners also may become involved in inventorship, or validity disputes. To counter or defend against such claims can be expensive and time consuming. In an infringement proceeding, a court may decide that a patent in which we have an interest is invalid or unenforceable, the other party' s use of our patented technology falls under the safe harbor to patent infringement under 35 U. S. C. § 271 (e) (1), or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented, or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations, and growth prospects. Intellectual property rights do not necessarily address all potential threats. The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example: • others may be able to make products that are similar to our product candidates or utilize similar technology but that are not covered by the claims of the patents that we license or may own; • our future licensors or collaborators, might not have been the first to invent the claimed inventions covered by the issued patents or pending patent applications that we license in the future; • we, or our current or future licensors or collaborators, might not have been the first to file patent applications covering certain of our or their inventions; • others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights; • it is possible that our current or future pending owned or licensed patent applications will not lead to issued patents; • issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties; • our competitors or other third parties might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; • we may not develop additional proprietary technologies that are patentable; • the patents of others may harm our business; and • we may choose not to file a patent application in order to maintain certain trade secrets or know- how, and a third party may subsequently file a patent application covering such intellectual property. Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations, and growth prospects. Risks Related to Our Operations We are highly dependent on our key personnel, and if we are not successful in attracting, motivating, and retaining highly qualified personnel, ~~especially in light of a competitive hiring and compensation environment,~~ we may not be able to successfully implement our business strategy. Our

ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract, motivate, and retain highly qualified managerial, scientific, and medical personnel. We are highly dependent on our leadership, including our Chief Executive Officer, Dr. Arnon Rosenthal. The loss of the services provided by any of our executive officers, other key employees, and other scientific and medical advisors, and our inability to either find suitable replacements in the event of such loss or to attract senior management personnel to fill open positions ~~, especially in light of a highly competitive hiring and wage environment,~~ could result in delays in the development of our product candidates and harm our business. We conduct our operations at our facility in South San Francisco, California, ~~in~~ a region that is headquarters to many other ~~biopharmaceutical~~ **biotechnology** companies ~~and~~ **as well as** many academic and research institutions ~~. Competition for skilled personnel is intense and the turnover rate can be high, especially in light of recent competitive hiring and wage environment~~ , which may limit our ability to hire **competitively** and retain highly qualified personnel ~~on acceptable terms or at all. We expect that we may need to recruit talent~~ from **or** outside of our region ~~and doing so may be costly and difficult~~ . To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided and will continue to provide restricted stock **units** , stock option grants, and other equity awards that vest over time. The value to employees of these equity grants that vest over time may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Although we have employment agreements with our key employees, these employment agreements provide for at- will employment, which means that any of our employees could leave our employment at any time, with or without notice. If we are unable to attract and incentivize quality personnel on acceptable terms, or at all, it may cause our business and operating results to suffer. We will need to effectively manage the size and capabilities of our organization. As of December 31, ~~2022~~ **2023** , we had ~~273~~ **244** full- time employees. As our development plans and strategies develop **, and as we progress development of our product candidates and move towards commercialization** , we will be required to add additional managerial, operational, financial, and other personnel. We will need to effectively manage the size and capabilities of our organization and any future growth through significant responsibilities on members of management, including: • identifying, recruiting, integrating, retaining, and motivating additional employees; • managing our internal development efforts effectively, including the clinical and FDA review process for our current and future product candidates, while complying with our contractual obligations to collaborators and other third parties; • expanding our operational, financial and management controls, reporting systems, and procedures; and • managing increasing operational and managerial complexity. Our future financial performance and our ability to continue to develop and, if approved, commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth. Our management may also have to divert a disproportionate amount of its attention away from day- to- day activities in order to manage these growth activities **. Our near- term financial performance and development plans also require that we manage our personnel, and we recently committed to a plan to reduce our workforce to better align our resources with our current strategic priorities. We initiated a reduction in force impacting approximately 30 employees across the organization effective March 2023. One- time restructuring charges associated with the reduction in force were approximately $ 1. 