

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2020

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO

Commission File Number 001-38792

Alector, Inc.

(Exact name of Registrant as specified in its Charter)

001-38792

(Commission File Number)

82-2933343

(IRS Employer
Identification No.)

Delaware

(State or other jurisdiction of incorporation)

131 Oyster Point Blvd, Suite 600

South San Francisco, California 94080

(Address of principal executive offices, including zip code)

(415) 231-5660

(Registrant's telephone number, including area code)

Not applicable

(Former name or former address, if changed since last report)

Securities registered pursuant to Section 12(b) of the Exchange Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock	ALEC	The Nasdaq Stock Market LLC (The Nasdaq Global Select Market)

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES NO

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES NO

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES NO

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). YES NO

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer Accelerated filer

Non-accelerated filer Smaller reporting company

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES NO

The aggregate market value of the common stock held by non-affiliates of the registrant as of June 30, 2020 (the last business day of the registrant's most recently completed second fiscal quarter) was approximately \$1,375.6 million, based on the closing price of the registrant's common stock, as reported by the Nasdaq Global Select Market on June 30, 2020 of \$24.44 per share.

The number of shares of the registrant's Common Stock outstanding as of February 15, 2021 was 79,584,442.

Portions of the registrant's Definitive Proxy Statement relating to the registrant's Annual Meeting of Shareholders are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. Such Definitive Proxy Statement will be filed with the Securities and Exchange Commission within 120 days after the end of the registrant's 2020 fiscal year ended December 31, 2020.

Alector, Inc.
Annual Report on Form 10-K

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements. All statements other than statements of historical facts contained in this report, including statements regarding our future results of operations and financial position, business strategy, product candidates, planned preclinical studies and clinical trials, results of clinical trials, research and development costs, regulatory approvals, timing and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements. These statements involve known and unknown risks, uncertainties, and other important factors that are in some cases beyond our control and may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “would,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential,” or “continue” or the negative of these terms or other similar expressions. Forward-looking statements contained in this report include, but are not limited to, statements about:

- our plans relating to the development and manufacturing of our product candidates and research programs;
- the ability of our clinical trials to demonstrate safety and efficacy of our product candidates, and other positive results;
- the timing and focus of our future clinical trials, and the reporting of data from those trials;
- the impact of the coronavirus (COVID-19) pandemic on our business;
- our plans relating to commercializing our product candidates, if approved, including the geographic areas of focus and sales strategy;
- the expected potential benefits of strategic collaborations with third parties and our ability to attract collaborators with development, regulatory and commercialization expertise;
- our estimates of the number of patients in the United States who suffer from the diseases we are targeting and the number of patients that will enroll in our clinical trials;
- the size of the market opportunity for our product candidates in each of the diseases we are targeting;
- our ability to expand our product candidates into additional indications and patient populations;
- the success of competing therapies that are or may become available;
- the beneficial characteristics, safety, efficacy, and therapeutic effects of our product candidates;
- the timing or likelihood of regulatory filings and approvals, including our expectation to seek special designations, such as orphan drug designation, for our product candidates for various diseases;
- our ability to obtain and maintain regulatory approval of our product candidates;
- our plans relating to the further development and manufacturing of our product candidates, including additional indications that we may pursue;
- existing regulations and regulatory developments in the United States and other jurisdictions;
- our continued reliance on third parties to conduct additional clinical trials of our product candidates, and for the manufacture of our product candidates for preclinical studies and clinical trials;
- our plans and ability to obtain or protect intellectual property rights, including extensions of existing patent terms where available and the outcome of our ongoing arbitration proceedings;
- the need to hire additional personnel and our ability to attract and retain such personnel;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements, and needs for additional financing;
- our financial performance; and

- the sufficiency of our existing cash and cash equivalents to fund our future operating expenses and capital expenditure requirements.

We have based these forward-looking statements largely on our current expectations and projections about our business, the industry in which we operate and financial trends that we believe may affect our business, financial condition, results of operations, and prospects, and these forward-looking statements are not guarantees of future performance or development. These forward-looking statements speak only as of the date of this report and are subject to a number of risks, uncertainties, and assumptions described in the section titled “Risk Factors” and elsewhere in this report. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein until after we distribute this Annual Report on Form 10-K, whether as a result of any new information, future events, or otherwise.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and you are cautioned not to unduly rely upon these statements.

Investors and others should note that we may announce material business and financial information to our investors using our investor relations website (<https://investors.alector.com>), Securities and Exchange Commission (SEC) filings, webcasts, press releases, and conference calls. We use these mediums, including our website, to communicate with our stockholders and public about our company, our products, and other issues. It is possible that the information that we make available may be deemed to be material information. We therefore encourage investors and others interested in our company to review the information that we make available on our website.

Item 1. Business.

Overview

Our mission is to develop therapies that empower the immune system to cure neurodegeneration and other diseases.

We are a clinical stage biopharmaceutical company pioneering immuno-neurology, a novel therapeutic approach for the treatment of neurodegeneration. Immuno-neurology targets immune dysfunction as a root cause of multiple pathologies that are drivers of degenerative brain disorders. We are developing therapies designed to simultaneously counteract these pathologies by restoring healthy immune function to the brain. Supporting our scientific approach, our Discovery Platform enables us to advance a broad portfolio of product candidates, validated by human genetics, which we believe will improve the probability of technical success over shorter development timelines. As a result, we have identified over 100 system targets, have advanced four product candidates, AL001, AL002, AL003, and AL101, into clinical development, and continue to develop our research pipeline.

AL001, our first product candidate, modulates progranulin (PGRN), a key regulator of immune activity in the brain with genetic links to multiple neurodegenerative disorders, including frontotemporal dementia (FTD), Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis (ALS). AL001 is initially designed to treat FTD, a severe, rapidly progressing neurodegenerative disorder that affects 50,000 to 60,000 people in the United States and roughly 110,000 people in the European Union, with potentially higher prevalence in Asia and Latin America.

AL001 is initially aimed at treating people with FTD who have a known genetic mutation that causes a deficiency in PGRN, which is called FTD-GRN. Our AL001 program has successfully demonstrated safety, target engagement, and proof-of-mechanism with a well-tolerated safety profile in the central nervous systems of healthy volunteers and FTD patients in our Phase 1a, Phase 1b, and Phase 2 clinical trials. In July 2020, we advanced AL001 into a global pivotal Phase 3 trial, named INFRONT-3, in both pre-symptomatic and symptomatic participants with FTD-GRN. We own worldwide rights to AL001.

