Risk Factors Comparison 2025-02-27 to 2024-02-28 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. " 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. Risk Factor Summary This summary of risks provides an overview of the principal risks we are exposed to. These risks are more fully described below. Risks Related to Our Business, Financial Condition and Capital Requirements • We are in 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 since our inception and anticipate that we will continue to incur net losses for the foreseeable future. • Drug development is a highly uncertain undertaking. We have never generated any revenue from product sales, and may never do so. • Due to the significant resources required for the development of our programs, and depending on our ability to access capital, we must prioritize development of certain product candidates. • A pandemic, epidemic **,** or outbreak of an infectious disease ~~, such as COVID- 19~~ , or the perception of its effects, may materially and adversely affect our business, operations, and financial condition. Risks Related to the Discovery, Development and Commercialization of Our Product Candidates • We are heavily dependent on the successful development of our ~~BBB~~ **TV** technology and the programs currently in our pipeline, which are in the preclinical and clinical development stages. • We may not be successful in our efforts to continue to create a pipeline of product candidates or to develop commercially successful products. • We have concentrated a substantial portion of our efforts on the treatment of neurodegenerative and ~~LSDs~~ **lysosomal storage diseases** , fields that have seen limited success in drug development. • 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. • We may encounter difficulties enrolling and / or retaining patients in our clinical trials, and our clinical development activities could thereby be delayed or otherwise adversely affected. • 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 or potency of our product candidates, which would prevent, delay ~~,~~ or limit the scope of regulatory approval and commercialization. • We face significant competition and our operating results may suffer if we fail to compete effectively ~~. • The manufacture of our product candidates, particularly those that utilize our BBB platform technology, is complex and we may encounter difficulties in production~~ . • If we are unable to establish sales and marketing capabilities or enter into agreements with third parties, we may not be successful in commercializing product candidates if and when they are approved. • If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates. 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. • We currently conduct clinical trials outside the United States, and the FDA, EMA and applicable foreign regulatory authorities may not accept data from such trials. • **To the extent we seek orphan drug designation for any of our product candidates, we may be unable to obtain such designations or to maintain the benefits associated with orphan drug status. •** Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations. • Our business is subject to complex and evolving U. S. and foreign laws and regulations, information security policies, and contractual obligations relating to privacy ~~and ,~~ data protection **, and data security** . Risks Related to Our Reliance on Third Parties • We depend on collaborations with third parties for the research, development ~~,~~ and commercialization of certain product candidates. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates. • We 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. • Our reliance on third parties for the manufacture of the significant majority of the materials for our research programs, preclinical studies, and clinical trials **. This reliance on third parties** may increase the risk that we will not have sufficient quantities of such materials or product candidates. • We depend on third- party suppliers for key raw materials used in our manufacturing, and the loss of these suppliers or their inability to supply us with adequate raw materials could harm our business. Risks Related to Our Intellectual Property • If we are unable to obtain and maintain patent protection for our product candidates or our ~~BBB~~ **TV** technology, our competitors could develop and commercialize products or technology similar or identical to ours, and adversely affect our ability to commercialize any product candidates. • If any of our owned or in- licensed patent applications do not issue as patents in any jurisdiction, we may not be able to compete effectively. • Our rights to develop and commercialize our ~~BBB~~ **TV** technology and product candidates are subject, in part, to the terms of licenses granted to us by others or licenses granted by us to others. • We may not be able to protect our intellectual property and proprietary rights throughout the world. • Our patent protection could be reduced or eliminated if we are unable to comply with requirements imposed by government patent agencies. • Changes in U. S. patent law could impair our ability to protect our products. • Issued patents covering our ~~BBB~~ **TV** technology, product candidates and other technologies could be found invalid or unenforceable if challenged. • Patent terms may be inadequate to protect our competitive

position on our product candidates for an adequate amount of time. • We may be subject to claims challenging the inventorship of our intellectual property. • If we are unable to protect the confidentiality of our trade secrets, our business would be harmed. • We may not be successful in obtaining, through acquisitions, in- licenses , or otherwise, necessary rights to our ~~BBB~~ TV platform ~~technology~~ , product candidates or other technologies. • 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. • Third - party intellectual property claims against us, our licensors or our collaborators may prevent or delay the development of our ~~BBB~~ TV platform ~~technology~~ , product candidates and other technologies. Risks Related to Our Operations • If we are not successful in attracting, motivating and retaining highly qualified personnel, we may not be able to successfully implement our business strategy. • We have engaged in and may in the future engage in acquisitions or strategic partnerships, which may increase our capital requirements, dilute our stockholders, or cause us to incur debt or assume contingent liabilities ~~. • The proposed spin out of our preclinical small molecule portfolio is subject to various risks and uncertainties or may not result in the expected benefits~~ . • Our internal computer systems, or those used by our collaborators, CROs or other contractors, may fail or suffer security breaches or incidents that could compromise the confidentiality, integrity, and availability of such systems and data, expose us to liability, and affect our reputation. • Our business is subject to risks associated with international operations. Risks Related to Ownership of Our Common Stock • The market price of our common stock has been and may continue to be volatile, which could result in substantial losses for investors. • If securities analysts publish negative evaluations of our stock, or if they do not publish research or reports about our business; the price of our stock and trading volume could decline. • 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. • Delaware law and provisions in our charter documents might prevent a change in control of our company or changes in our management, depressing the trading price of our common stock. • Our amended and restated certificate of incorporation provides exclusive forums for disputes between us and our stockholders, limiting their ability to obtain a favorable judicial forum. We are in 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 business and predict our future success and viability. We are a clinical- stage biopharmaceutical company with a limited operating history, focused on developing therapeutics for neurodegenerative diseases, including Alzheimer' s disease, Parkinson' s disease and ALS, and ~~LSDs~~ **lysosomal storage diseases** , including Hunter syndrome and Sanfilippo syndrome. We commenced operations in May 2015, 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. Our clinical- stage programs are in various phases ranging from Phase 1 through Phase 3. 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 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 companies, 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 significant net losses since our inception. Our net losses were $ **422. 8 million, $** 145. 2 million, **and** $ 326. 0 ~~million, and $ 290. 6~~ million for the years ended December 31, **2024,** 2023, **and** 2022 ~~, and 2021~~ , respectively. As of December 31, ~~2023~~ **2024** , we had an accumulated deficit of $ 1. ~~12~~ **54** billion. We have invested significant financial resources in research and development activities, including for our preclinical and clinical product candidates and our TV platform. ~~We do not expect to generate revenue from product sales for several years, if at all.~~ 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. 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; • progress our current and any future product candidates through preclinical and clinical development; • **manufacture** ~~initiate and conduct additional preclinical, clinical, or other studies for our~~ product candidates ~~; • work~~ **at our manufacturing facility and** with our contract manufacturers ~~to scale up the manufacturing processes for our product candidates or, in the future, establish and operate a manufacturing facility~~ ; • change or add additional 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; • acquire or in- license product candidates, intellectual property ~~,~~ and technologies; • make milestone, royalty ~~,~~ or other payments due under any license or collaboration agreements; • obtain, maintain, protect, and enforce our intellectual property portfolio, including intellectual property obtained through license agreements; • attract, hire, and retain qualified personnel and incur increased stock- based compensation, especially in light of a competitive 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; • experience any delays or encounter other issues related to our operations; • meet the requirements and demands of being a public company; **and** • defend against any product liability claims or other lawsuits related to our products ~~; and • build clinical manufacturing capabilities and capacity~~ . 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. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We have never generated any revenue from product sales, and we may never generate product revenue or be profitable. We have no products approved for commercial sale and have not generated any revenue from product sales. To obtain revenue 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 significantly on many factors, including: • successfully prioritizing and completing research and preclinical and clinical development of our product candidates; • 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, including those that utilize our TV platform, 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 by collaborating with a partner or, if launched independently, by establishing a 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 milestone and other payments under our current and any future collaboration arrangements; • maintaining, protecting, expanding, and enforcing our portfolio of intellectual property rights; • attracting, hiring, and retaining qualified personnel; • general economic conditions ~~, including conditions resulting from rising inflation and interest rates, recent bank failures and instability in the financial services sector, geopolitical uncertainty and instability or war~~ ; and • addressing any delays in our clinical trials or other impacts from a pandemic or other global health emergency. 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 current or our 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 commercializing any approved product candidate and ongoing compliance efforts. Even if we are able to generate revenue from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations. Revenue from the sale of any product candidate for which regulatory approval is obtained will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price, and whether we own the commercial rights for that territory. If the number of addressable patients is not as significant as we anticipate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice, or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates, or continue our operations and cause a decline in the value of our common stock, all or any of which may adversely affect our viability. If we fail to obtain additional financing, we may be unable to complete the development and, if approved, commercialization of our product candidates. Our operations have required substantial amounts of cash since inception. We currently fund our operations primarily with the proceeds from our follow- on ~~offerings~~ **offering** completed in ~~January 2020 and~~ October 2022, ~~and~~ payments received from our collaboration agreements with Biogen, Sanofi, ~~and~~ Takeda **, and a strategic private offering transaction completed in February 2024** . We have a diversified portfolio with numerous programs at various stages of research, discovery, preclinical and clinical development. 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 , obtaining regulatory approvals~~ and ~~launching and~~ **prepare for potential** ~~commercializing~~ **commercialization** ~~any product candidate will require substantial additional funding~~ . As of December 31, ~~2023~~ **2024** , we had $ 1. ~~03~~ **19** billion in cash, cash equivalents ~~,~~ and marketable securities. We believe that our existing cash, cash equivalents ~~,~~ and marketable securities will be sufficient to fund our projected operations through at least the next twelve months. 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 be proven inaccurate, and we could use our available capital resources sooner than we currently expect. Changing circumstances, some of which may be beyond our control, such as recent bank failures, geopolitical uncertainty, rising inflation or interest rates, or a perceived or actual economic downturn, may cause us to increase our spending significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. We may also need to raise additional funds sooner than we anticipate if we choose to expand more rapidly than we presently anticipate. We **have no committed source of additional capital, and we** cannot be certain that additional funding will be available when we need it, on terms acceptable to us or at all ~~. Other than the PIPE financing that was announced on February 27, 2024, we have no committed source of additional capital~~ . 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, which could materially affect our business, financial condition, results of operations, and growth prospects and cause the price of our common stock to decline. **We** ~~Due to the significant resources required for the development of our programs, 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 and 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 a diversified portfolio with numerous programs at various stages of research, discovery, preclinical and clinical development. These programs require significant capital investment. We seek to maintain a process of prioritization and resource allocation to maintain an optimal balance between aggressively advancing lead programs and replenishing our portfolio. We regularly review the programs in our portfolio, and terminate those programs which do not meet our development criteria, which we have done a number of times in the past.~~ Due to the significant resources required for the development of our programs, we must focus our programs 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 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. Similarly, our potential decisions to delay, terminate, **divest** ~~spin out~~, 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 and ~~LSDs~~ **lysosomal storage diseases**, our business, financial condition, results of operations **,** and growth prospects could be materially adversely affected. ~~As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forgo 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. A pandemic, epidemic or outbreak of an infectious disease, such as COVID- 19, or the perception of its effects, may materially and adversely affect our business, operations and financial condition. Public health outbreaks, such as epidemics or pandemics may significantly disrupt our business. Such outbreaks pose the risk that we or our employees, contractors, suppliers, and other partners may be prevented from conducting business activities for an indefinite period of time due to the spread of the disease, due to shutdowns that may be requested or mandated by federal, state, and local governmental authorities or certain employers, or due to the economic consequences associated with the pandemic. Business disruptions could include disruptions or restrictions on our ability to travel, as well as temporary closures of our facilities and the facilities of our partners, clinical trial sites, service providers, suppliers, or contract manufacturers. For example, the COVID- 19 pandemic caused a temporary disruption in our ability to recruit participants for our clinical trials in the calendar year 2020 and the first quarter of 2021. While it is not possible to predict whether another pandemic, epidemic, or infectious disease outbreak similar to COVID- 19 will materialize, any measures taken by governments and local authorities in response to such future health crises have the potential to disrupt and delay the initiation of new clinical trials, the progress of our ongoing clinical trials and our preclinical activities, and potentially the manufacture or shipment of both drug substance and finished drug product of our product candidates for preclinical testing and clinical trials, as well as adversely impact our business, financial condition, or operating results. The continued impact of the COVID- 19 pandemic may materially and adversely affect our business, operations and financial condition. 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 remain in effect. The full impact of the termination of the public health emergency on the FDA and other regulatory policies and operations remains unclear. In response to the COVID- 19 pandemic, we implemented policies that enabled some of our employees to work remotely, which policies may continue for an indefinite period. Due to telecommuting patterns, modified work schedules, and enhanced safety protocols, our laboratory operations have at times and may again operate with decreased efficiency. Furthermore, our clinical trial sites for our clinical studies were impacted by the COVID- 19 pandemic: in 2020, we experienced a pause in enrollment in our BIIB122 / DNL151 Phase 1 and Phase 1b trials, our DNL343 Phase 1 and Phase 2 / 3 trials, and our ETV: IDS program observational biomarker study, and we have subsequently experienced certain delays in patient enrollment. The FDA issued a number of COVID- 19 related guidance documents for manufacturers and clinical trial sponsors in 2020 and 2021, many of which have expired or were withdrawn with the expiration of the COVID- 19 public health emergency in May 2023, although some COVID- 19 related guidance documents remain in effect. Should the FDA issue additional guidance that mandates material changes to our clinical trials in response to a pandemic or other public health outbreaks, the costs of such clinical trials may increase. To the extent we experience any ongoing pandemic disruptions or other public health emergencies, including a resurgence of COVID- 19 cases, potential impacts to our business may include delays or difficulties in enrolling patients, difficulties interpreting data impacted by trial disruptions, supply chain issues, staffing shortages, and disruptions to the operations of our service providers, any of which could have a material adverse effect on our business and clinical development plans. To the extent another pandemic or other public health outbreak adversely affects our business, operations and financial condition in the future, it may also have the effect of heightening many of the risks described in this " Risk Factors " section.~~ Risks Related to the Discovery, Development, and Commercialization of Our Product Candidates ~~Research and development of biopharmaceutical products is inherently risky.~~ We are heavily dependent on the successful development of our ~~BBB~~ **TV** platform ~~technology~~ and the programs currently in our pipeline ~~, which are in preclinical and clinical development stages~~. 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 at~~ **Investment in biopharmaceutical product development involves significant risk that any product candidate will fail to demonstrate adequate efficacy or potency, or** an **acceptable safety profile, gain regulatory approval,** ~~early stage of development of many of the product candidates currently in our programs~~ and **become commercially viable** ~~are further developing our BBB platform technology~~. To date, we have invested substantially all of our efforts and financial resources to identify, acquire intellectual property for, and develop our ~~BBB~~ **TV** platform ~~technology~~ and our programs, including conducting preclinical studies and clinical trials, and providing 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; • our drug delivery platform technology may not be clinically viable; • 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 **or platform technologies** that render our product candidates **or platform** obsolete or less attractive; • ~~our competitors may develop~~ **the product candidates and TV** platform ~~technologies to deliver large molecule therapeutics across the BBB that render our platform technology obsolete or less attractive; • the product candidates and BBB platform technology~~ that we develop may not be sufficiently covered by intellectual property for which we hold exclusive rights; • the product candidates and ~~BBB~~ **TV** platform ~~technology~~ 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 commercial quantities 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; 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 could have a material adverse effect on our business ~~. We may not be successful in our efforts to further develop our BBB platform technology and 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. Our product candidates are in the early stages of development and 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 have previously discontinued the development of certain molecules prior to completion of preclinical development because we did not believe they met our criteria for potential clinical success. Further, we cannot be certain that any of our product candidates will be successful in clinical trials. For instance, in August 2023, together with our collaboration partner Takeda, we discontinued development of TAK- 920 / DNL919 (ATV: TREM2) in Alzheimer' s disease, based on data from the Phase 1 study and the rapidly evolving treatment landscape **,** and ~~shifted our efforts to exploring back- up molecules~~ **, in January 2025, we announced that the Phase 2 / 3 HEALEY ALS Platform Trial evaluating DNL343 for ALS did not meet primary and key secondary endpoints** . We may in the future advance product candidates into clinical trials and terminate such trials 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 EU, 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, and may never receive such regulatory approval even if a product candidate successfully completes 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 or potency, purity, chemistry, 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 time frame 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. If we are unable to obtain approval for our product candidates in multiple jurisdictions, our revenue, business, financial condition, results of operations and 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 and LSDs or other diseases, we cannot assure you 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 potency, 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. ~~We may not be successful in our efforts to continue to create a pipeline of product candidates or to develop commercially successful products. If we fail to successfully identify and develop additional product candidates, our commercial opportunity may be limited.~~ One of our strategies is to identify and pursue clinical development of additional product candidates. We currently have several programs in the research, discovery ~~,~~ and preclinical stages of development. Identifying, developing, obtaining regulatory approval for, and commercializing additional product candidates for the treatment of neurodegenerative and ~~LSDs~~ **lysosomal storage diseases** will require substantial additional funding and is prone to the risks of failure inherent in drug development. We cannot provide you 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~~ **Our product candidates** are **based** ~~unable to successfully identify, acquire, develop, and commercialize additional product candidates, our commercial opportunity may be limited. We have concentrated a substantial portion of our research and development efforts~~ on **novel technology in** ~~the treatment of neurodegenerative and LSDs,~~ fields that have seen limited success in drug development ~~. Further, our product candidates are based on new approaches and novel technology~~ , which makes it difficult to predict the time