7 million, primarily consisting of personnel expenses such as salaries, one- time severance payments, and other benefits. Most cash payments related to these expenses were paid out during the first half of 2023. Any future reductions in or restructurings of our workforce, whether due to market downturns, uncertainty in capital markets, other macroeconomic changes or any other reason, may generate severance and other costs that may cause our business and operating results to suffer** . We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors, and consultants to provide certain services. There can be no assurance that the services of these independent organizations, advisors, and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, if at all. If we are not able to effectively **manage or** expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop our product candidates, our clinical trials may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval of our product candidates, and accordingly, may not achieve our research, development, and commercialization goals. We have engaged in strategic collaborations and may in the future engage in acquisitions, collaborations, or strategic partnerships, which may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks. We have engaged in strategic collaborations in the past, such as our strategic collaborations with AbbVie ~~, Innovent~~ and GSK, and we may engage in various acquisitions, collaborations, and strategic partnerships in the future, including licensing or acquiring complementary products, intellectual property rights, technologies, or businesses. Any acquisition, collaboration, or strategic partnership may entail numerous risks, including: • increased operating expenses and cash requirements; • volatility with respect to the financial reporting related to such arrangements, such as our expected variability in the recognition of revenue each quarter from the AbbVie and GSK Agreement based on the percentage- of- completion basis under the applicable accounting rules; • assumption of indebtedness or contingent liabilities; • potential goodwill impairment resulting from such acquisitions; • issuance of our equity securities which would result in dilution to our stockholders; • assimilation of operations, intellectual property, products, and product candidates of an acquired company by our partners, including difficulties associated with integrating new personnel; • diversion of our management' s attention from our existing product programs and initiatives in pursuing such an acquisition, collaboration or strategic partnership; • retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships; • risks and uncertainties associated with the other party to such a transaction, including the

prospects of that party and their existing products or product candidates and regulatory approvals ~~;~~ **,** that may impact their ability to fulfill their obligations under such transaction; • risks that the other party to such a transaction may exercise its rights under the applicable agreement in a way that negatively impacts us; and • our inability to generate revenue from acquired or partnered intellectual property, technology, and / or products sufficient to meet our objectives or even to offset the associated transaction and maintenance costs. In addition, if we undertake such a transaction, we may issue dilutive securities, assume or incur debt obligations, incur large one- time expenses, and acquire intangible assets that could result in significant future amortization expense. ~~Our~~ **We have experienced cyber- attacks in the past, and our** internal computer systems, or those used by ~~our~~ third ~~- party~~ **parties with which we engage, such as** research institution collaborators, **clinical trial sites, and** CROs or other **vendors,** contractors or consultants, may fail or suffer other breakdowns, cyberattacks, or information security breaches **or sensitive data loss** that could compromise the confidentiality, integrity, and availability of such systems and data, result in material disruptions of our development programs and business operations, risk disclosure of confidential, financial, or proprietary information, and affect our reputation. **We have experienced cyberattacks in the past that have not had a material effect on our business operations, and we face the risk of future cyberattacks that may or may not have a material effect.** Despite the implementation of security measures, our internal computer systems and those of ~~our future~~ **third parties with which we engage, such as research institution collaborators, clinical trial sites, and** CROs and other **vendors,** contractors and consultants **,** may be vulnerable to damage **, interruption, or other disruption** from **various causes, including** computer viruses and **other malicious code, and may be vulnerable to** unauthorized access **. Likewise, data privacy or security breaches or breaches by employees or others may pose a risk that sensitive data, including our intellectual property, trade secrets, or personal information of our employees, patients, customers, or other business partners, may be exposed to unauthorized persons or to the public or may otherwise be misused** . As the cyber- threat landscape evolves, especially as certain of our employees have engaged in remote or hybrid work ~~as a result of, or after, the COVID- 19 pandemic~~ , these attacks are growing in frequency, sophistication, and