AL101, our second product candidate in our PGRN portfolio, is designed to treat people suffering from more prevalent neurodegenerative diseases including Alzheimer's disease and Parkinson's disease, in addition to FTD. In line with our therapeutic hypothesis for FTD, mutations that moderately reduce the expression levels of PGRN have been shown to increase the risk of developing Alzheimer's disease and Parkinson's disease, and increased PGRN levels have been demonstrated to be protective for these diseases in animal models. We initiated our AL101 clinical study in January 2020, and we expect to start receiving Phase 1a data in 2021. We also own worldwide rights for AL101.

Our AL002 product candidate is aimed at treating patients with Alzheimer's disease and is being developed in collaboration with AbbVie. Alzheimer's disease is a chronic neurodegenerative disease that is the most common cause of dementia, affecting nearly six million people in 2020 and that number is projected to rise to nearly 14 million by 2050. Alzheimer's disease is the sixth leading cause of death in the United States. AL002 is focused on modulating check-point receptors on the brain's immune cells, targeting Triggering Receptor Expressed on Myeloid cells 2 (TREM2). AL002 has demonstrated a safety and tolerability profile that supports further development, target engagement, and proof-of-mechanism in the central nervous systems of healthy volunteers in a Phase 1 trial. We initiated a Phase 2 trial evaluating AL002 in patients with early Alzheimer's disease in January 2021.

AL003 is another product candidate designed to treat patients with Alzheimer's disease and is also being developed in collaboration with AbbVie. AL003 focuses on modulating check-point receptors on the brain's immune cells, targeting sialic acid binding Ig-like lectin 3 (SIGLEC 3). AL003 has demonstrated a safety and tolerability profile that supports further development and peripheral target engagement in healthy volunteers in a Phase 1a study. AL003 has also completed enrollment of Alzheimer's disease patients in a Phase 1b study that continues to progress.

Our newest development program, AL044, is developing our latest prioritized product candidate that targets *MS4A4A*, a major risk gene for Alzheimer's disease that encodes a transmembrane receptor protein that is expressed selectively in microglia in the brain and is associated with control of microglia functionality and potential viability. We own worldwide rights for our AL044 development program.

We are also expanding our discovery platform to other indications, such as the field of immuno-oncology. We believe that products focused on innate immune biology will complement and expand the efficacy of current immuno-oncology drugs that target the adaptive immune system.

The Immune System is Central to Neurodegeneration

The loss of healthy immune function in the brain, due to cellular aging or mutations of genes that regulate key immune cells, underlies the onset and progression of multiple neurodegenerative disorders. Genomic analyses have shown that there is a strong correlation between genetic mutations that predispose individuals to neurodegeneration and dysfunction in the immune system. As a result of these genetic mutations, the brain's immune function deteriorates and subsequently would fail to carry out critical activities, which include:

- clearing or counteracting pathological neurodegenerative proteins such as amyloid-beta, TAU, alpha-synuclein, and TDP-43;
- providing metabolic and functional support to nerve cells;
- regulating synaptic connections;
- protecting nerve cells by stimulating the regeneration of myelin sheaths around nerve fibers; and
- controlling the neurotoxic activities of activated astrocytes and rogue microglia.

We believe that restoring the immune system's ability to perform all of these vital functions in the brain is crucial to addressing neurodegeneration given that past approaches focusing on single degenerative pathologies have proved inadequate to date.

Since the early 20th century, the root cause of neurodegeneration has been thought to be misfolded and aggregated pathological proteins. Other observable pathologies, including destruction of synapses, accelerated nerve cell death, and dysfunction of the brain support cells, were all thought to be consequences of these pathological misfolded proteins. As a result, attempts to develop therapies for neurodegeneration have been centered on blocking the synthesis of, and removing or dis-aggregating misfolded proteins. These attempts have been largely unsuccessful, as the disease continues to progress despite significant clearance of the misfolded protein. We believe that the multiple pathologies found in degenerative brain disorders become independent of the misfolded proteins, and each other, at early disease stages and are driven primarily by dysfunction of the brain's immune system.

Specifically, the brain's immune system undergoes gradual deterioration of functional characteristics as part of normal biological aging or due to harmful genetic mutations that are linked to neurodegeneration and are associated with accelerated senescence of the brain immune cells. These cells are no longer capable of executing their beneficial and protective roles and instead often become harmful and destructive to the brain. Based on our understanding of the role of genetic mutations in neurodegeneration, we have designed our product candidates to target the mutated genes linked to neurodegeneration, with the goal of slowing or reversing the deterioration of the brain's immune cells to achieve therapeutic benefit. By restoring healthy immune function in the brain, we believe we can simultaneously counteract the multiple independent pathologies responsible for neurodegeneration.

Our Strategy

Our goal is to develop therapies that empower the immune system to cure neurodegeneration and other diseases. The key tenets of our business strategy to achieve this goal include:

- ***Building the leading, fully-integrated company focused on delivering innovative immuno-therapies, validated by human genetics, for the treatment of neurodegeneration.*** We believe that building a fully integrated company will allow us to more rapidly and efficiently develop therapies for patients as

well as create value for our stakeholders. We are focused on building an independent research, development, clinical, and ultimately commercial organization in order to prosecute the full potential of our immuno-neurology approach and Discovery Platform.

- ***Applying our proprietary development capabilities to rapidly advance our product candidates through clinical proof-of-concept studies and beyond.*** We are focused on maximizing the probability of success of our product candidates by leveraging immunology, neurobiology, and human genetics, as well as our state-of-the-art bioinformatics, to enable better and earlier target selection. In addition, we are also focused on a biomarker-driven approach, including proprietary tools and assays, to confirm target engagement, inform patient selection, and follow clinical outcomes.
- ***Maximizing the therapeutic potential of our existing targets and product candidates.*** Given the central physiological roles played by the distinct targets of our product candidates, we believe that there is significant potential for us to address multiple indications with single targets. Our goal is to expand the therapeutic and commercial potential of our existing targets and product candidates to additional indications, such as immuno-oncology. However, we will remain disciplined about advancing this strategy, leveraging our Discovery Platform capabilities to inform expansion areas of maximum value and highest probability of success.
- ***Continuing to focus on discovering new targets and product candidates, validated by human genetics, to prosecute the full power of our insights and platform.*** Our Discovery Platform is central to our efforts to rapidly identify new product candidates with compelling clinical promise. We will continue to invest in our Discovery Platform, including evolving our proprietary analytical tools and assays, to further investigate several of our identified immune system targets as well as generate additional targets and product candidates.