and cost of product candidate development and subsequently obtaining regulatory approval. We have focused our research and development efforts on addressing neurodegenerative and ~~LSDs~~ **lysosomal storage diseases** . Collectively, efforts by biopharmaceutical companies in the fields of neurodegenerative and ~~LSDs~~ **lysosomal storage diseases** have seen limited success in drug development. There are few effective therapeutic options available for patients with neurodegenerative diseases, such as Alzheimer' s disease, Parkinson' s disease, and ALS, and ~~LSDs~~ **lysosomal storage diseases** , such as Hunter syndrome and Sanfilippo syndrome. Our future success is highly dependent on the successful development of our ~~BBB~~ **TV** platform ~~technology~~ and our product candidates for treating neurodegenerative and ~~LSDs~~ **lysosomal storage diseases** . Developing and, if approved, commercializing our product candidates for treatment of neurodegenerative and ~~LSDs~~ **lysosomal storage diseases** subjects us to a number of challenges, including engineering product candidates to cross the BBB to enable optimal concentration of the therapeutic in the brain 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 and ~~LSDs~~ **lysosomal storage diseases** aims to identify and select targets with a genetic link to neurodegenerative and ~~LSDs~~ **lysosomal storage diseases** , as applicable, identify and develop molecules that engage the intended target, identify and develop biomarkers, which are biological molecules found in blood, other bodily fluids or tissues that are signs of a normal or abnormal process or of a condition or disease, to select the right patient population and demonstrate target engagement, pathway engagement and impact on disease progression of our molecules, and engineer our molecules to cross the BBB and act directly in the brain. This strategy may not prove to be successful. We may not be able to discover, develop, and utilize biomarkers to demonstrate target engagement, pathway engagement, and the impact on disease progression of our molecules. We cannot be sure that our approach will yield satisfactory therapeutic products that are safe and effective, scalable, or profitable. Moreover, public perception of drug safety issues, including adoption of new therapeutics or novel approaches to treatment, may adversely influence the willingness of subjects to participate in clinical trials, or if approved, of physicians to subscribe to novel treatments. 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 trial design; • delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites; • delays in identifying, recruiting and training suitable clinical investigators; • delays in obtaining required IRB approval at each clinical trial site; • imposition of a temporary or permanent clinical hold by regulatory agencies for a number of reasons, 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; a negative finding from an inspection of our clinical trial operations or trial sites; developments ~~on~~ **in** trials conducted by competitors for related technology that ~~raises~~ **raise** FDA or EMA concerns about risk to patients of the technology broadly; or if the FDA or EMA finds 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 requirements; • failure to perform in accordance with the FDA' s or any other regulatory authority' s current good clinical practices (" cGCPs") requirements, 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 approval policies or regulations of the FDA or other regulatory authorities; • 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 us or our collaborators deciding, or regulators requiring us, to conduct additional clinical trials or abandon product development programs; • transfer of manufacturing processes from our academic collaborators to larger- scale facilities operated by a CDMO or by us, and delays or failure by our CDMOs or us to make any necessary changes to such manufacturing process; • 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; and • delays associated with a pandemic or other public health emergency. 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 or our collaborators may be required **to** or 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, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. We could also encounter delays if a clinical trial is suspended or terminated by us or our collaborators, by the data safety monitoring board for such trial, or by any 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 **, developments on trials conducted by us or our competitors for related technology that raises regulatory concerns about risk to patients of the technology broadly** , or lack of adequate funding to continue the clinical trial. For example, in January 2022, we announced that the TAK- 920 / DNL919 (ATV: TREM2) IND application had been placed on clinical hold by the FDA. In August 2023 we announced that, in agreement with Takeda, we would discontinue clinical development of TAK- 920 / DNL919 in Alzheimer' s disease. We cannot assure you that we will ever resume the clinical program for TAK- 920 / DNL919, nor can we assure you that our other product candidates will not be subject to new, partial, or full clinical holds in the future, which may impact development plans. We ~~or our collaborators~~ may **also** ~~in the future advance product candidates into clinical trials and terminate such trials prior to their completion, which could adversely affect our business. Further, after the commencement of clinical trials, we or our collaborators may discontinue advancement of lead molecules, such as the TAK- 920 / DNL919 program, or~~ pause the advancement of lead molecules in favor of a backup molecule with a superior safety or efficacy profile, such as we did in our RIPK1 program, switching our focus from DNL747 to SAR443820 / DNL788. 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. 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 may experience difficulties in patient enrollment and retention in our clinical trials for a variety of reasons, including: • public health crises ~~, such as the COVID- 19 pandemic~~ ; • 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; • competing clinical trials for similar therapies or targeting patient populations meeting our patient eligibility criteria; • 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, for any reason, including the risk of higher drop- out rates if participants become infected with the **global** ~~COVID- 19~~ virus or other infectious diseases that impact their participation in our trials. Our inability to enroll and retain a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays **and retention challenges** in our clinical trials may result in increased development costs for our product candidates **, delay our ability to obtain clinical data,** and jeopardize our ability to obtain marketing approval for the sale of our product candidates. **Our** ~~Furthermore, even if we are able to enroll a sufficient number of patients for our~~ clinical trials ~~, we~~ may ~~have difficulty maintaining participation in~~ **reveal significant adverse events, toxicities,** ~~our~~ **or** ~~clinical trials through the~~ **other** ~~treatment~~ **side effects** and ~~any follow- up periods~~ **may fail to demonstrate substantial evidence of the safety and efficacy or potency of our product candidates** , which ~~could~~ **would prevent,** delay **,** ~~or negatively impact the anticipated readouts from our~~ **or limit the scope of** ~~clinical trials, delay our~~ regulatory **approval** ~~submissions,~~ and **commercialization** ~~increase the costs of the clinical trials~~ . 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 clinical trials of our product candidates may not be predictive of the results of later- stage clinical trials. The results of clinical trials in 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 or potency 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 protocols and the rate of dropout among clinical trial participants. Open- label extension studies may also extend the timing and increase the cost of clinical development substantially. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy or potency 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 potency or unacceptable safety issues, notwithstanding promising results in earlier trials. This is particularly true in neurodegenerative and ~~LSDs~~ **lysosomal storage 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. 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, results of operations and growth prospects. Even if such clinical trials are successfully completed, we cannot guarantee that the FDA will approve the product candidates for the