intensity, and are becoming increasingly difficult to detect **, mitigate, and defend against. Such threats are prevalent and continue to rise, are increasingly difficult to detect, and come from a variety of sources, including traditional computer " hackers, " threat actors, " hacktivists, " organized criminal threat actors, personnel (such as through theft or misuse), sophisticated nation states, and nation- state- supported actors. During times of war and other conflicts, we and our business counterparties, including third parties upon which we rely, may be vulnerable to a heightened risk of these attacks** . Such attacks ~~could include~~ **might involve** the use of **sophisticated** ~~key loggers or other harmful and virulent~~ malware, including ransomware or ~~other denials~~ **various types** of service ~~, and~~ **denial tactics. They** can be ~~deployed~~ **initiated** through ~~malicious~~ **harmful** websites **or by leveraging phishing strategies** , ~~the use of~~ social engineering **tactics** , ~~and /~~ or **credential stuffing. This might also include brute force attacks, along with** other ~~means~~ **contemporary malicious methods which are always changing** . If a breakdown, cyberattack, or other information security breach ~~were to~~ **or incident** ~~occur~~ **occurs** ~~and cause interruptions in our operations~~ , it could **cause damage to or interruptions or other disruptions in our operations or those of third parties with which we engage, and could** result in ~~a~~ **damage to, the loss or unavailability of, or** misappropriation **or other unauthorized use or processing** of **, sensitive data, including personal information and** confidential information, ~~including~~ **such as** our intellectual property or financial information, and a material disruption of our development programs and our business operations. For example, the loss **or unavailability** of **, or damage to,** clinical trial data from completed, ongoing, or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third- party research institution collaborators **, clinical trial sites,** and CROs **and other vendors, consultants and contractors** for research and development of our product candidates **,** and **we rely on** other third parties ~~for the~~ **, such as CDMOs and CROs, to** manufacture ~~of~~ our product candidates and to conduct clinical trials, **respectively. Supply- chain attacks against third- party actors like these have increased in frequency and severity, and we cannot guarantee that third- party infrastructure in our supply chain or our third- party partners' supply chains have not been compromised. Cyberattacks, security breaches and incidents, and disruptions, interruptions,** and similar events relating to their computer systems **and operations** could also have a material adverse effect on our business. **We and** ~~To the extent that any disruption or~~ **our business counterparties** ~~security breach were to result in a loss of~~ , ~~or damage to~~ **including third parties on which we rely** , **may be unable to anticipate** ~~our~~ - **or** ~~data~~ **prevent techniques used to obtain unauthorized access to or to compromise** ~~or~~ **our or our business counterparties'** systems **because such techniques change frequently and are generally not detected until after** ~~, or inappropriate disclosure of confidential, financial, or proprietary information, including data related to our personnel, we could incur liability or risk disclosure of confidential, financial, or proprietary information, and~~ - **an incident has occurred** ~~the further development and commercialization of our product candidates could be delayed~~ . There can be no assurance that we and our business counterparties will be successful in efforts to detect, prevent, or fully recover systems or data from all breakdowns, service interruptions **or other disruptions** , attacks, or **compromises of, or security** breaches ~~of~~ **or incidents impacting,** systems that could adversely affect our business and operations and / or result in the loss **or unavailability** of **, or damage to,** critical or sensitive data **. Any disruption or security breach or incident resulting in loss or unavailability of** , **or damage to, our data or systems, or those of third parties on** which **we rely, or inappropriate use, disclosure, or modification of personal, sensitive, confidential or proprietary information,** could result in **our being subject to claims, demands, and litigation, investigations and other regulatory proceedings, and fines and other liabilities, as well as in delays to further development and commercialization of our product candidates. While we have invested, and continue to invest, in the protection of our data and information technology infrastructure, there can be no assurance that our efforts will prevent service disruptions, or prevent or identify vulnerabilities or security breaches or incidents, that could adversely affect our business and operations or result in the loss, unavailability, or corruption of, or inappropriate access to or use of, confidential, personal, or other sensitive information or company resources. Any such interruptions, breaches or**