Our Approach

The Role of the Innate Immune System and Microglia in Neurodegeneration

Significant evidence in the last decade has shown that neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, FTD, and ALS, are linked to a dysfunctional brain immune system. In contrast to the dual adaptive and innate components that characterize the broader human immune system, the brain's immune system consists primarily of innate immune cells, known as microglia. These brain resident macrophages account for 10% to 15% of all cells found within the brain and are responsible for many aspects of brain health and maintenance. As the key innate immune cells in the brain, microglia respond to infection and damage, clear cell debris and pathological proteins, nurture neurons and the brain support cells, and control the number and functionality of inter-neuronal connections. Microglia have been our initial focus and new scientific advances have made it possible to understand how these key innate immune cells in the brain represent a crucial focal point for intervening, treating, or preventing neurodegenerative diseases (Figure 1).

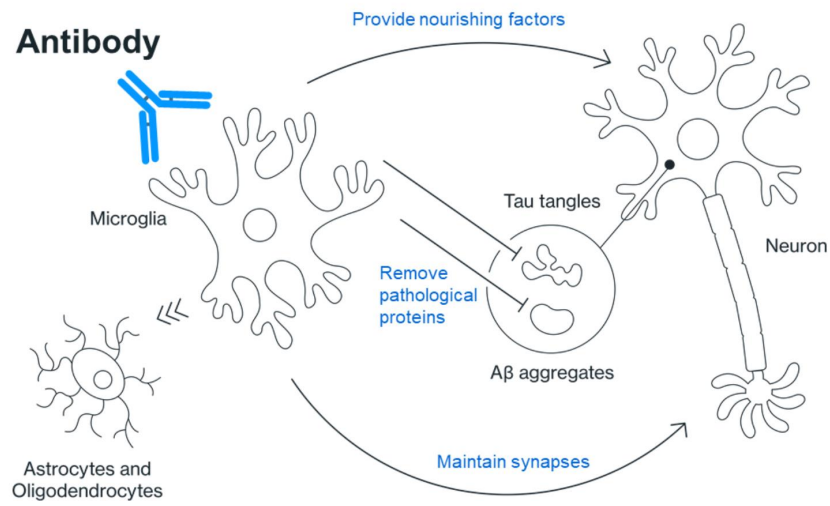


Figure 1. Our antibody product candidates target microglia to harness their many potential beneficial roles in treating neurodegenerative diseases.

Significant Scientific Data Support Our Hypothesis

Understanding how the brain's immune cells affect its structure and function, in both normal and diseased states, is in our view, the key to understanding many neurological diseases. Human genetic evidence has supported the importance of the interactions between the brain and the innate immune system. For example, 22 of the top 29 risk genes for Alzheimer's disease, identified using genetic linkage studies, candidate gene analysis, genome-wide association (GWAS) studies, and whole-genome or whole-exome sequencing, regulate immune function in the brain. Many of these risk genes have been shown to express predominantly in microglia and to control the function of these cells (Figure 2).

of AD risk genes are microglia specific (red)

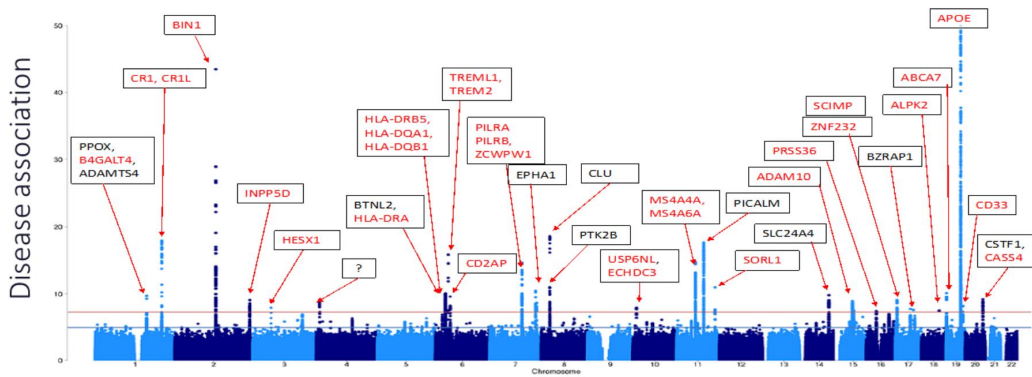


Figure 2. Expression of genes linked to Alzheimer's disease is highly enriched in microglia.¹

Microglia have been shown to be key cells in overall brain maintenance, health, and function and are the brain's first line of immune defense. These innate immune cells are tooled with "microglial sensomes" which enable them to constantly survey brain cells to identify and respond to subtle signs of pathology or dysfunction. Microglia scavenge the brain for toxic misfolded proteins, cell debris, damaged or unnecessary nerve cells, dysfunctional or aged synapses, and infectious agents. In addition, microglia support the generation of new neurons and synapses and remodel neuronal circuits. Microglia also control the survival and function of astrocytes and oligodendrocytes, the main brain support cells which control brain metabolism and blood supply and replenish aged or damaged nerve fibers after injury. Further, microglia have been shown to modulate the permeability of the blood brain barrier allowing access to peripheral immune cells, to assist against infection or injury. Microglia can also change their morphology, functionality, and number in response to changing brain environment.

Analysis of gene transcription at the single-cell level in microglia from normal and diseased brains revealed that multiple microglia subtypes exist which may respond to specific disease pathologies in the brain. Our product candidates are designed to recruit microglia subtypes by targeting microglia check-point proteins that control their survival, proliferation, migration, and function. This allows us to differentially modulate microglia activity as needed to counteract a given degenerative brain disorder.

Findings in the fields of human genetics, immunology, and neuroscience have indicated that as a result of normal aging or genetic mutations, the beneficial functions of the microglia deteriorate leading to massive death of neurons and consequently to neurodegeneration.

¹ Hansen, D., Hanson, J., Sheng, M. "Microglia in Alzheimer's disease." *Journal of Cell Biology*. Volume 217, Number 2, February 2018

The following table outlines the key impact of functional and dysfunctional microglia:

<u>Functional Microglia</u>	<u>Dysfunctional Microglia</u>
•Clear/counteract and form a barrier around pathological proteins such as amyloid-beta	•Reduced ability to remove, or to limit the damage caused by pathological proteins leading to dysfunction of neuronal connections and ultimately leading to neuronal cell death
•Provide metabolic and functional support to nerve cells	•Reduced ability to provide nourishing factors to neurons leading to neuronal cell death
•Regulate healthy synaptic connections	•Indiscriminate destruction of synapses leading to reduced number of synapses and dysfunctional neuronal connections
•Control the function of astrocytes, the brain's star shaped support cells that help maintain the blood-brain barrier, provide nutrients to neurons, repair the nerve tissue following injury, and facilitate neurotransmission	•Inducement and conversion of beneficial astrocytes to toxic astrocytes leading to neuronal cell death
•Control the survival and function of oligodendrocytes that provide protective myelin sheaths around nerve fibers	•Failure to support oligodendrocytes, leading to neuronal dysfunction

Our Discovery Platform

Our Discovery Platform leverages human genetic datasets, advanced tools in bioinformatics and imaging, and insights in neurodegeneration and immunology to: (1) identify immune system targets that play a critical role in the development of multiple neurodegenerative diseases, and rapidly develop antibody therapeutics to these targets, (2) interrogate and prioritize those targets for activity using biomarkers and related proprietary assays and preclinical models, and (3) clinically test product candidates in genetically defined patient populations that are most likely to respond to treatment. We believe that these platform capabilities provide us with the tools to solve the conceptual and technical challenges associated with development of drug candidates for neurodegeneration.