proposed indications, and more trials could be required before we submit our product candidates for approval. **For instance, while we plan to submit a biologics license application (" BLA") for accelerated approval of DNL310, we expect the FDA will require us to conduct a confirmatory trial post any 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, or 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, such as requiring us to narrow our indications to a smaller subset, may also limit its commercial potential. **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,our collaborators,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.Our most advanced product candidates,DNL310,DNL126,BIIB122 / DNL151,eclitasertib (SAR443122 / DNL758),TAK** - 594 / DNL593 **,and DNL343,** are currently our only clinical stage product candidates.Adverse events and other side effects may result from higher dosing,repeated dosing,and / or longer- term exposure to our product candidates and could lead to delays and / or termination of the development of these product candidates.For example,in August 2023,together with our collaboration partner Takeda,we made the strategic decision to discontinue clinical development of TAK- 920 / DNL919 in Alzheimer' s disease following a clinical hold by the FDA.In 2020,we paused clinical studies with DNL747 in our RIPK1 program.Chronic toxicity studies with DNL747 in cynomolgus monkeys showed dose- and duration- dependent adverse preclinical findings at exposures higher than those tested in the clinic.These findings,which are considered off- target and molecule- specific,may impact the ability to increase the dose of DNL747 and achieve higher levels of target inhibition without time consuming additional clinical safety studies in patients to evaluate the long- term safety and tolerability.Drug- related side effects could affect patient recruitment,the ability of enrolled patients to complete the trial,and / or result in potential product liability claims. ~~We are required to maintain product liability insurance pursuant to certain of our license 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 cause our stock price to decline and,if judgments exceed our insurance coverage,could adversely affect our results of operations and business.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.~~ Additionally,if one or more of our product candidates receives marketing approval,and we or others,including our collaborators,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 product;• regulatory authorities may require additional warnings on the label;• we may be required to change the way the product is administered or conduct additional clinical trials or post- approval studies;• we may be required to create a Risk Evaluation and Mitigation Strategy plan 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 cannot predict whether our product candidates will cause toxicities in humans that would preclude or lead to the revocation of regulatory approval based on nonclinical studies or clinical trials.** Interim, topline, and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available, and are subject to audit and verification procedures that could result in material changes in the final data. From time to time, we may publicly disclose preliminary, interim, or topline data from our nonclinical studies and clinical trials, which are based on a preliminary analysis of then- available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations, and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, preliminary, interim, or topline data should be viewed with caution until the final data are available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Adverse changes between interim data and final data could significantly harm our business and prospects. Further, additional disclosure of interim data by us or by our competitors in the future could result in volatility in the price of our common stock. Further, others, including our collaborators or regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions, or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approval or commercialization of the particular product candidate and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is typically selected from a more extensive amount of available information. You or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the preliminary or topline data that we report differ from late, final, or actual results, or if others, including our collaborators or regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for,

and commercialize our product candidates may be harmed. We face significant competition in an environment of rapid technological and scientific change, and our operating results may suffer if we fail to compete effectively. The development and commercialization of new drug products is highly competitive. Moreover, the neurodegenerative and lysosomal storage fields are characterized by strong and increasing competition. Our potential competitors include pharmaceutical companies, biotechnology companies, academic institutions, government agencies, and other public and private research organizations that conduct research. Our competitors, either alone or with collaborative partners, may succeed in developing, acquiring, or licensing on an exclusive basis drug or biologic products that are more effective, safer, more easily commercialized, or less costly than our product candidates or may develop proprietary technologies or secure patent protection that we may need for the development of our technologies and products. A number of large pharmaceutical and biotechnology companies are developing products for the treatment of the neurodegenerative and ~~LSD~~ **lysosomal storage disease** indications for which we have research programs, including Alzheimer' s disease, Parkinson' s disease, Hunter syndrome, and ALS. Companies that we are aware are developing therapeutics in the neurodegenerative and ~~LSD~~ **lysosomal storage disease** areas include companies with significant financial resources. In addition to competition from other companies targeting neurodegenerative indications, any products we may develop may also face competition from other types of therapies, such as gene- editing therapies. Many of our current or potential competitors 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. Mergers and acquisitions 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. Our competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop. Furthermore, currently approved products could be discovered to have application for treatment of neurodegenerative or ~~LSD~~ **lysosomal storage disease** indications, which could give such products significant regulatory and market timing advantages over any of our product candidates. Our competitors also may obtain regulatory approval for their products more rapidly than we do, and may obtain orphan product exclusivity 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. **We may fail to successfully manufacture our product candidates, operate our own manufacturing facility, or obtain regulatory approval to utilize or commercialize from our manufacturing facility, which could adversely affect our clinical trials and the commercial viability of our product candidates.** The **processes involved in** ~~manufacture~~ **manufacturing** ~~of~~ our **drug and biological** product candidates, particularly those that utilize our ~~BBB~~ **TV** platform ~~technology, is complex and we may encounter difficulties in production. We may fail to successfully manufacture our product candidates, operate our own manufacturing facility, or obtain regulatory approval to utilize or commercialize from our manufacturing facility, which could adversely affect our clinical trials and the commercial viability of our product candidates. The processes involved in manufacturing our drug and biological product candidates, particularly those that utilize our BBB platform technology~~ , are complex, expensive, highly regulated and subject to multiple risks. Additionally, the manufacture of biologics involves complex processes, including developing cells or cell systems to produce the biologic, growing large quantities of such cells, and harvesting and purifying the biologic produced by them. As a result, the cost to manufacture a biologic is generally far higher than traditional small molecule chemical compounds, and the biologics manufacturing process is less reliable and is difficult to reproduce. Manufacturing biologics is highly susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics, and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects, and other supply disruptions. 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 small and large quantities. Our manufacturing partners may be unable to successfully increase the manufacturing 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 our manufacturing partners are unable to successfully scale up the manufacture of 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, which could significantly harm our business. The same risks would apply to our internal manufacturing facilities and capabilities ~~, which we are actively building in Salt Lake City, Utah~~ . Under **a** ~~an operating~~ lease for approximately 60, 000 rentable square feet of laboratory, office, and warehouse premises, we ~~have initiated~~ **substantially completed** the build- out of our Utah site ~~to expand~~ **and are in the process of establishing** our clinical manufacturing capabilities for biologic therapeutics including the manufacture of materials for toxicology studies and drug substance for early human clinical studies. ~~In addition, building internal manufacturing capacity carries 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. To date, we have experienced delays with the manufacturing site build- out, and there~~ **There** can be no