incidents, or the perception that any have occurred, could result in financial, legal, business, or reputational harm to us **. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyberattacks and other privacy and security breaches or incidents. Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims** . Business disruptions, including as a result of global pandemics, could seriously harm our future revenue and financial condition and increase our costs and expenses. Our operations, and those of our collaborators, CROs, CDMOs, suppliers, and other contractors and consultants, could be subject to pandemic events and other events beyond our control, such as the spread of disease, earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, political unrest, including the **ongoing conflicts between** Russia ~~-~~ **and** Ukraine ~~conflict~~ **and between Israel and Hamas,** and other natural or man- made disasters or business interruptions, for which we are either totally or partly uninsured. In addition, we rely on our third- party research institution collaborators for conducting research and development of our product candidates, and they may be affected by government shutdowns or withdrawn funding. ~~The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.~~ We rely on third- party manufacturers to produce and process our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man- made or natural disaster, global pandemics, or other business interruption **. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses** . The majority of our operations including our corporate headquarters are located in a facility in South San Francisco, California. Damage or extended periods of interruption to our corporate, development, or research facilities due to fire, natural disaster, global pandemics, power loss, communications failure, unauthorized entry, earthquakes or other events could cause us to cease or delay development of some or all of our product candidates. Although we maintain property damage and business interruption insurance coverage on these facilities, our insurance might not cover all losses under such circumstances **,** and our business may be seriously harmed by such delays and interruption. Our business is subject to economic, political, regulatory, and other risks associated with international operations. Our business is subject to risks associated with conducting business internationally. Some of our CDMOs and clinical trial sites, for example **,** are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including: • economic weakness, including inflation, or political instability in particular in non- U. S. economies and markets; • differing and changing regulatory requirements in non- U. S. countries; • challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States; • difficulties in compliance with non- U. S. laws and regulations; • changes in non- U. S. regulations and customs, tariffs, and trade barriers; • changes in non- U. S. currency exchange rates and currency controls; • changes in a specific country' s or region' s political or economic environment; • shipping of biologics / drugs; • trade protection measures, import or export licensing requirements, or other restrictive actions by U. S. or non- U. S. governments; • negative consequences from changes in tax laws; (including the provisions of the recently enacted federal tax legislation titled the Inflation Reduction Act); • compliance with tax, employment, immigration, and labor laws for employees living or traveling abroad; • workforce uncertainty in countries where labor unrest is more common than in the United States; • difficulties associated with staffing and managing international operations, including differing labor relations; • potential liability under the FCPA, UK Bribery Act, or comparable foreign laws; and • business interruptions resulting from geo- political actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods, droughts, extreme temperatures, and fires. These and other risks associated with our planned international operations may materially adversely affect our ability to attain profitable operations. Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited. As of December 31, ~~2022~~ **2023** , we had federal and state net operating loss (NOL) carryforwards of approximately **zero and** $ ~~40~~ **202** . **2** ~~3 million and $ 203. 5~~ million, respectively. Federal NOL carryforwards have an indefinite life **but** ~~and deductions~~ cannot ~~exceed~~ **offset more than** 80 % of taxable income. Pursuant to Internal Revenue Code Sections 382 and 383, annual use of the Company' s net operating loss and research and development credit carryforwards may be limited in the event that a cumulative change in ownership of more than 50 % occurs within a three- year period. As a result of our initial public offering in February 2019 and follow- on public offering in January 2020, and other transactions that have occurred since our incorporation, we may have experienced such an ownership change. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which are outside our control. As a result, our ability to use our pre- change net operating loss carryforwards and other pre- change tax attributes to offset post- change taxable income or taxes may be subject to limitation. **Additionally** ~~In addition~~ , **our** ~~the enacted legislation commonly referred to as the Tax Cuts and Jobs Act of 2017 (the TCJA), as amended by the Coronavirus Aid, Relief, and Economic Security Act of 2020 (CARES Act), also provides that NOLs from tax years that began after December 31, 2017 may offset no more than 80 % of current taxable income annually for taxable years beginning after December 31, 2022. Our~~ NOLs may also be subject to limitations under state law. Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition. We are or may become subject to income and non- income taxes in the United States under federal, state, and local jurisdictions and in certain foreign jurisdictions in which we operate. Tax laws, regulations and administrative practices in these jurisdictions may be subject to significant change, with or without advance notice. For example, on January 1, 2022, a provision of the TCJA went into effect that eliminates the option to deduct domestic research and development costs in the year incurred and instead requires taxpayers to amortize such costs over five years for domestic costs and 15 years for foreign costs. ~~The~~ **As a result, the** Company ~~is~~