We rely on proprietary immuno-neurology bioinformatics algorithms and methodologies to analyze large genetic datasets from diseased and healthy individuals, brain-based gene expression profiling, brain-based proteomics, and human pathology. These proprietary capabilities allow us to rapidly identify tractable targets, pharmacodynamic biomarkers, and patient populations associated with aberrant immune function which lead to neurodegeneration. Specifically, the three priorities of our platform efforts are:

- **Target Selection.** Our target selection capabilities address a wide array of factors that we believe inform efficient, optimized therapeutic outcomes, including genetic and mechanistic rationale. We leverage our state-of-the-art bioinformatics to identify genetic mutations in the brain immune system that we believe are the root cause of neurodegeneration. We employ a suite of genetic tools to elucidate the immune dysfunction caused by these mutations. We then seek to engineer immune modulating antibody product candidates to functionally counteract the harmful consequence of these genetic mutations. We leverage *in vitro* and *in vivo* functional tools to validate the activity of our product candidates and their ability to cross the blood brain barrier at sufficient quantities to be therapeutically effective.
- **Biomarker Selection.** We are able to identify and employ molecular biomarkers, assays, and imaging techniques that are tailored to our product candidates to confirm target engagement and quantify their therapeutic impact, allowing us to potentially obtain clinical data earlier than would be expected using traditional clinical measures.
- **Patient Selection.** We utilize genetic screening and biomarkers to better align a patient's specific diagnosis with the targeted intervention in our clinical studies.

We employ gene expression profiling, proteomics, brain imaging, and data on disease pathology as well as our own preclinical and clinical data to continually refine our proprietary immuno-neurology algorithms and

methodologies. Using our Discovery Platform to identify targets that are validated by human genetics, disease biomarkers, and responsive patient populations, we believe that we are positioned for greater probability of technical success on more efficient timelines relative to historical drug development in neurodegeneration.

Our Pipeline Programs

Figure 3. The following table highlights our clinical programs.

TARGET	RESEARCH	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER
Progranulin	FTD-GRN					
	FTD-C9orf72					
Progranulin	Neurology					
TREM2	Alzheimer's disease (AD)					abbvie
SIGLEC3	Alzheimer's disease (AD)					abbvie
MS4A4A	Alzheimer's disease (AD)					
SIRP-alpha	Cancer					Innovent
Multi-Siglec	Cancer					

In addition to our pre-clinical and clinical programs described above, we continue to expand the number of research programs in our pipeline focused on targeting Alzheimer's disease, Parkinson's disease, ALS, progressive multiple sclerosis, and oncology.

Our Progranulin Program

Our first development program is focused on modulating levels of PGRN, a key regulator of microglia function in the brain with strong genetic links to FTD and other neurodegenerative disorders. Healthy individuals carry two copies of PGRN that function together to produce healthy levels of PGRN throughout the body. Mutations in both copies of the PGRN gene lead to a neurodegenerative disease called neuronal ceroid lipofuscinosis, which is typified by childhood dementia, vision loss, and epilepsy. Mutations in a single copy of PGRN lead to a drop of between 50% and 70% in the level of PGRN and consequently lead to development of FTD with about 90% penetrance by 75 years of age² with greater than 90% probability. Moreover, large scale human genetic studies have shown that mutations in the gene for PGRN, which leads to a more modest decrease in the level of PGRN, increases the risk for Alzheimer's disease and Parkinson's disease, making PGRN a significant risk gene for these disorders as well.

Healthy levels of PGRN are associated with many cellular processes that include, but are not limited to, normal microglial activities, neuronal survival, and lysosome function. As shown in the figure below (Figure 4), PGRN deficiency disrupts microglia-neuronal homeostasis in the brain and promotes neurodegeneration through the release of cytotoxic cytokines and complement factors by dysfunctional microglia. Moreover, these microglia activate astrocytes, which in turn, damage neurons. Thus, lack of PGRN leads to disrupted health and function of both neurons and microglia and if not corrected, rapid neurodegeneration.

² Cruts et al. Nature. 2006;442:920-4. [[PubMed](#)]

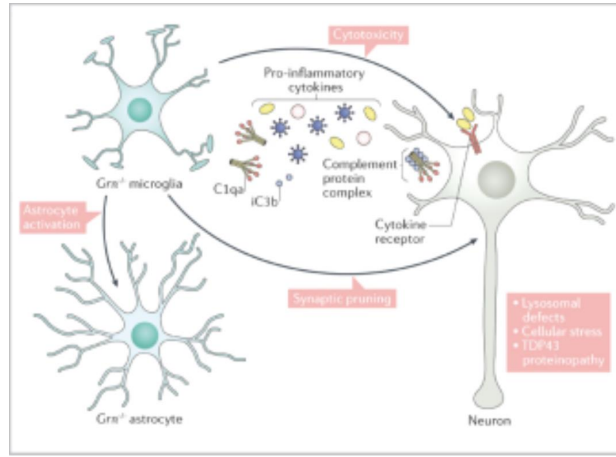


Figure 4. PGRN deficiency disrupts homeostasis between microglia and neurons, and promotes neurodegeneration during aging.³

SORT1 Controls PGRN Levels in the Body

Human and mouse genetic studies have identified the neurotrophic factor PGRN degrading receptor Sortilin (SORT1) as a major negative regulator of PGRN levels in plasma and the brain. SORT1 is a sorting receptor on the cell surface and on the endoplasmic reticulum-Golgi apparatus within the cell. SORT1 binds to extracellular PGRN in the plasma and brain and transports it into the cells for degradation by the lysosome resulting in decreasing levels of extracellular PGRN. SORT1 deficiency increases PGRN plasma and brain levels by two to three-fold in mouse models, while variants that modestly reduce expression of SORT1 increase the level of PGRN in humans.

Moreover, genetic loss of SORT1 in mice does not lead to the adverse effects associated with genetic loss of PGRN, and PGRN continue to function as expected in the absence of SORT1. These studies and others have indicated to us that blocking SORT1 with a pharmacological agent would be a safe and effective approach in increasing the level of functional PGRN in the brain.