assurance that our current and future efforts to scale our internal manufacturing capabilities will succeed. In addition, the manufacturing process, including any material modifications in the manufacturing process for any products that we may develop, is subject to regulatory authority approval processes and continuous oversight, and we will need to contract with manufacturers who can meet all applicable 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 regulatory authorities, 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 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 candidate, 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 **initiated a build- out of** a sales ~~or~~ **and** marketing infrastructure and **may enter into arrangements with** ~~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~~ **for commercialization of** future ~~, we may choose to build a focused sales, marketing, and commercial support infrastructure to sell, or participate in sales 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 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; • the inability of reimbursement professionals 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; • 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 product candidates 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 or potency and safety of such product candidates as demonstrated in pivotal 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; • 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; • sufficient third- party coverage or reimbursement; 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. Even if we are able to commercialize any product candidates, such products may become subject to unfavorable pricing regulations, third- party reimbursement practices, or healthcare reform initiatives, which would harm our business. The regulations that govern marketing approvals, pricing, and reimbursement for new drugs vary widely from country to country. In the United States, 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 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 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 (" VA"), 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 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 ~~and materially~~ . ~~Should sales decline,we may have to write off a portion or all of the intangible assets associated with the affected product and our results of operations and cash flows could be materially and adversely affected.See " Risks Related to Our Intellectual Property."~~ Our biologic,or large molecule,product candidates for which we intend to seek approval may face competition sooner than anticipated.Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors,our large molecule product candidates may face competition from biosimilar products.In the United States,our large molecule product candidates **,including DNL310,** are regulated by the FDA as biologic products and we intend to seek approval for these product candidates pursuant to **a** ~~the biologics license application (" BLA "),~~ pathway.The Biologics Price Competition and Innovation Act of 2009 (the" 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 large molecule product candidates.We believe that any of our large molecule 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,potentially creating the opportunity for generic 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 similar 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,if competitors are able to obtain marketing **approval for biosimilars referencing our large molecule product candidates,such products 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** . If any of our small molecule product candidates obtain regulatory approval, additional competitors could enter the market with generic versions of such drugs, which may result in a material decline in sales of affected products. Under the Drug Price Competition and Patent Term Restoration Act of 1984 (the" Hatch- Waxman Act"), a pharmaceutical manufacturer may file an abbreviated new drug application (" ANDA") seeking approval of a generic copy of an approved, small molecule innovator product. Under the Hatch-Waxman Act, a manufacturer may also submit a new drug application (" NDA") under section 505 (b) (2) that references the FDA' s prior approval of the small molecule innovator product. A 505 (b) (2) NDA product may be for a new or improved version of the original innovator product. ~~The Hatch- Waxman Act also provides for certain periods of regulatory exclusivity, which preclude FDA approval (or in some circumstances, FDA filing and reviewing) of an ANDA or 505 (b) (2) NDA. These include, subject to certain exceptions, the period during which an FDA- approved drug is subject to orphan drug exclusivity. In addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed with the product in the FDA publication, " Approved Drug Products with Therapeutic Equivalence Evaluations, " known as the " Orange Book. " If there are patents listed in the Orange Book, a generic or 505 (b) (2) applicant that seeks to market its product before expiration of the patents must include in the ANDA a " Paragraph IV certification, " challenging the validity or enforceability of, or claiming non- infringement of, the listed patent or patents. Notice of the certification must be given to the innovator, too, and if within 45 days of receiving notice the innovator sues to protect its patents, approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court.~~ Accordingly, if any of our small molecule product candidates are approved, competitors could file ANDAs for generic versions of our small molecule drug products or 505 (b) (2) NDAs that reference our small molecule drug products, respectively. If there are patents listed for our..... product candidates may have received approval. 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. 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 would require significant costs to defend litigation and a diversion of management' s time and resources. Regardless of the merits or eventual outcome, liability claims may result in a decreased or interrupted demand for our products, injury to our reputation, withdrawal of clinical trial participants and inability to continue clinical trials, and initiation of investigation by regulators. Any successful liability claims could result in 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; the inability to commercialize any product candidate; and a decline in our share price. 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. 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. ~~For example~~ **In June 2024** , ~~if~~ the **U. S.** Supreme Court **overruled** ~~reverses or curtails~~ the Chevron doctrine, which gives deference to regulatory agencies **' statutory interpretations** in litigation against **federal government agencies, such as** the FDA ~~and~~ **, where** ~~other~~ -- **the** ~~agencies,~~ **law is ambiguous. This landmark Supreme Court decision may invite** more companies ~~may~~ **and other stakeholders to** bring lawsuits against the FDA to challenge longstanding decisions and policies of the FDA **, including the FDA' s statutory interpretations of market exclusivities and the" substantial evidence" requirements for drug approvals** , which could undermine the FDA' s authority, lead to uncertainties in the industry, and disrupt the FDA' s normal operations, **any of** which could delay the FDA' s review of our ~~marketing applications~~ **regulatory submissions. We cannot predict the full impact of this decision, future judicial challenges brought against the FDA, or the nature or extent of government regulation that may arise from future legislation or administrative action** . 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. Moreover, regulatory authorities may fail to approve companion diagnostics that we contemplate using with our therapeutic product candidates. We have not submitted 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. **Changes to the leadership at federal agencies under the new administration, as well as executive orders and actions, such as a freeze on hiring and a freeze on implementing new regulations and on external communications, may impact our clinical development and timelines.** 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: • regulatory authorities may disagree with the design, implementation, or results of our clinical trials; • regulatory authorities may determine that our product candidates are not safe and effective, only moderately 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 or potency and safety in the full population for which we seek approval ~~; • we may be unable to demonstrate to the regulatory authorities that a product candidate' s risk- benefit ratio when compared to the standard of care is acceptable~~ ; • 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 regulatory authorities that a product candidate' s risk- benefit ratio for its proposed indication is acceptable; • regulatory authorities may fail to approve ~~the~~ **our** manufacturing processes, test procedures and specifications, or facilities **or those** of **our** third- party manufacturers ~~with which we contract for clinical and commercial supplies~~ ; and • the approval policies or regulations of the regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval. 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 prospects . Our product candidates may cause undesirable..... studies or early- stage clinical trials . We currently and may in the future 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 conduct clinical trials outside the United States, including in Europe, and may continue to do so in the future. The acceptance of 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. 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. 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, and 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 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 to comply with the regulatory requirements in international markets or fail 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 regulatory scrutiny. If any of our product candidates are approved, they will be subject to ongoing regulatory requirements, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities. While healthcare professionals are free to use and prescribe drug products for off- label uses, the FDA strictly regulates manufacturers' promotional claims of drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the FDA- approved labeling. A company that is found to have improperly promoted off- label uses may be subject to large civil and criminal fines, penalties, and enforcement actions. If we cannot successfully manage the promotion of our approved product candidates, we could become subject to significant liability, which could materially adversely affect our business and financial condition. 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 the 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 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 **. In certain indications, regulatory approval may limit the market of a product candidate to target patient populations when patient selection biomarkers are used. In these indications, regulatory authorities may require us to run additional clinical trials prior to expanding the label for approval that includes a broader patient population** . 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 non- biologic products or safety, purity, and potency for our biologic products, in general or in specific patient subsets. **We plan to seek** ~~If original marketing approval was obtained via the~~ accelerated approval ~~pathway~~ **of DNL310. If successful** , we ~~could be~~ **expect the FDA will** ~~required~~ **require us** to conduct a **confirmatory study** ~~successful post- marketing clinical trial~~ to ~~confirm~~ **verify the predicted** clinical benefit **and safety profile. The results from the confirmatory study may not support the clinical benefit** ~~for~~ **or** ~~our products~~ **safety profile, which would result in approval being withdrawn** . The Food and Drug Omnibus Reform Act reformed the accelerated approval pathway, such as requiring the FDA to specify conditions for post- approval study requirements and setting forth procedures for the FDA to withdraw a product on an expedited basis for non- compliance with post- approval requirements. An unsuccessful post- marketing study or failure to complete such a study could result in the withdrawal of marketing approval. ~~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.~~ 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, impose penalties, suspend regulatory approvals, or require a product recall. Any of these actions by a regulatory agency could require us to expend significant time and resources, generate negative publicity, and adversely affect the value of our company. To the extent we seek orphan drug designation for any of our product candidates, 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 where 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. Once granted, orphan drug designation entitles a party to financial incentives and certain exclusivity protections. In February 2019, the FDA granted orphan drug designation for our DNL310 program in Hunter syndrome. However, the FDA can still approve other drugs that have a different active ingredient for use in treating the same indication or disease, and can waive orphan exclusivity if we are unable to manufacture sufficient supply of our product. We plan to seek orphan drug designations for some other product candidates, but we may be unable to obtain such designations. Further, in response to Catalyst Pharms., Inc. v. Becerra, 14 F. 4th 1299 (11th Cir. 2021), the FDA clarified in a January 2023 notice that the FDA intends to continue to apply its longstanding interpretation of the regulations to matters outside of the scope of the Catalyst order – that is, the agency will 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 have not yet been approved. It is unclear how future litigation, legislation, agency decisions, and administrative actions will impact the scope of the orphan drug exclusivity ~~. We have received Fast Track designation from the FDA for SAR443820 / DNL788, and may seek Fast Track designation from the FDA for additional product candidates. Even if one or more of our product candidates receives Fast Track designation, we may be unable to obtain or maintain the benefits associated with the Fast Track designation. The FDA has granted Fast Track designation to SAR443820 / DNL788. Fast Track designation is designed to facilitate the development and expedite the review of therapies to treat serious conditions and fill an unmet medical need. However, if we do not continue to meet the criteria of the Fast Track designation, or if our clinical trials are delayed, suspended or terminated, or put on clinical hold due to unexpected adverse events or issues with clinical supply, we will not receive the benefits associated with the Fast Track program. 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. Fast Track designation also does not guarantee our product candidate will be approved in a timely manner, if at all~~ . We may face difficulties from changes to current regulations and future legislation. Current and future legislation may increase the difficulty and cost for us to commercialize our drugs, if approved, and affect the prices we may obtain, including changes in coverage and reimbursement policies in certain market segments for our product candidates, which could make it difficult for us to sell our product candidates, if approved, profitably. 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 health care system that could impact our ability to sell our products profitably. These include the enactment of the Affordable Care Act of 2010 (" ACA "), the American Rescue Plan Act of 2021, which will eliminate a statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs, and the July 2021 executive order," Promoting Competition in the American Economy," with

multiple provisions aimed at increasing competition for prescription drugs. In August 2022, Congress passed the Inflation Reduction Act of 2022 (" IRA"), 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. Various industry stakeholders, including pharmaceutical companies, the U. S. Chamber of Commerce, and the Pharmaceutical Research and Manufacturers of America, have initiated lawsuits against the federal government asserting that the price negotiation provisions of the **IRA** ~~Inflation Reduction Act~~ are unconstitutional. The impact of these judicial changes **, future litigation brought in view of the Supreme Court' s overrule of the Chevron doctrine** , legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the government on us and the pharmaceutical industry as a whole is unclear. At the state level, 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. Since its enactment, there have been executive, judicial ~~,~~ and congressional challenges to certain aspects of the ACA **and IRA** . It is unclear how future litigation or healthcare measures promulgated by the Biden administration 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 material adverse effect on our business. We expect that the ACA and IRA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, lower reimbursement, and new payment methodologies. This could lower the price that we receive for any approved product. 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. There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future. 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 any product candidates that are approved, our ability to receive or set a price we believe is fair for our products, our ability to attract investment, our ability to generate revenue or achieve profitability, the level of taxes we are required to pay, and the availability of capital. ~~Our~~ **If we or our** employees, independent contractors, consultants, commercial partners, and vendors **fail to comply** ~~may engage in misconduct or other improper activities, including noncompliance~~ with **healthcare laws or** regulatory ~~standards and~~ requirements **, we could face substantial penalties and our business, operations, and financial conditions could be adversely affected** . 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 regulatory authorities; comply with manufacturing standards we have established; 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 **. The laws that may impact our operations include the federal Anti- Kickback Statute, the False Claims Act, the federal Health Insurance Portability and Accountability Act of 1996 (" HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (" HITECH"), the federal Physician Payment Sunshine Act, federal consumer protection and unfair competition laws, and analogous state and foreign laws and regulations** . 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~~ **the promotion** , sales, **and** marketing **of healthcare items and services is subject to extensive laws and regulations designed to prevent fraud** , ~~education~~ **kickbacks, self- dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive,** 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~~ . Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. 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. Further, 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. 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, state, local, and foreign healthcare fraud and abuse laws. The laws that may impact our operations include the federal Anti- Kickback Statute, the False Claims Act, the federal Health Insurance Portability and Accountability Act of 1996 (" HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (" HITECH"), the federal Physician Payment Sunshine Act, federal consumer protection and unfair competition laws, and analogous state and foreign laws and regulations. These laws may impact, among other things, our clinical research program, as well as our proposed and future sales, marketing, and education programs. In particular, the promotion, sales, and marketing of healthcare items and services is subject to extensive laws and regulations 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, marketing and promotion, sales commission, customer incentive, and other business arrangements. 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. Our business is subject to complex and evolving U. S. and foreign laws and regulations, information security policies, and contractual obligations relating to privacy and data protection **and security** , including the use, processing, and cross- border transfer of personal information. 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. We receive, generate, ~~and~~ store **, and otherwise process** significant and increasing volumes of sensitive information and business- critical information, including employee and personal data (including protected health information), research and development information, commercial information, and business and financial information. We heavily rely on external security and infrastructure vendors to manage our information technology systems and data centers. We face a number of risks relative to protecting this critical information, including the loss of access, inappropriate use or disclosure, inappropriate modification, and the risk of our being unable to adequately monitor, audit, and modify our controls over our critical information. This risk extends to third- party vendors and subcontractors we use to manage this sensitive data. A wide variety of provincial, state, national, and international laws and regulations apply to the collection, use, retention, protection, disclosure, transfer, and other processing of ~~personal~~ data **relating to individuals** . These laws and regulations are evolving and may result in ever- increasing regulatory and public scrutiny and escalating levels of enforcement and sanctions. For example, the collection and use of personal data in the EU are governed by the EU General Data Protection Regulation (" GDPR"), which became fully effective on May 25, 2018. The GDPR imposes stringent data protection requirements, including, for example, more robust disclosures to individuals and a strengthened individual data rights regime, shortened timelines for data breach notifications, limitations on retention of information, increased requirements pertaining to special categories of data, such as health data, and additional obligations when we contract with third- party processors in connection with the processing of the personal data. The GDPR also imposes strict rules on the transfer of personal data out of the EU to the United States and other countries, and in the context of clinical trials we currently rely on patient informed consent as the legal basis for such transfers. In addition, the GDPR provides that EU member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data. The GDPR provides for penalties for noncompliance of up to the greater of € 20 million or four percent of worldwide annual revenues. The GDPR applies extraterritorially, and we may be subject to the GDPR because of our data processing activities that involve the personal data of individuals located in the EU, such as in connection with any EU clinical trials. Additionally, the UK has implemented legislation that substantially implements the GDPR (the" UK GDPR"), with **substantial** penalties for noncompliance ~~of up to the greater of £ 17. 5 million or four percent of worldwide revenues. Aspects of UK data protection laws and regulations remain unclear. On June 28, 2021, the European Commission announced a decision of" adequacy" concluding that the UK ensures an equivalent level of data protection to the GDPR, which provides some relief regarding the legality of continued personal data flows from the European Economic Area (" EEA") to the UK. Some uncertainty remains, however, as this adequacy determination must be renewed after four years and may be modified or revoked in the interim. We cannot fully predict how the UK GDPR and data protection laws or regulations may develop in the medium- to- long term. We may incur liabilities, expenses, costs, and other operational losses under the GDPR and UK GDPR as well as privacy and data protection laws of Switzerland, the United Kingdom, and applicable EU member states. We may find it necessary or appropriate to make additional changes to the ways we or our service providers collect, disclose, transfer, and otherwise process data within the EEA, Switzerland, and the UK, and to our related policies and practices. This may be onerous and may interrupt or delay our development activities, and adversely affect our business, financial condition, results of operations and prospects~~ . Further, various states, such as California, Massachusetts, and Washington have implemented privacy laws and regulations that impose restrictive requirements regulating the use and disclosure of health information and other personal information. Where state laws are more protective than HIPAA, we must comply with the stricter provisions. In addition to fines and penalties imposed upon violators, some of these state laws also afford private rights of action to individuals who believe their personal information has