~~currently evaluating the potential impact~~ **recognizes taxable income earlier than anticipated**. Also, the United States recently enacted the Inflation Reduction Act **of 2022 (the IRA)**, which introduced a 15 % minimum tax on book income and a 1 % excise tax on **certain** stock buybacks. Changes in tax laws (including provisions of the **IRA** ~~Inflation Reduction Act~~), regulations, or rulings, changes in interpretations of existing laws and regulations, or changes in accounting principles could negatively or materially affect our financial position, cash flows and results of operations. General Risk Factors The market price of our common stock may continue to be volatile, which could result in substantial losses for investors. Although our common stock is listed on the NASDAQ Global Select Market, the market for our shares has demonstrated varying levels of trading activity. The trading price of our common stock has been and may continue to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations and progression of our product pipeline may not meet the expectations of public market analysts and investors, and, as a result of these and other factors, the price of our common stock may fall. Some of the factors that may cause the market price of our common stock to fluctuate or decline include: • the success of existing or new competitive products or technologies; • the timing and results of clinical trials for our current product candidates and any future product candidates that we may develop; • commencement or termination of collaborations for our product development and research programs; • failure to achieve development, regulatory, or commercialization milestones under our collaborations; • failure or discontinuation of any of our product development and research programs; • results of preclinical studies, clinical trials, or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors; • regulatory or legal developments in the United States and other countries; • developments or disputes concerning patent applications, issued patents, or other proprietary rights; • the recruitment or departure of key personnel; • the level of expenses related to any of our research programs, clinical development programs, or product candidates that we may develop; • the results of our efforts to develop additional product candidates or products; • actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts; • announcement or expectation of additional financing efforts; • sales of our common stock by us, our insiders, or other stockholders, such as if we use our at- the- market facility; • expiration of market standoff or lock- up agreements; • variations in our financial results or those of companies that are perceived to be similar to us; • changes in estimates or recommendations by securities analysts, if any, that cover our stock; • changes in the structure of healthcare payment systems; • market conditions in the pharmaceutical and biotechnology sectors; • general economic, political, industry, and market conditions, including a rising rate of inflation or a period of economic recession; and • the other factors described in this " Risk Factors " section. In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Broad market and industry factors, such as inflationary concerns, may seriously affect the market price of our common stock, regardless of our actual operating performance. Following periods of such volatility in the market price of a company' s securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management' s attention and resources from our business. If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline. The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. If one or more of the analysts covering our business cease to cover us or downgrade their evaluations of our stock or if we fail to meet their operating results estimates for us, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline. Sales of substantial amounts of our common stock in the public markets, or the perception that such sales might occur, could cause the market price of our common stock to decline significantly, even if our business is doing well. Sales of a substantial number of shares of our common stock in the public market could occur at any time. If our stockholders sell, or the market perceives that our stockholders intend to sell, substantial amount of our common stock in the public market, the market price of our common stock could decline significantly. Certain holders of shares of our common stock have rights **may, in the future**, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. Registration of these shares under the Securities Act would result in the shares becoming freely tradeable in the public market, subject to the restrictions of Rule 144 in the case of our affiliates. Any sales of securities by these stockholders could have a material adverse effect on the market price for our common stock. Raising additional capital may cause dilution to our existing stockholders, restrict our operations, or require us to relinquish rights to our technologies or product candidates. We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances, and licensing arrangements. We, and indirectly, our stockholders, will bear the cost of issuing and servicing such securities. Because our decision to issue debt or equity securities in any future offering will depend on market conditions and other factors beyond our control, we cannot predict or estimate the amount, timing, or nature of any future offerings. To the extent that we raise additional capital through the sale of equity or debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell, or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We **have** ~~plan to file~~ an omnibus shelf registration statement on Form S- 3 with the SEC, which **became** ~~, upon becoming~~ effective **on May 1**, ~~will~~ **2023, which** ~~permit~~ **permits** us to issue up to $ 400 million in common stock, other equity securities and / or debt securities **. On November 7, 2023, we entered into an**