We have developed two distinct product candidates that target SORT1, AL001 and AL101, designed to increase PGRN levels in the brain of patients to counteract the damage sustained due to low PGRN levels in neurodegenerative disorders. Our first product candidate, AL001, is initially intended to target orphan disorders, including genetic forms of FTD such as in patients that are missing a functional copy of the PGRN gene (FTD-GRN). Our second PGRN product candidate, AL101, is intended to target widely prevalent neurodegenerative disorders such as Alzheimer’s disease and Parkinson’s disease, in addition to FTD. We have worldwide development and commercial rights to our PGRN product candidates.

AL001 for the Treatment of FTD

Our first product candidate, AL001, is a humanized recombinant monoclonal antibody that is intended to be delivered by intravenous, peripheral infusion to the blood stream to increase the levels of PGRN in the brains of FTD-GRN patients. AL001 functions by shutting down the SORT1 degradation mechanism for PGRN and increasing the circulating half-life of the functional PGRN in the brain. AL001 received orphan drug designation from the FDA for the treatment of FTD in 2018 as well as Fast Track designation for the treatment of patients with

³ Kao, A., McKay, A., Singh, P., Brunet, A., Huang, E. “Progranulin, lysosomal regulation and neurodegenerative disease.” *Nature Reviews Neuroscience*. Volume 18, Number 6, June 2017.

FTD-GRN. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of market exclusivity. This exclusivity precludes the FDA from approving another marketing application for the same indication for that time period, unless the later product is clinically superior. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. Fast Track designation is designed to facilitate the development and expedite the review of therapies which treat serious conditions and fill an unmet medical need. Programs with Fast Track designation may benefit from early and frequent communications with the FDA, potential priority review, and additionally, a rolling submission of the marketing application.

Overview of FTD

FTD is a rapidly progressing and severe degenerative brain disease with no approved treatment. FTD is a form of dementia found most frequently in individuals less than 65 years old at time of diagnosis. Patients with FTD exhibit a range of symptoms including personality changes including compulsive behavior, lack of restraint, apathy, and anxiety as well as language and behavioral problems. Average life expectancy in FTD patients is seven to 10 years after the start of symptoms. FTD symptoms have an insidious onset with clinical symptoms usually appearing between 45 to 65 years of age at an average age of 58. Hence, FTD is considered an early-onset dementia as compared to late-onset Alzheimer's disease, and is more common than Alzheimer's disease in early-onset dementia under the age of 60 years.

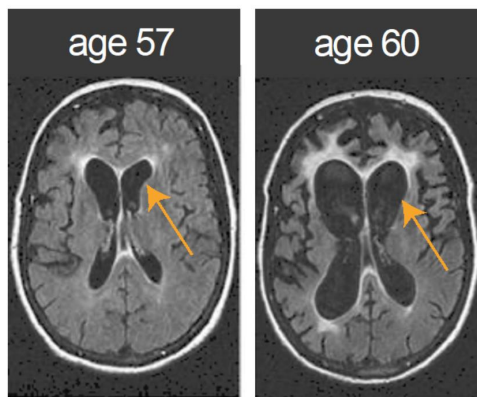


Figure 5. MRI of frontal and temporal atrophy in FTD.

Although FTD was poorly understood and thought to be rare, over the past decade the scientific community has gained a knowledge about the biology of FTD as well as an awareness of disease prevalence. FTD affects roughly 50,000 to 60,000 people in the United States and roughly 110,000 in the European Union. There are multiple heritable forms of FTD, and FTD-GRN, and FTD-GRN patients represent 5% to 10% of all people with FTD. There are currently no approved treatments options available for FTD. Healthy individuals carry two copies of PGRN that function together to produce sufficient levels of PGRN throughout the body. Mutations in a single copy of PGRN lead to a drop of between 50% and 70% in the level of PGRN and consequently lead to development of FTD with about 90% penetrance by 75 years of age⁴ with greater than 90% probability. Researchers have identified over 70 inherited loss of function mutations in PGRN that lead to FTD to date.

⁴ Cruts et al. Nature. 2006;442:920–4. [[PubMed](#)]

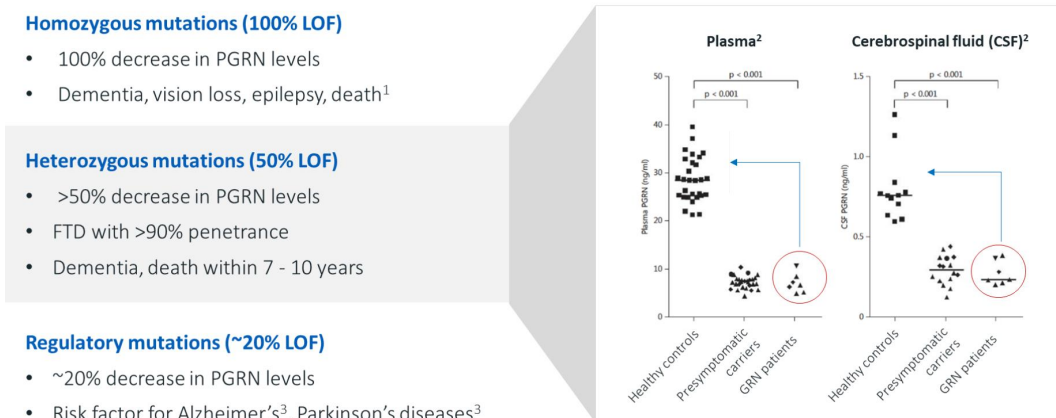


Figure 6. Mutations in a single copy of PGRN lead to a 50% or greater decrease in the level of PGRN and lead to development of FTD with a greater than 90% probability.

The rate of disease progression in FTD is faster than in Alzheimer's disease, suggesting that clinical trials with disease-modifying agents have the potential to obtain clinical data more quickly and with fewer subjects in FTD than in Alzheimer's disease. For example, the median survival from symptom onset in FTD is shorter than in Alzheimer's disease.

We believe that we can establish rapid clinical proof-of-concept in FTD-GRN patients given its genetically-defined patient population, fast rate of disease progression, and our ability to leverage fluid and imaging biomarkers. In FTD-GRN patients, inhibition of SORT1 through AL001 represents a potential mechanism to compensate for the over 50% reduction of PGRN. AL001 is intended to reduce the ability of SORT1 to bind to and degrade PGRN, leading to increases in the levels of PGRN through increasing its circulating half-life (Figure 7). We have tested our PGRN program antibodies in various animal models, healthy volunteers, and FTD-GRN patients and have achieved significantly elevated, long-lasting levels of PGRN in the brain after intravenous administration.