been misused. For example, California has enacted legislation, the California Consumer Privacy Act (" CCPA"), ~~that~~ **which** , among other things, requires covered companies to provide new disclosures to California consumers, and affords such consumers new abilities to opt- out of certain sales of personal information ~~. The CCPA became effective on January 1, 2020~~ . The CCPA, as amended and expanded by the California Privacy Rights Act (" CPRA"), requires covered companies to provide new disclosures to individuals and consumers in California, and afford such individuals and consumers new data protection rights, including the ability to opt- out of certain sales of personal information. Numerous other states in the United States have proposed or enacted similar legislation. Further, some states have enacted more specific legislation, such as Washington' s enactment of the My Health, My Data Act, which includes a private right of action. The U. S. federal government is also contemplating federal privacy legislation. **Additionally, the U. S. Department of Justice recently issued a final rule that takes effect in April 2025 and places limitations, and in some cases prohibitions, on certain transfers of sensitive personal data to business partners located in China or with other specified links to China (and other designated countries).** The GDPR, UK GDPR, CCPA, CPRA, and many other federal, state, and foreign laws and regulations relating to privacy and data protection are still being tested in courts, and they are subject to new and differing interpretations by courts and regulatory officials. Additionally, the interplay of federal and state laws may be subject to varying interpretations by courts and government agencies, creating complex compliance issues for us and data we receive, use and share, potentially exposing us to additional expense, adverse publicity and liability. ~~We are working to comply with the GDPR, UK GDPR, CCPA, CPRA and other privacy and data protection laws and regulations that apply to us, and we anticipate needing to devote significant additional resources to complying with these laws and regulations. These and future laws and regulations may increase our compliance costs and potential liability.~~ It is possible that the GDPR, UK GDPR, CCPA, CPRA, or other laws and regulations relating to privacy and data protection may be interpreted and applied in a manner that is inconsistent from jurisdiction to jurisdiction or inconsistent with our current policies and practices. We cannot guarantee that we **or our vendors** are in compliance with all such applicable data protection laws and regulations and we cannot be sure how these regulations will be interpreted, enforced or applied to our operations. Furthermore, other jurisdictions outside the EU are similarly introducing or enhancing **laws and regulations addressing** privacy and data **protection and** security ~~laws, rules, and regulations~~ , which could increase our compliance costs and the risks associated with noncompliance. It is possible that these laws **, regulations, or other actual or asserted obligations** may be interpreted and applied in a manner that is inconsistent with our practices and our **compliance** efforts ~~to comply with the evolving data protection rules~~ may be unsuccessful. We cannot guarantee that we or our vendors may be in compliance with all applicable international laws and regulations as ~~they are~~ **currently maintained and** enforced ~~now~~ or as they evolve. ~~For example, our privacy policies may be insufficient to protect any personal information we collect, or may not comply with applicable laws.~~ Our **actual or alleged** non- compliance could result in government- imposed fines or orders requiring that we change our practices, which could adversely affect our business. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations ~~at the federal and state level~~ may be costly and require ongoing modifications to our policies, procedures and systems. In addition, if we are unable to properly protect the privacy and security of protected health information, we could be alleged or found to have breached ~~our~~ **certain** ~~contracts~~ **contractual obligations** . Our actual or perceived failure to adequately comply with applicable laws and regulations or other actual or asserted obligations relating to privacy and data protection **and security** , or to protect personal data and other data we process or maintain, could result in regulatory enforcement actions against us, including fines, imprisonment of company officials and public censure, claims for damages by affected individuals, other lawsuits or reputational damage, all of which could materially affect our business, financial condition, results of operations and growth prospects. 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 the success of 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 growth prospects. Our business activities may be subject to the Foreign Corrupt Practices Act and similar anti- bribery and anti- corruption laws, as well as U. S. and certain foreign export controls, trade sanctions, and import laws and regulations. Our business activities may be subject to the

Foreign Corrupt Practices Act of 1977, as amended (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 certain 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 health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA. Recently the Securities and Exchange Commission (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. In addition, **if** ~~in the future once~~ we enter a commercialization phase, our products may be subject to U. S. and foreign export controls, trade sanctions, and import laws and regulations. Governmental regulation of the import or export of our products, or our failure to obtain any required import or export authorization for our products, when applicable, could harm our international sales and adversely affect our revenue. ~~Compliance with applicable regulatory requirements regarding the export of our products may create delays in the introduction of our products in international markets or, in some cases, prevent the export of our products to some countries altogether. Furthermore, U. S. export control laws and economic sanctions prohibit the shipment of certain products and services to countries, governments, and persons targeted by U. S. sanctions. If we fail to comply with export and import regulations and such economic sanctions, we may be fined or other penalties could be imposed, including a denial of certain export privileges. Moreover, any new export or import restrictions, new legislation or shifting approaches in the enforcement or scope of existing regulations, or in the countries, persons, or technologies targeted by such regulations, could result in decreased use of our products by, or in our decreased ability to export our products to existing or potential customers with international operations. Any limitation on our ability to export or sell access to our products would likely adversely affect our business.~~ Inadequate funding for the FDA, ~~the~~ **USPTO,** SEC **,** and other government agencies could hinder **or result in the suspension of** 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~~ **operations** ~~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 FDA have fluctuated in recent years as a result. In addition, government funding of the SEC **, USPTO,** and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other government 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. For example, over the last several years the U. S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical government employees and stop critical activities. **The new administration' s freeze on hiring and return- to- office policy may disrupt normal operations of federal agencies, including the FDA.** If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, or to provide feedback on our clinical development plans, which could have a material adverse effect on our business. Further, future government shutdowns or other disruptions to normal operations could impact our ability to access the public markets and obtain the funding necessary to properly capitalize and continue our operations **. We depend on collaborations with third parties for the research, development, and commercialization of certain product candidates. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates** . We anticipate seeking third- party collaborators for the research, development, and commercialization of certain of the product candidates we may develop. For example, we have collaborations with F- star, Takeda, Sanofi, Biogen, and others to further our development of product candidates and to enhance our research efforts directed to better understanding neurodegenerative and ~~LSDs~~ **lysosomal storage diseases** . Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies, biotechnology companies, and academic institutions. If we enter into any such arrangements with any third parties, we will likely have 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 any collaboration that we enter into. Collaborations involving our research programs, or any product candidates we may develop, pose the following risks to us: • collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations; • 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 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 on our ability to obtain and maintain regulatory approval of our products 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 may decide to **terminate or** not pursue development and commercialization of any product candidates we develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator' s strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities; • collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing; • collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our 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 marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing and distribution of such product candidates; • we may lose certain valuable rights under circumstances identified in our agreements with our collaborators, 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, or if they terminate our collaborations with them, we may not be able to develop or commercialize product candidates as planned; **and** • 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 ~~;• 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, including our BBB platform technology; and • collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our development or commercialization program under such collaboration could be delayed, diminished, or terminated~~ . We may face significant competition in seeking appropriate collaborations. Recent 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. If we enter into collaborations to develop and potentially commercialize any product candidates, we may not be able to realize the benefit of such transactions 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. The failure to develop and commercialize a product candidate pursuant to our agreements with our current or future collaborators could prevent us from receiving future payments under such agreements, which could negatively impact our revenues. 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 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. 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 database within certain time frames. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions. Our third- party service providers are not our employees, and we are therefore unable to directly monitor whether or not they devote sufficient time and resources to our clinical and nonclinical programs. These third- party service providers may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for any product candidates we may develop and 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. Our reliance on third parties for the manufacture of the ~~significant~~ majority of the materials for our research programs, preclinical studies, and clinical trials 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. Although we have ~~initiated~~ **substantially completed** the build- out of our Utah site to ~~expand~~ **enable** our clinical manufacturing capabilities for biologic therapeutics, we ~~do not have any operational~~ **are in the process of scaling up** manufacturing ~~facilities~~ **activities** . We currently rely on third- party manufacturers for the manufacture of our materials for preclinical studies and clinical trials and expect to continue to do so for some or all of our materials for preclinical studies, clinical trials **,** and for commercial supply of any product candidates that we may develop. We may be unable to establish any further agreements with third- party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third- party manufacturers, reliance on third- party manufacturers entails additional risks, including the possible breach, termination, or non- renewal of the agreement by the third party, which may be costly or inconvenient, and the inability of the third party to produce the required volume in a timely manner. We may also be exposed to the risks of relying on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting. Third- party manufacturers may not be able to comply with U. S. export control regulations, cGMP regulations, or similar regulatory requirements outside the United States. Our failure, or the failure of our third- party manufacturers, to comply with applicable regulations could result in a need to replace current third- party manufacturers including the possibility of supply delays, 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 growth 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 manufacturers could delay clinical development or marketing approval. ~~We do not currently have arrangements in place for redundant supply for many components of our product candidates.~~ 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 third parties for the manufacture of ~~any~~ **our** 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 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 could harm our business. We rely on third- party suppliers for the raw materials required for the production of our product candidates. Our dependence on these third- party suppliers and the challenges we may face in obtaining adequate supplies of raw materials involve several risks, including limited control over pricing, availability, quality **,** and delivery schedules. As a small company, our negotiation leverage is limited and we are likely to get lower priority than our larger competitors. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Further, we have in the past and may in the future experience delayed shipments of raw materials due to interruptions relating to the aforementioned events **. We do not currently have arrangements in place for redundant supply for certain components of our product candidates** . We may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business. If we are unable to obtain and maintain patent protection for any product candidates we develop or for our ~~BBB~~ **TV** platform ~~technology~~ , our competitors could develop and commercialize