at- the- market sales agreement with Cowen and Company, LLC (TD Cowen) pursuant to which we may offer and sell from time to time through TD Cowen up to $ 125, 000, 000 of shares of our common stock, in such share amounts as we may specify by notice to TD Cowen. On January 17, 2024, we entered into an underwriting agreement with Cantor Fitzgerald & Co. (Cantor), pursuant to which we offered and sold 10, 869, 566 shares of the Company' s common stock at a price per share of $ 6. 57 paid by Cantor . Additionally, any future collaborations we enter into with third parties may provide capital in the near term but limit our potential cash flow and revenue in the future. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms unfavorable to us. Our principal stockholders and management own a significant percentage of our stock and will be able to exercise significant influence over matters subject to stockholder approval. Our directors, executive officers, holders of more than 5 % of our outstanding stock and their respective affiliates beneficially own ~~50~~ **40** . ~~2~~ **9** percentage of our outstanding common stock as of February ~~21~~ **22** , ~~2023~~ **2024** . As a result, these stockholders, if they act together, may significantly influence all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company that our other stockholders may believe is in their best interests. This in turn could have a material adverse effect on our stock price and may prevent attempts by our stockholders to replace or remove the board of directors or management. We have incurred and will continue to incur significant additional costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices. As a public company, we have incurred and will continue to incur significant legal, accounting, and other expenses that we did not incur as a private company. The Sarbanes- Oxley Act, the Dodd- Frank Wall Street Reform, and Consumer Protection Act, the listing requirements of NASDAQ, and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We have hired, and expect that we will need to continue to hire, additional accounting, finance, and other personnel in connection with our ~~becoming~~ --- **being** , and our efforts to comply with the requirements of being, a public company, and our management and other personnel have devoted and will continue to devote a substantial amount of time towards maintaining compliance with these requirements. These requirements have increased and will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that the rules and regulations applicable to us as a public company may make it more difficult and more expensive for us to maintain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We are currently evaluating these rules and regulations and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. If we are unable to maintain effective internal controls, our business, financial position, and results of operations could be adversely affected. As a public company, we are subject to reporting and other obligations under the Exchange Act, including the requirements of Sarbanes- Oxley Act Section 404 (a), which require annual management assessments of the effectiveness of our internal control over financial reporting. Section 404 (b) of the Sarbanes- Oxley Act also requires our independent auditors to attest to, and report on, this management assessment. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing **,** and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes- Oxley Act of 2002. These reporting and other obligations place significant demands on our management and administrative and operational resources, including accounting resources. If we are not able to comply with the requirements of Section 404 or if we or our independent registered public accounting firm are unable to attest to the effectiveness of our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our stock could decline and we could be subject to sanctions or investigations by ~~Nasdaq~~ **NASDAQ** , the SEC, or other regulatory authorities, which would require additional financial and management resources. Our operations are subject to the effects of a rising rate of inflation. The United States has recently experienced historically high levels of inflation. According to the U. S. Bureau of Labor Statistics, the annual consumer price index increase for the United States was approximately ~~6~~ **3** . ~~5~~ **4** % for the 12 months ended December 31, ~~2022~~ **2023** . If the inflation rate continues to increase, it will affect our expenses, such as employee compensation and research and development charges. Research and development expenses account for a significant portion of our operating expenses. Such increased charges may not be readily recoverable during the period of time that we are bringing the product candidates to market. Additionally, the United States is experiencing an acute workforce shortage, which in turn, has created a very competitive wage environment that may increase the Company' s operating costs. To the extent inflation results in rising interest rates and has other adverse effects on the market, it may adversely affect our consolidated financial condition and results of operations **. Market conditions and changing circumstances, some of which may be beyond our control, could impair our ability to access our existing cash, cash equivalents and investments and to timely pay key vendors and others. Market conditions and changing circumstances, some of which may be beyond our control, could impair our ability to access our existing cash, cash equivalents and investments and to timely pay key vendors and others. For example, on March 10, 2023, Silicon Valley Bank (SVB), where we maintained certain immaterial deposit accounts at the time, was placed into receivership with the Federal Deposit Insurance Corporation (FDIC), which resulted in all funds held at SVB being temporarily inaccessible by SVB' s customers. If other banks and financial institutions with whom we have banking relationships enter**