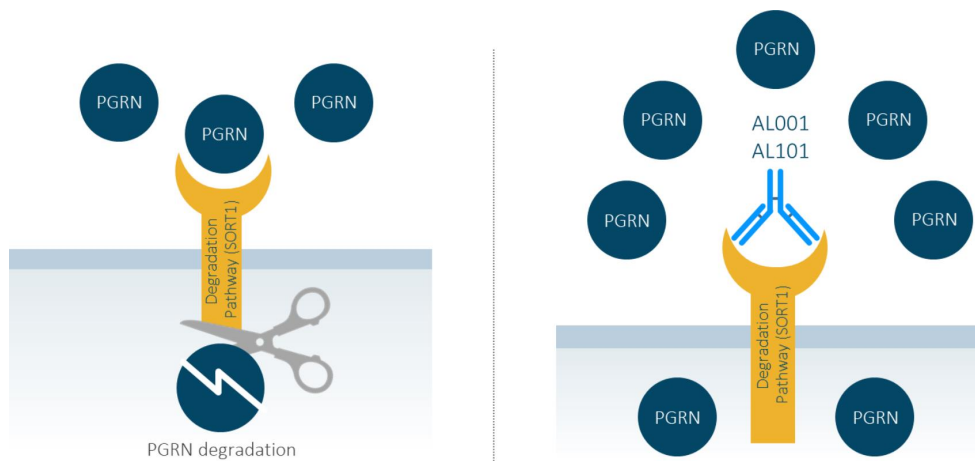


Figure 7. Mechanism of action for our PGRN programs. AL001 binds to SORT1 and prevents degradation of PGRN, increasing its circulating half-life significantly. A similar mechanism of action is also applicable for AL101.

AL101 for the Treatment of Alzheimer’s Disease and Parkinson’s Disease

We are developing a second product candidate in our PGRN program, AL101, that targets SORT1 for large patient populations such as Alzheimer’s disease and Parkinson’s disease. The FDA has granted orphan drug designation for the treatment of FTD to AL101, as well as Fast Track designation for the treatment of patients with FTD-GRN.

Mutations that moderately reduce the amount of PGRN in the brain increase the risk for Alzheimer’s disease and Parkinson’s disease. Moreover, some Parkinson’s disease patients have been shown to have reduced levels of PGRN. In line with our therapeutic hypothesis, we plan to target PGRN as a potential disease modifying therapeutic for patients suffering from Alzheimer’s disease and/or Parkinson’s disease.

Overview of Alzheimer’s Disease

Alzheimer’s disease is a chronic neurodegenerative disease that usually starts slowly in people over 65 years of age and worsens over time. It is the most common cause of dementia, accounting for 60% to 70% of all cases. The most common early symptom of Alzheimer’s disease is difficulty in remembering recent events. As the disease advances, symptoms can include problems with language, disorientation, mood swings, loss of motivation, failure to manage self-care, and behavioral issues. As a person’s condition declines, they often withdraw from family and society. Gradually, bodily functions are lost, leading to death. Although the speed of progression can vary, the typical life expectancy following diagnosis is eight to ten years.

While estimates of the prevalence of Alzheimer’s disease vary, the Alzheimer’s Association estimates that in 2020, there were more than five million Americans age 65+ suffering from Alzheimer’s disease and that number is projected to nearly triple by 2050. Alzheimer’s disease is the sixth leading cause of death in the United States and the fifth-leading cause of death for those ages 65 and older.

In addition to its debilitating effect on patients’ cognition and day-to-day functioning, Alzheimer’s disease places a significant burden on the healthcare system. According to the Alzheimer’s Association, the aggregate cost of care in 2020 for patients with Alzheimer’s disease and other types of dementia in the United States was estimated to be \$305 billion, with nearly two-thirds over half of which is borne by the Medicare system. Total payments for health care, long-term care and hospice care for people with Alzheimer’s and other dementias are projected to increase to more than \$1.1 trillion in 2050.

Overview of Parkinson's Disease

Parkinson's disease is a long-term degenerative disorder of the central nervous system that mainly affects the motor system. Early in the disease, the most obvious symptoms are shaking, rigidity, slowness of movement, and difficulty with walking. Cognitive and behavioral problems may also occur. Dementia becomes common in the advanced stages of the disease. Depression and anxiety are also common, occurring in more than a third of people with Parkinson's disease. Other symptoms include sensory, sleep, and emotional problems. Parkinson's disease typically occurs in people over the age of 60. The average life expectancy following diagnosis is between three to 10 years after the onset of symptoms.

There is no disease modifying treatment for Parkinson's disease, and the options for patients are limited to treatments that improve symptoms. Initial treatment is typically with the anti-Parkinson's drug medication levodopa, with dopamine agonists being used once levodopa becomes less effective. As the disease progresses and neurons continue to be lost, these medications become less effective while at the same time they produce a complication marked by involuntary writhing movements.

According to the Parkinson's Foundation, more than 10 million people worldwide are living with Parkinson's disease. Approximately 60,000 Americans are diagnosed with Parkinson's disease each year and an estimated one million Americans will be living with Parkinson's disease by the year 2040. According to the Parkinson's Foundation, the combined direct and indirect cost of Parkinson's, including treatment, social security payments and lost income, is estimated to be nearly \$52 billion per year in the United States alone. It is estimated that by 2040, over 12 million people globally will have Parkinson's disease.

Our PGRN Product Candidates Development Plan

We initiated our AL001 Phase 1a clinical study in September 2018. Our AL001 product candidate has demonstrated target engagement and increases in the disease associated pharmacodynamic marker PGRN in the brains of primates, healthy volunteers, and FTD-GRN patients. We initiated our AL101 Phase 1a clinical study in January 2020, and we expect to start receiving Phase 1a data in 2021. AL001 successfully demonstrated proof-of-mechanism in a Phase 1a study (n=50) in healthy volunteers and in the Phase 1b portion of the study (n=14) in FTD-GRN patients by showing a statistically significant increase in PGRN levels relative to baseline when compared to pooled placebo in plasma and in CSF at the pre-specified follow-up time point. The primary endpoints of the study are safety and tolerability. The secondary endpoints include pharmacokinetic and pharmacodynamic measurements, including changes of PGRN in serum and the CSF. Pharmacodynamic characteristics include the biochemical and physiological effects of a product candidate, and pharmacokinetic characteristics describe the time course, for example, product candidate absorption, distribution, metabolism, and excretion.