products or technology similar or identical to ours, and our ability to successfully commercialize any product candidates we may develop, and our technology 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 ~~BBB~~ **TV** platform ~~technology~~ and any proprietary product candidates and other technologies we may develop. We seek to protect our proprietary position by in- licensing intellectual property and filing patent applications in the United States and abroad relating to our ~~BBB~~ **TV** platform ~~technology~~, programs and product candidates, as well as other technologies that are important to our business. Given that the development of our technology and product candidates is at an early stage, our intellectual property portfolio with respect to certain aspects of our technology and product candidates is also at an early stage. In addition, we cannot be certain that any patents we own or in-license in the United States adequately cover the Fc domain portion of our ~~BBB~~ **TV** platform ~~technology~~ that binds to transferrin receptor, or adequately cover the antibodies, enzymes or proteins being developed in our ~~ATV: TREM2, ETV: IDS, ETV: SGSH, ETV: IDUA, PTV: PGRN, ATV: Abeta, OTV, or other~~ TV- enabled programs. We have filed or intend to file patent applications on these aspects of our technology and product candidates; however, there can be no assurance that any such patent applications will issue as granted patents. Furthermore, in some cases, we have only filed provisional patent applications on certain aspects of our technology and product candidates and each of these provisional patent applications is not eligible to become an issued patent until, among other things, we file a non- provisional patent application within twelve 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 ~~BBB~~ **TV** platform ~~technology~~, 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 ~~BBB~~ **TV** platform ~~technology~~, 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 ~~BBB~~ **TV** platform ~~technology~~, programs and product candidates could have a material adverse effect on our business, financial condition, results of operations and growth prospects. 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 owned and licensed patents. With respect to both in- licensed and owned intellectual property, we cannot predict whether the patent applications we and our licensors 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 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, including delays as a result of **a global** ~~the COVID- 19~~ pandemic impacting our or our licensors' operations. 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, 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 licensors were the first to make the inventions claimed in any of our owned or licensed patents or pending patent applications, or that we or our licensors were the 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 owned or in- licensed pending and future patent applications may not result in patents being issued which protect our ~~BBB~~ **TV** platform ~~technology~~, 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 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 that we own or in- license may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether our ~~BBB~~ **TV** platform ~~technology~~, 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 growth 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 licensors may be subject to a third- party preissuance submission of prior art to the USPTO, or become involved in opposition, derivation, revocation, reexamination, post- grant and inter partes review, or interference proceedings or other similar proceedings challenging our owned or licensed patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render

unenforceable, our owned or in- licensed patent rights, allow third parties to commercialize our ~~BBB~~ TV platform ~~technology~~, product candidates or other technologies and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third- party patent rights. Moreover, we, or one of our licensors, may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post- grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our or our licensor' s priority of invention or other features of patentability with respect to our owned or in- licensed 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 of our ~~BBB~~ TV platform ~~technology~~, 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 priority or inventorship dispute, we may be required to obtain and maintain licenses from third parties, including parties involved in any such interference proceedings or other priority or inventorship disputes. 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 sufficient rights to exclude others from commercializing products similar or identical to ours. Some of our owned and in- licensed patents and patent applications are, and may in the future be, co- owned with third parties. For example, we currently, and may in the future, co- own certain patents and patent applications relating to our ~~BBB~~ TV platform ~~technology~~ with F- star. In addition, certain of our licensors co- own the patents and patent applications we in- license with other third parties with whom we do not have a direct relationship. Our exclusive rights to certain of these patents and patent applications are 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 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. 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 growth prospects. Our rights to develop and commercialize our ~~BBB~~ TV platform ~~technology~~ and product candidates are subject, in part, to the terms and conditions of licenses granted to us by others or licenses granted by us to others. We are heavily reliant upon licenses to certain patent rights and proprietary technology from third parties that are important or necessary to the development of our ~~BBB~~ TV platform ~~technology~~ and product candidates. For example, in June 2016, we entered into a license agreement with Genentech pursuant to which we received an exclusive license to certain of Genentech' s intellectual property relating to our LRRK2 program, including our BIIB122 / DNL151 product candidate. Our agreements with F- star and other license agreements may not provide exclusive rights to use certain licensed intellectual property and technology 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. For example, F- star retains the right to use itself, and to license to others, its modular antibody technology for any purpose other than the targets which we have agreed with F- star would or may be exclusively available to us. As a result, we may not be able to prevent competitors or other third parties from developing and commercializing competitive products that also utilizes technology that we have in- licensed. In addition, subject to the terms of any such license agreements, we do 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 patents and patent applications covering the technology that we license from third parties. For example, under our agreements with F- star and Genentech, the licensors control prosecution and, in the case of F- star and in specified circumstances, enforcement of certain of the patents and patent applications licensed to us. Also, under our agreements with Takeda, Sanofi and Biogen, they control prosecution, and in specified circumstances, enforcement of certain of the patents and patent applications licensed to them. We cannot be certain that our in- licensed or out- licensed patents and patent applications that are controlled by our licensors or licensees will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If our licensors or licensees fail to prosecute, maintain, enforce, and defend such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, our right to develop and commercialize our ~~BBB~~ TV platform ~~technology~~ and any of our product candidates that are subject of such licensed rights could be adversely affected, and we may not be able to prevent competitors from making, using and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed to and from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensees, our licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution. Furthermore, our owned and in- licensed patents may be subject to a reservation of rights by one or more third parties. For example, our license to certain intellectual property owned by Genentech is subject to certain research rights Genentech granted to third parties prior to our license agreement. In addition, certain of our in- licensed intellectual property relating to RIPK1 was funded in part by the U. S. government. As a result, the U. S. government may have certain rights to such intellectual property. If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose

license rights that are important to our business. We have entered into license agreements with third parties and may need to obtain additional licenses from others to advance our research or allow commercialization of product candidates we may develop or our ~~BBB~~ **TV** platform ~~technology~~. It is possible that we may be unable to obtain additional licenses 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 or continue to utilize our existing ~~BBB~~ **TV** platform ~~technology~~, which could harm our business, financial condition, results of operations, and growth prospects significantly. We cannot provide any assurances that third- party patents do not exist which might be enforced against our current technology, including our ~~BBB~~ **TV** platform ~~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 current license agreements, and we expect our future agreements, will impose various development, diligence, commercialization, and other obligations on us. Certain of our license agreements also require us to meet development timelines, or to exercise commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the licenses. In spite of our efforts, our licensors might conclude that we have materially breached our obligations under such license agreements and might therefore terminate the license agreements, thereby removing or limiting our ability to develop and commercialize products and technology covered by these license agreements. If these in- licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties would have the freedom to seek regulatory approval of, and to market, products identical to ours and we may be required to cease our development and commercialization of certain of our product candidates or of our current ~~BBB~~ **TV** platform ~~technology~~. 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 licensing agreement, including: • the scope of rights granted under the license agreement and other interpretation- related issues; • the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement; • the sublicensing of patent and other rights under our collaborative development relationships; • our diligence obligations under the license agreement and what activities satisfy those diligence obligations; • the inventorship and ownership of inventions and know- how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and • the priority of invention of patented technology. In addition, the agreements under which we currently 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 licensed prevent or impair our ability to maintain our current licensing 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. In addition, the United States federal government retains certain rights in inventions produced with its financial assistance under the Patent and Trademark Law Amendments Act, or the Bayh- Dole Act. The federal government retains a " nonexclusive, nontransferable, irrevocable, paid- up license " for its own benefit. The Bayh- Dole Act also provides federal agencies with " march- in rights. " March- in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a " nonexclusive, partially exclusive, or exclusive license " to a " responsible applicant or applicants. " If the patent owner refuses to do so, the government may grant the license itself. If, in the future, we co- own or license in technology which is critical to our business that is developed in whole or in part with federal funds subject to the Bayh- Dole Act, our ability to enforce or otherwise exploit patents covering such technology may be adversely affected **.** Filing, prosecuting, and defending patents on our ~~BBB~~ **TV** platform ~~technology~~, 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. Further, our ability to pursue patents throughout the world may be delayed or affected due to **a public health crisis such as** the ~~COVID- 19~~ global pandemic. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with our 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. **in** ~~European~~ -- **Europe** ~~applications will soon have the option~~ **as** ~~upon grant~~ of ~~a patent~~ **June 1** , **2023,** ~~of becoming a Unitary Patent which will be subject to the jurisdiction of~~ the Unitary Patent Court (" UPC") **has exclusive jurisdiction over Unitary Patents and offers a uniform and specialized framework for patent litigation at the European level. Furthermore, European applications have the option, upon grant of a patent, of becoming a Unitary Patent and therefore subject to UPC** . This will be a significant change in European patent practice. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty.

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 claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Geopolitical actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the United States and foreign government actions related to Russia' s invasion of Ukraine may limit or prevent filing, prosecution, and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees that have citizenship or nationality in, are registered in, or predominately have primary place of business or profit-making activities in the United States and other countries that Russia has deemed unfriendly without consent or compensation. Consequently, we may be unable to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors 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 growth 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 be paid 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 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 are also dependent on our 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. Geopolitical actions in the United States and in foreign countries could prevent us from continuing to make these periodic payments in certain locations. For example, the United States and foreign government actions related to Russia' s invasion of Ukraine may limit our ability to make or prevent us from making these payments in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia, which could adversely affect our business. 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. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy- Smith America Invents Act (the" America Invents Act"), enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before us could therefore 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 will require us to be cognizant going forward of the time from invention to filing of a patent application. Since 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 or our licensors were the first to either (i) file any patent application related to our ~~BBB~~ **TV** platform ~~technology~~, product candidates or other technologies or (ii) invent any of the inventions claimed in our or our licensor' s patents or patent **applications. Further, changes in the leadership of the PTO and other federal agencies under the new administration may lead to new policies and changes in the regulations that may impact the timelines of our patents** applications. The America Invents Act also includes a number of significant changes that affect the way patent applications will be 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 first 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 first 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 owned or in- licensed patent applications and the enforcement or defense of our owned or in- licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and growth prospects. In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U. S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. For example, the Supreme Court of the United States held in Amgen v. Sanofi (2023) that a functionally claimed genus was invalid for failing to comply with the enablement requirement of the Patent Act. In addition, the Federal circuit recently issued a decision involving the interaction of patent term adjustment (**"** PTA **"**), terminal disclaimers, and obvious- type double patenting. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. 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. For example, in Assoc. for Molecular Pathology v. Myriad Genetics, Inc. (2013), the U. S. Supreme Court held that certain claims to DNA molecules are not patentable. While we do not believe that any of the patents owned or licensed by us will be found invalid based on this decision, we cannot predict how future decisions by the courts, the U. S. Congress or the USPTO may impact the value of our patents. **For example, the IRA passed by Congress authorizes the Secretary of the Department of Health and Human Services (" HHS") to negotiate prices directly with participating manufacturers for selected medicines covered by Medicare even if these medicines are protected by an existing patent. For small molecule medicines, the process begins seven years after initial approval by the FDA. While we do not believe that the IRA or its effects will impact our ability to obtain patents in the near future, we cannot be certain whether it will affect our patent strategy in the long run.** Issued patents covering our ~~BBB~~ **TV** platform ~~technology~~, 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 or one of our licensors initiated legal proceedings against a third party to enforce a patent covering our ~~BBB~~ **TV** platform ~~technology~~, product candidates or other technologies, the defendant could counterclaim that such patent is invalid or unenforceable or raise a defense to infringement. 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 subject matter eligibility for patenting, novelty, obviousness, or non- enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Grounds for defenses to infringement include statutory exemptions to patent infringement for uses related to submitting information to regulatory authorities to seek certain regulatory approvals. Third parties may raise claims challenging the validity or enforceability of our owned or in- licensed 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, interference proceedings, 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 ~~BBB~~ **TV** platform ~~technology~~, product candidates or other technologies. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, a judge or jury could find that our patent claims laws of nature or are otherwise ineligible for patenting, and 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 ~~BBB~~ **TV** platform ~~technology~~, 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. Patent rights are of limited duration. In the United States, if all maintenance fees are paid timely, the natural expiration of a patent is generally 20 years after its first effective filing date. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such product candidates are commercialized. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from biosimilar or generic products. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours. Upon issuance in the United States, the term of a patent can be increased by patent term adjustment, which is based on certain delays caused by the USPTO, but this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. The term of a United States patent may also be shortened if the patent is terminally disclaimed over an earlier- filed patent. A patent term extension (**"** PTE **"**) based on regulatory delay may be available in the United States. However, only a single patent can be extended for each marketing approval, and any patent can be extended only once, for a single product. Moreover, the scope of protection during the period of the PTE does not extend to the full scope of the claim, but instead only to the scope of the product as approved. Laws governing analogous PTEs in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. If we are unable to obtain PTE or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing

products following our patent expiration and may take advantage of our investment in development and clinical trials by referencing our clinical and nonclinical data to launch their product earlier than might otherwise be the case, and our revenue could be reduced, possibly materially. We may be subject to claims challenging the inventorship of our patents and other intellectual property. We or our licensors may be subject to claims that former employees, collaborators, or other third parties have an interest in our owned or in- licensed patents, trade secrets, or other intellectual property as an inventor or co- inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our ~~BBB~~ **TV** platform ~~technology~~, product candidates, or other technologies. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in- licensed patents, trade secrets, or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our ~~BBB~~ **TV** platform ~~technology~~, 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 ~~BBB~~ **TV** platform ~~technology~~, 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. 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 nondisclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants as well as 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. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time- consuming, and the outcome is unpredictable. In addition, some courts inside and outside 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, in- licenses, or otherwise, necessary rights to our BBB platform technology, product candidates or other technologies. We~~ currently have rights to intellectual property, through licenses from third parties, to identify and develop our ~~BBB~~ **TV** platform ~~technology~~ and product candidates. Many pharmaceutical companies, biotechnology companies, and academic institutions are competing with us in the fields of neurodegenerative and ~~LSDs~~ **lysosomal storage diseases** and BBB technology ~~or~~ **and** may have patents and have filed and plan to file 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 BBB technologies that we are evaluating for use with our current or future product candidates. In addition, with respect to any patents we co- own with third parties, we may require licenses to such co- owners' interest to such patents. However, we may be unable to secure such licenses or otherwise acquire or in- license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for our current or future product candidates and our ~~BBB~~ **TV** platform ~~technology~~. The licensing or acquisition of third- party intellectual property rights is a competitive area, and several 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 licensors, 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, our licensors, or our collaborators may prevent or delay the development and commercialization of our ~~BBB~~ **TV** platform ~~technology~~, product candidates, and other technologies. The fields of discovering treatments for neurodegenerative and ~~LSDs~~ **lysosomal storage diseases**, especially using BBB technology, is highly competitive and dynamic. Due to the focused research and development that is taking place by several companies, including us and our competitors, in these fields, the intellectual property landscape is in flux, and it may remain uncertain in the future. As such, there may be significant intellectual property litigation and proceedings relating to our owned, in- licensed, and other third- party intellectual property and proprietary rights in the future. Our commercial success depends in part on our, our licensors' and our collaborators' ability to avoid 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, as well as administrative proceedings for challenging patents, including interference, derivation, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. As discussed above, recently, due to changes in U. S. law referred to as patent reform, new procedures including inter partes review and post- grant review have been implemented. As stated above, this reform adds uncertainty to the possibility of challenge to our patents in the future. Numerous U. S. and foreign issued patents and pending patent applications owned by third parties exist relating to BBB technology and 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 ~~BBB~~ **TV** platform ~~technology~~, product candidates, and other technologies may give rise to claims of infringement of the patent rights of others. We cannot assure you that our ~~BBB~~ **TV** platform ~~technology~~, 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 our ~~BBB~~ **TV** platform ~~technology~~, product candidates, and other technologies might assert are infringed by our current or future ~~BBB~~ **TV** platform ~~technology~~, product candidates or other technologies, including claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover our ~~BBB~~ **TV** platform ~~technology~~, 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 ~~BBB~~ **TV** platform ~~technology~~, product candidates, or other technologies, could be found to be infringed by our ~~BBB~~ **TV** platform ~~technology~~, 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 ~~BBB~~ **TV** platform ~~technology~~, product candidates, or other technologies may infringe. **Generative artificial intelligence (" AI") resources that are publicly available may also present a risk that a company may inadvertently obtain, incorporate or use a third party' s intellectual property.** Third parties may have patents or obtain patents in the future and claim that the manufacture, use, or sale of our ~~BBB~~ **TV** platform ~~technology~~, 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 ~~BBB~~ **TV** platform ~~technology~~, product candidates, or other technologies. In this case, the holders of such patents may be able to block our ability to 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 ~~BBB~~ **TV** platform ~~technology~~, 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 ~~BBB~~ **TV** platform ~~technology~~, 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 ~~BBB~~ **TV** platform ~~technology~~, 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, or results of operations or growth prospects. We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, 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, priority, 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 owned and in- licensed patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our owned or in- licensed 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, 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. We are highly dependent on our key personnel, and if we are not successful in attracting, motivating and retaining highly qualified personnel, 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 management, particularly our Chief Executive Officer, Dr. Ryan Watts, and our scientific and medical personnel. 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 find suitable replacements, could result in delays in the development of our product candidates and harm our business. We primarily conduct our operations at our facility in South San Francisco, a region that is headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel is intense and the turnover rate can be high, which may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. We expect that we may need to recruit talent from 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 restricted stock and stock option grants 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. **Our** ~~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. We do not maintain " key man " insurance policies on the lives of ~~all of these individuals or the lives of~~ any of our ~~other~~ employees. 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 grow the size and capabilities of our organization, and we may experience difficulties in managing this growth. As of December 31, ~~2023~~ **2024** , we had approximately ~~445~~ **422** employees, all of whom were full- time. As our development plans and strategies develop, we must add a significant number of additional managerial, operational, financial, and other personnel. Future growth will impose significant added responsibilities on members of management, including recruiting, integrating, and retaining additional employees; managing our internal development efforts; and expanding our controls, reporting systems, and procedures. 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. 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 our growth, we may not be able to successfully implement the tasks necessary to further develop our product candidates and, accordingly, may not achieve our research, development, and commercialization goals. We have engaged in and may in the future engage in acquisitions 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 in the past engaged in acquisitions and strategic partnerships, and we may engage in various acquisitions and strategic partnerships ~~, or spin outs of businesses~~ in the future, including licensing or acquiring complementary products, intellectual property rights, technologies, or businesses as part of our business strategy. For example, we have collaboration agreements with Takeda, Sanofi and Biogen, and issued stock in connection with entering into certain of those agreements in 2018 and 2020. Any such transaction may entail numerous risks, including: • increased operating expenses and cash requirements; • the assumption of indebtedness or contingent liabilities; • the 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, including difficulties associated with integrating new personnel; • the diversion of our management' s attention from our existing product programs and initiatives in pursuing such an acquisition or strategic partnership; • the loss of key employees, 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; and • our inability to generate revenue from acquired intellectual property, technology and / or products sufficient to meet our objectives or 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. ~~The proposed spin- out of our preclinical small molecule portfolio is subject to various risks and uncertainties and may not be completed on the terms or timeline currently contemplated, or at all, or may not result in the expected benefits, which might harm our business or operations. On January 8, 2024, we announced our intention to spin- out our preclinical small molecule portfolio into a new, independently- funded company (" NewCo"). Unanticipated developments could delay, prevent, or otherwise adversely affect the proposed spin- out, including but not limited to disruptions in general or financial market conditions, litigation or other legal challenges to the spin- out, or potential problems or delays in licensing our intellectual property to NewCo. We cannot assure you that we will be able to complete the spin- out on the terms or the timeline that we announced, if at all. Furthermore, the anticipated benefits of the spin- out are based on a number of assumptions; if some of these prove incorrect, the Company may not be able to achieve the full expected strategic and financial benefits of the transaction. The price of the Company' s common stock may be more volatile around the time of the spin- out, and the Company cannot predict the effect of the spin- out on the trading price of shares of its common stock. Moreover, following the spin- out, the price of shares of the Company' s common stock may fluctuate.~~ Our internal computer systems, or those used by our third- party research institution collaborators, CROs, or other contractors or consultants, may fail or suffer other breakdowns, cyberattacks, or information security breaches or incidents that could compromise the confidentiality, integrity, and availability of such systems and data, expose us to liability, and affect our reputation. We are increasingly dependent upon information technology systems, infrastructure, and data to operate our business. We also rely on third- party vendors and their information technology systems. Despite the implementation of security measures, our internal computer systems and those of our collaborators, CROs, and other contractors and consultants may be vulnerable to damage, outages and interruptions resulting from computer viruses and other malicious code or unauthorized access, or breached, compromised, or otherwise subject to security incidents due to operator error, malfeasance, or other system disruptions. Geopolitical events, such as war and armed conflicts, may increase the risks of cyber- attacks, disruptions, and security breaches and incidents that we and these third parties face. **Security threats can come from a variety of sources, ranging in sophistication from an individual hacker to a state- sponsored attack. Cyber threats may be broad- based or otherwise generic in nature, or they may be custom- crafted against our information systems or those of our collaborators, CROs, or other contractors or consultants.** As the cyber- threat landscape evolves ~~, attacks are growing in frequency, sophistication, and intensity, and are becoming increasingly difficult to detect. Security threats can come from a variety of sources, ranging in sophistication from an individual hacker to a state- sponsored attack. Cyber threats may be broad- based or otherwise generic in nature, or they may be custom- crafted against our information systems or those of our collaborators, CROs, or other contractors or consultants. Over the past few years~~ , cyber- attacks have become more prevalent, intense, sophisticated, and much harder to detect and defend against. Such attacks could include the use of key loggers or other harmful and virulent malware, including ransomware or other denials of service, and can be deployed through malicious websites, the use of social engineering and / or other means. We and our collaborators, CROs, or other contractors and consultants may not be able to anticipate all types of security threats, and we may not be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched, and can originate from a wide variety of sources. Although to our knowledge we have not experienced any such material system failure or security breach or incident to date, if a breakdown, cyberattack or other information security breach or incident were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to loss or misappropriation of trade secrets or loss of, or unauthorized modification, unavailability, disclosure, or other unauthorized processing of other proprietary information or other similar disruption and we could incur liability and reputational damage. For example, any corruption, loss, or other unavailability of 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 our third- party research institution collaborators for research and development of our product candidates and other third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. Cyber- attacks, breaches, interruptions, or other data security incidents could result in legal claims or proceedings by private parties or governmental authorities, liability under federal or state laws that protect the privacy of personal information, regulatory penalties, significant remediation costs, disrupt key business operations, and divert attention of management and key information technology resources. In the United States, notice of breaches must be made to affected individuals, the U. S. Secretary of the Department of Health and Human Services (" HHS"), and for extensive breaches, notice may need to be made to the media or U. S. state attorneys general. Such a notice could harm our reputation and our ability to compete. In addition, U. S. state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. There can be no assurance that we, our collaborators, CROs, contractors, consultants, and any other business counterparties will be successful in efforts to detect, prevent, protect against, or fully recover systems or data from all break- downs, service interruptions, attacks, or security breaches or incidents. Although we maintain standalone cybersecurity insurance, the costs related to significant security breaches, incidents, or disruptions could be material and exceed the limits of any insurance coverage we have, and may result in increases in our insurance costs. Relevant insurance may in the future become unavailable to us on commercially reasonable terms or at all. Any disruption or security breach or incident that results in or is perceived to have resulted in a loss of, or damage to, our data or systems, or inappropriate disclosure, use, acquisition, transfer, modification, unavailability, or other processing of confidential or proprietary information, including data related to our personnel, could result in the loss, unauthorized modification, use, unavailability, disclosure or other unauthorized processing of critical or sensitive data, and could cause us to incur liability. Further, in any such event, the development and commercialization of our product candidates could be delayed and our business and operations could be adversely affected. Any of the foregoing could result in financial, legal, business, or reputational harm to us. 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 third- party research institution collaborators, CROs, CDMOs, suppliers, **clinical trial sites,** and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, **public** health **crises** ~~epidemics such as COVID- 19~~ , and other natural or man- made disasters or business interruptions, for which we are partly uninsured **. For example, the global pandemic caused a temporary disruption in our ability to recruit participants for our clinical trials in the calendar year 2020 and the first quarter of 2021** . 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 bank failures or instability in the financial services sector, 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. **Government responses** ~~We rely on third- party manufacturers~~ to **such events, such as** ~~produce and process our product candidates. Our ability~~ to ~~obtain clinical supplies~~ **public health crises, may also result in disruption and delay** of ~~our product candidates could be disrupted if the operations of these suppliers are affected by a man- made or~~ **our** ~~natural disaster or other~~ business ~~interruption~~ . The majority of our operations ~~including our corporate headquarters~~ are located ~~in a single facility~~ in South San Francisco, California **and Salt Lake City, Utah** . Damage or extended periods of interruption to our corporate, development ~~or~~ **,** research **, or manufacturing** facilities due to fire, extreme weather conditions or natural disaster, power loss, communications failure, unauthorized entry, 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. **In addition to a subsidiary located in Zurich, Switzerland,** ~~Some~~ **some** of our suppliers and collaborative relationships are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including: • economic weakness, including inflation, rising interest rates or political instability in certain 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 non- U. S. countries that do not offer the same level of intellectual property protection 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; • trade protection measures, import or export licensing requirements, or other restrictive government actions; • negative consequences from changes in tax laws; • 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; • business interruptions resulting from geopolitical actions, including war and armed conflict, terrorism, natural disasters including earthquakes, typhoons, floods, and fires, or health epidemics ~~such as COVID- 19~~ ; and • cyberattacks, which are growing in frequency, sophistication and intensity, and are becoming increasingly difficult to detect. **In particular, given the new administration in the United States, there is currently significant uncertainty about the future relationship between the United States and various other countries, most significantly China, with respect to trade policies, treaties, tariffs, taxes, and other limitations on cross- border operations. The U. S. government has and continues to make significant additional changes in U. S. trade policy and may continue to take future actions that could negatively impact U. S. trade. For example, legislation has been introduced in Congress to limit certain U. S. biotechnology companies from using equipment or services produced or provided by**