receivership or become insolvent in the future, we may be unable to access, and we may lose, some or all of our existing cash, cash equivalents and investments to the extent those funds are not insured or otherwise protected by the FDIC. In addition, in such circumstances we might not be able to timely pay key vendors and others. We regularly maintain cash balances that are not insured or are in excess of the FDIC' s insurance limit. Any delay in our ability to access our cash, cash equivalents and investments (or the loss of some or all of such funds) or to timely pay key vendors and others could have a material adverse effect on our operations and cause us to need to seek additional capital sooner than planned . We do not expect to pay any dividends for the foreseeable future. Investors may never obtain a return on their investment. You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. In addition, any future credit facility may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock. Delaware law and provisions in our amended and restated certificate of incorporation and bylaws might discourage, delay, or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock. Provisions in our amended and restated certificate of incorporation and bylaws may discourage, delay, or prevent a merger, acquisition, or other change in control that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares of our common stock. These provisions may also prevent or frustrate attempts by our stockholders to replace or remove our management. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our charter documents: • establish that our board of directors is divided into three classes, Class I, Class II, and Class III, with each class serving staggered three- year terms; • provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum; • provide that our directors may only be removed for cause; • eliminate cumulative voting in the election of directors; • authorize our board of directors to issue shares of preferred stock and determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval; • provide our board of directors with the exclusive right to elect a director to fill a vacancy or newly created directorship; • permit stockholders to only take actions at a duly called annual or special meeting and not by written consent; • prohibit stockholders from calling a special meeting of stockholders; • require that stockholders give advance notice to nominate directors or submit proposals for consideration at stockholder meetings; • authorize our board of directors, by a majority vote, to amend the bylaws; and • require the affirmative vote of at least 66 2 / 3 % or more of the outstanding shares of common stock to amend many of the provisions described above. In addition, Section 203 of the General Corporation Law of the State of Delaware (DGCL), prohibits a publicly- held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15 % of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. Any provision of our amended and restated certificate of incorporation, amended and restated bylaws, or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock. Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees. Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, another State court in Delaware or the federal district court for the District of Delaware) is the exclusive forum for the following (except for any claim as to which such court determines that there is an indispensable party not subject to the jurisdiction of such court (and the indispensable party does not consent to the personal jurisdiction of such court within 10 days following such determination), which is vested in the exclusive jurisdiction of a court or forum other than such court ~~,~~ or for which such court does not have subject matter jurisdiction): • any derivative action or proceeding brought on our behalf; • any action asserting a claim of breach of fiduciary duty; • any action asserting a claim against us arising under the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws; and • any action asserting a claim against us that is governed by the internal- affairs doctrine. This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act or any other claim for which the U. S. federal courts have exclusive jurisdiction. Our amended and restated bylaws further provide that the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. These exclusive- forum provisions may limit a stockholder' s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage lawsuits against us and our directors, officers , and other employees. Any person or entity purchasing or otherwise acquiring any interest in any of our securities shall be deemed to have notice of and consented to these provisions. There is uncertainty as to whether a court would enforce such provisions, and the enforceability of similar choice of forum provisions in other companies' charter documents has been challenged in legal proceedings. It is possible that a court could find these types of provisions to be inapplicable or unenforceable, and if a court were to find either exclusive- forum provision in our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business.