Sustained increase in CSF PGRN in AL001 Phase 1b study

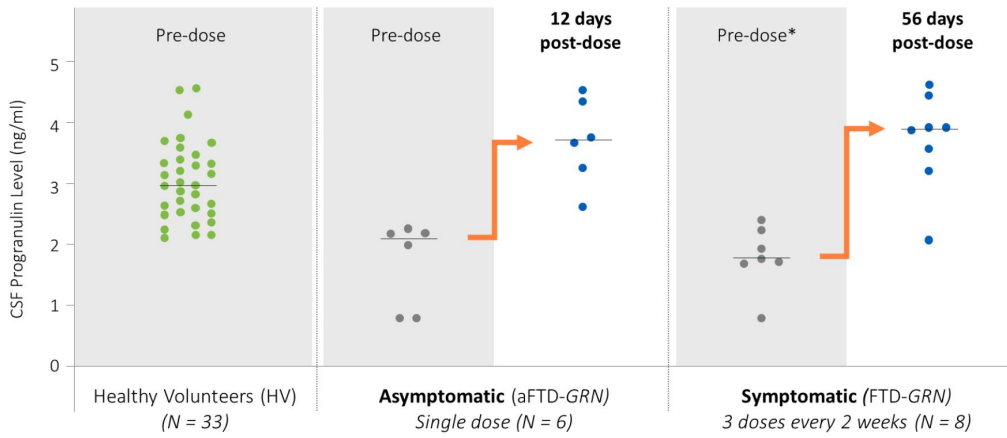


Figure 8. AL001 restores PGRN levels back to normal range in healthy volunteers and symptomatic and asymptomatic FTD-GRN patients.

Results showed that AL001 was generally safe and well-tolerated, with no drug-related serious adverse events or dose-limiting adverse events reported in the study, achieving the primary objective of the study. There were no drug-related serious adverse events or dose limiting adverse events reported in the study, achieving the primary endpoint. Moreover, in our Phase 1a and 1b studies, statistically significant increases in plasma and CSF PGRN levels relative to baseline were also observed, and the magnitude and duration of the effect in plasma and CSF PGRN levels appeared to be dose dependent.

In the third quarter of 2019, we advanced AL001 into a Phase 2 study. Our preliminary Phase 2 preliminary results similarly showed that there were no drug-related serious adverse events or dose limiting adverse events reported in the study and significant increases in plasma PGRN levels relative to baseline back to the normal range were also observed, and the magnitude and duration of the effect in plasma PGRN levels appeared to be dose dependent. The Phase 2 study also includes an additional genetic subset of FTD patients (FTD-C9orf72). We plan to continue this 96-week open-label Phase 2 study and present additional data from the study participants in 2021.

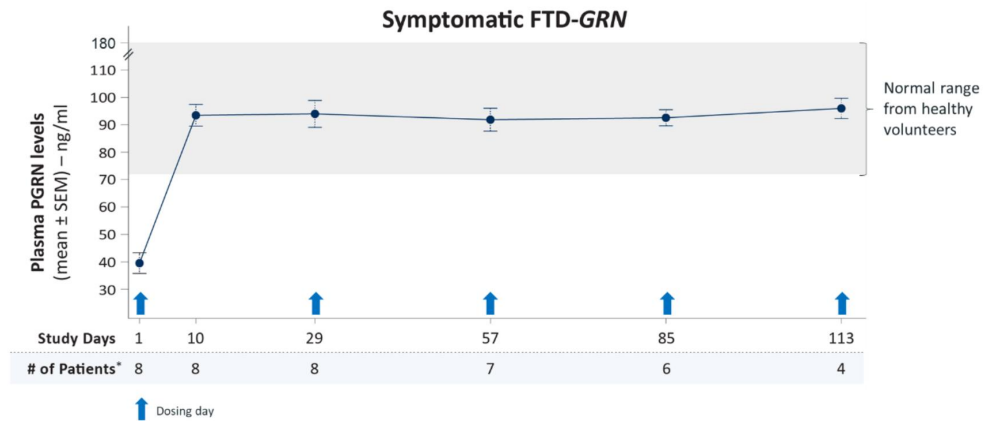


Figure 9. Phase 2 data shows plasma PGRN restored to normal in FTD-GRN participants.

We review and monitor biomarker data from these studies to confirm target engagement and quantify their therapeutic impact. In addition to reviewing PGRN levels in plasma and CSF, we evaluate disease-associated proteins, including inflammatory (i.e. SPP1, CHIT1) and lysosomal (i.e. CTSB) biomarkers and neurofilament light chain (NfL). NfL has been associated with disease progression in FTD patients and identified as a marker of treatment effect in neurodegenerative diseases such as amyotrophic lateral sclerosis, spinal muscular atrophy, and multiple sclerosis in peer-reviewed journals. We have previously reported results from our AL001 Phase 1b study and preliminary data from our AL002 study which showed normalization in a number of disease-associated proteins, further validating our decision to progress AL001 into a Phase 3 study.

In July 2020, we advanced AL001 into a global pivotal Phase 3 trial in both pre-symptomatic and symptomatic participants with FTD-GRN, named INFRONT-3. The randomized, double-blind, placebo-controlled trial will enroll up to 180 FTD-GRN mutation carriers across approximately 50 sites in the United States, Europe and Australia. Symptomatic and pre-symptomatic participants will be randomized to receive AL001 or placebo intravenously every four weeks. Participants will also be given the option to continue receiving treatment in an open-label extension study. The primary endpoint of the pivotal Phase 3 trial is to measure the effect of AL001 on clinical decline by utilizing the CDR® plus NACC FTLD-SB assessment, which evaluates clinical impairments in behavior, language, memory, judgment, and functional activities in trial participants. In addition, the trial will assess secondary clinical endpoints, multiple biomarkers and safety.

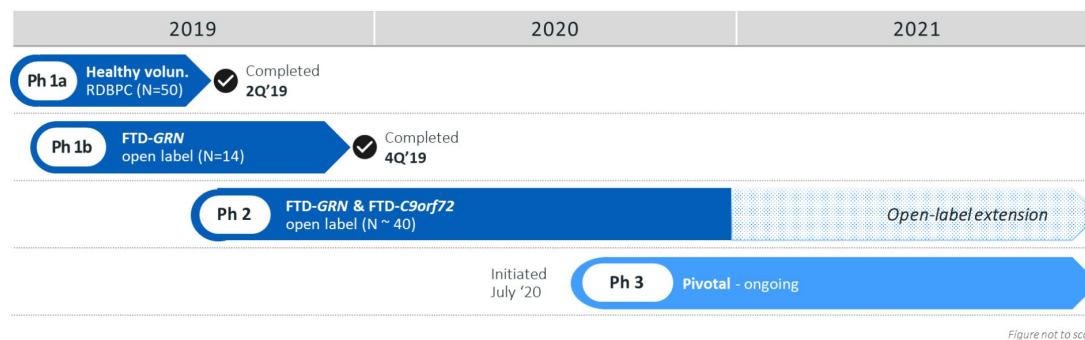


Figure 10. Clinical plan for AL001 in FTD-GRN. (Figure not to scale.)