select Chinese biotechnology companies, and others in Congress have advocated for the use of existing executive branch authorities to limit those Chinese service providers' ability to engage in business in the U. S. We cannot predict what actions may ultimately be taken with respect to trade relations between the United States and China or other countries, what products and services may be subject to such actions or what actions may be taken by the other countries in retaliation. If we are unable to obtain or use services from existing service providers or become unable to export or, if approved, sell our products, our business, liquidity, financial condition, and / or results of operations would be materially and adversely affected. 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, ~~2023~~ **2024**, we had federal net operating loss carryforwards of approximately $ ~~290~~ **436**. 6 million, federal research and development tax credit carryforwards of approximately $ ~~53~~ **64**. ~~1~~ **2** million, and orphan tax credit carryforwards of approximately $ ~~37~~ **56**. ~~4~~ **9** million, some of which will begin to expire in 2034. Under Sections 382 and 383 of the United States Internal Revenue Code of 1986, as amended, (the" Code"), if a corporation undergoes an " ownership change " (generally defined as a greater than 50- percentage- point cumulative change (by value) in the equity ownership of certain stockholders over a rolling three- year period), the corporation' s ability to use its pre- change net operating loss carryforwards and other pre- change tax attributes to offset its post- change taxable income or taxes may be limited. We have experienced ownership changes in the past, and we may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership, including in connection with our October 2022 offering, some of which are outside our control. ~~As a result~~ **Limitations may also apply under state law. For example**, ~~our ability to~~ **recently enacted California legislation limits the** use **of state** ~~our pre- change~~ net operating loss carryforwards **for tax years beginning on or after January 1, 2024** and **before January 1, 2027. As a result of this legislation or** other **unforeseen reasons, we** ~~pre- change tax attributes to offset post- change taxable income or taxes~~ may **not** be ~~subject~~ **able** to **utilize some** ~~limitation. We may be subject to adverse legislative or regulatory tax changes that could negatively impact our~~ **or all of** ~~financial condition. The rules dealing with U. S. federal, state, and local income taxation are constantly under review by legislators and by the IRS and the U. S. Treasury Department. Changes to tax laws (which changes may have retroactive application) have occurred and are likely to continue to occur in the future, which could adversely affect our shareholders. For example, in August 2022, the United States enacted the Inflation Reduction Act, which implemented a 15 % minimum tax on book income for certain companies and introduced a 1 % excise tax on stock buybacks. In addition, the current tax administration has proposed changes to the orphan drug tax credit. Changes in tax laws, regulation, or~~ **our net operating loss carryforwards, even if we attain profitability** ~~enforcement could adversely affect our stockholders or require us to implement changes to minimize increases in our tax liability~~. 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. In addition to the factors discussed in this" Risk Factors" section and elsewhere in this report, these factors 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; • the timing and ability to obtain regulatory approval on our lead product candidates, including DNL310; • failure to achieve development, regulatory, or commercialization milestones under our collaborations; • failure or discontinuation of any of** 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; • failure to~~ develop our ~~BBB~~ **TV** platform ~~technology~~; • results of preclinical studies, clinical trials, or regulatory approvals of product candidates of our competitors, or announcements about new research programs ~~or~~ **,** product candidates **, or technologies** 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; • variations in our financial results or those of companies that are perceived to be similar to us; • changes in the structure of healthcare payment systems or in accounting standards; • ineffectiveness of our internal controls; • significant lawsuits, including patent or stockholder litigation; • market conditions in the pharmaceutical and biotechnology sectors; and • other events or factors affecting general economic, industry, and market conditions, including bank failures or instability in the financial services sector, geopolitical events, such as war and armed conflict, **natural** ~~and outbreaks of pandemic diseases~~ **disasters**, **and public health crises** ~~such as COVID- 19~~. 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 may seriously affect the market price of our common stock, regardless of our actual operating performance. In the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit against us, the defense and disposition of any such lawsuits could be costly and divert the time and attention of our management and harm our operating results, regardless of the merits of such a claim. If securities analysts publish negative evaluations of our stock, or if they do not publish research or reports about our business, the price of our stock and trading volume 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 downgrade their evaluations of our stock, or if we fail to meet the expectations of analysts, 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 or trading volume 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, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock. Sales of our common stock by current stockholders may make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we deem reasonable or appropriate, and make it more difficult for you to sell shares of our common stock. Certain holders of shares of our common stock have rights, 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. For example, on February 27, 2024, we entered into a ~~securities purchase agreement (the "~~ Purchase Agreement ~~")~~ with certain existing accredited investors in connection with ~~the recently announced PIPE financing,~~ **a strategic private offering transaction.** ~~pursuant~~ **Pursuant** to ~~which the~~ **this transaction, we entered into an agreement granting an** ~~investors~~ **investor** ~~were granted~~ certain registration rights ~~. Furthermore, in connection with the PIPE financing, we have agreed to enter into a registration rights agreement with an investor~~ following such time that **the** investor may be deemed an affiliate of the Company ~~, pursuant to which the investor is entitled to certain resale registration rights~~ . Any sales of securities by these stockholders, or the perception that sales will be made in the public market, could have a material adverse effect on the market price for our common stock. We have registered on Form S- 8 all shares of common stock that are issuable under our 2017 Equity Incentive Plan and 2017 Employee Stock Purchase Plan. As a consequence, these shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates. 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. For example, ~~in August~~ **on February 27,** ~~2020~~ **2024** , we **announced a strategic private offering transaction** ~~entered into the Provisional Biogen Collaboration Agreement, and~~ in **which we** ~~connection therewith issued and~~ sold ~~13~~ **3** , ~~310~~ **244** , ~~243~~ **689** shares of our common stock ~~to Biogen in September 2020 for an~~ **and** ~~aggregate~~ **pre- funded warrants to** purchase ~~price~~ **26, 046, 065 shares** of **our common stock, resulting in net proceeds of approximately** $ ~~465~~ **499** . ~~0~~ **3** million **. Our security holders may be further diluted by the exercise of the pre- funded warrants issued** . We, and indirectly, our stockholders, will bear the cost of issuing and servicing all such securities. Additionally, 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 ~~. In January 2020, we sold 9. 0 million shares of common stock in an underwritten follow- on offering pursuant to a shelf registration statement filed in March 2019 and, in October 2022, we sold 11. 9 million shares of common stock in an underwritten public offering pursuant to a second shelf registration statement filed in February 2022. Also in February 2022, we entered into an equity distribution agreement with Goldman Sachs & Co. LLC, SVB Securities LLC, and Cantor Fitzgerald & Co., as sales agents, to establish an at- the- market facility pursuant to which we may offer and sell from time to time up to $ 400. 0 million in shares of our common stock. On February 27, 2024, we announced a PIPE financing in which we have agreed to sell 3, 244, 689 shares of our common stock and pre- funded warrants to purchase 26, 046, 065 shares of our common stock and which is expected to result in gross proceeds of approximately $ 499. 7 million. We have also granted a certain investor certain director nomination and additional registration rights, subject to certain exceptions, conditions, and limitations. Our decision to issue debt or equity securities in any future offering will depend on market conditions and other factors beyond our control, and therefore 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. In addition, any sales of our common stock or other securities under our shelf registration statement could put downward pressure on our stock price ~~. Additionally, 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 a significant percentage of our outstanding common stock. 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. If we are unable to maintain effective internal controls, our business, financial position and results of operations and growth prospects could be adversely affected. As a public company, we are subject to reporting and other obligations under the Securities Exchange Act of 1934, as amended, (" Exchange Act"), including the requirements of Section 404 of the Sarbanes- Oxley Act, which require annual management assessments of the effectiveness of our internal control over financial reporting. The rules governing the standards that must be

met for management and our auditors 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 or auditors may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes- Oxley Act. These reporting and other obligations place significant demands on our management and administrative and operational resources, including accounting resources. Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States (" U. S. GAAP"). Any failure to maintain effective internal controls could have an adverse effect on our business, financial position, results of operations, and growth prospects ~~. Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud. We are subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC~~ . We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well- conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision- making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected. We do not expect to pay any dividends for the foreseeable future. Investors may never obtain a return on their investment. We have never paid cash dividends on our common stock and do not anticipate that we will pay any dividends in the foreseeable future. We currently intend to retain our future earnings, if any, to maintain and expand our existing operations. If we do not pay dividends, our common stock may be less valuable because a return on your investment will only occur if our stock price appreciates, which may never occur. Delaware law and provisions in our charter documents 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 amended and restated 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 issues 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, (the" 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. 0 % 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 common stock and could also affect the price that some investors are willing to pay for our common stock. Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America will be the exclusive forums 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 certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for: • any derivative action or proceeding brought on our behalf; • any action asserting a 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. Our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America 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. If a court were to find either exclusive- forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action or we do not enforce such provision, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business.