Potential Additional Applications for Our PGRN Program

Our initial PGRN program is currently targeted only at patients with FTD-GRN, which is a subset of the total FTD patient population. Beyond FTD-GRN, we believe AL001 has the potential to treat other rare diseases that share pathological mechanisms with FTD-GRN. In order to treat any other rare diseases and the broader FTD patient population, we will be required to conduct additional clinical studies in order to obtain the applicable approvals for that specific patient population. We are enrolling an additional genetic subset of FTD patients (FTD-C9orf72) in our Phase 2 clinical trial of AL001 and may expand to additional FTD subpopulations in the future, and we will evaluate AL001 in patients with ALS caused by C9orf72 repeats, which share TDP-43 pathology with FTD-GRN. In addition, polymorphic mutations that moderately reduce the expression levels of PGRN have also been shown to increase the risk of developing Alzheimer’s disease and Parkinson’s disease, and increased PGRN levels have been demonstrated to be protective for these diseases in animal models. We are developing AL101 ultimately to target these large chronic neurodegenerative diseases (Figure 11). The study is a randomized, double-blind, placebo-controlled Phase 1 trial expected to enroll up to 42 healthy volunteers at a single clinical study site in the United States. The study is designed to assess the safety, tolerability, pharmacokinetics, pharmacodynamics, and bioavailability profile of intravenously and subcutaneously administered doses of AL101. For our other programs, we anticipate following a similar development approach to expand into additional patient populations as appropriate.

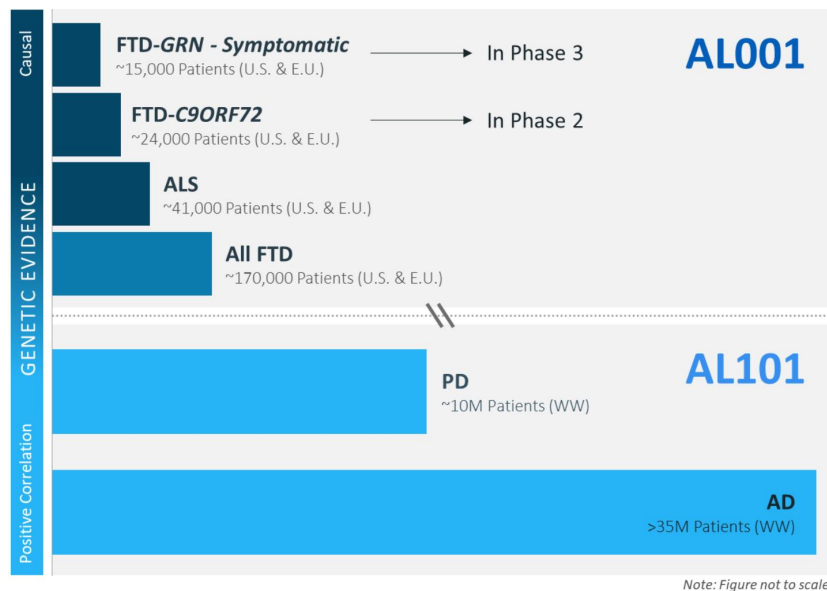


Figure 11 Our PGRN programs have broad therapeutic potential, including FTD and other more prevalent neurodegenerative diseases. (Figure not to scale.)

Our TREM2 Program

TREM2 is a transmembrane receptor protein that is expressed on a subset of innate immune cells and selectively on microglia in the brain. TREM2 on microglia cells is thought to promote improved cell migration to the site of injury, improved cell survival, increased phagocytosis, and increased cell proliferation. Rare individuals with homozygous TREM2 mutations, or mutations on both chromosomal copies, may develop neurodegeneration by the age of 40 with an average lifespan of 10 years following diagnosis. A gene variant in one of the two copies of TREM2 is found to increase the risk of Alzheimer’s disease by threefold. Not only do mutations in a single copy of TREM2 increase the risk of Alzheimer’s disease significantly, but Alzheimer’s disease patients with TREM2 mutations exhibit an earlier onset of symptoms by three years and an increased rate of brain volume loss compared to individuals without such mutation. Evidence also suggests that gain of function mutation leading to increased extension of TREM2 confer a protective phenotype against Alzheimer’s disease.

The discovery of strong genetic linkage of TREM2 to Alzheimer’s disease in 2013 was one of the first examples in which large scale genomic analyses were used to identify a rare gene variation and link it to an increase in the risk of late-onset Alzheimer’s disease.

TREM2 binds to membrane lipids and lipoproteins such as Apolipoprotein E (ApoE) which are normally found in the brain. Mutations in the gene for ApoE are also known to significantly increase the risk of development of Alzheimer’s disease and is the single highest risk factor for Alzheimer’s disease.

AL002 for the Treatment of Alzheimer’s Disease

Our product candidate, AL002, is a humanized, TREM2 activating, monoclonal antibody that is intended to be delivered by intravenous, peripheral infusion into the blood stream (Figure 12). AL002 is a microglia cell regulator that modulates the TREM2 receptor and is being developed for the treatment of Alzheimer’s disease in collaboration with AbbVie.

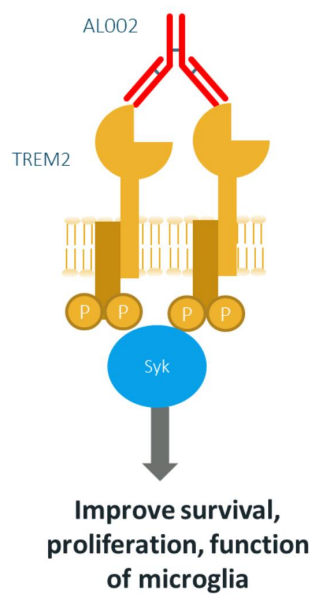


Figure 12. Mechanism of action of our TREM2 activating product candidate AL002.

There are currently no cures or approved disease-modifying therapies for Alzheimer’s disease, and there are only two classes of approved therapies for symptomatic treatment: acetylcholinesterase inhibitors and glutamatergic modulators. These drugs are designed to help preserve neuronal communication, but only provide temporary benefit and do not slow or halt neuronal death. In addition, antidepressants and antipsychotics are often prescribed off-label to treat the symptoms of severe Alzheimer’s disease in patients suffering from agitation, aggressive behaviors, psychosis, and depression.

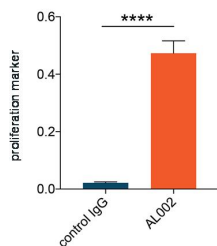
Recent drug candidates under development for Alzheimer’s disease include those focused on blocking synthesis, enhancing clearance or disaggregating misfolded amyloid-beta or TAU proteins in the brain, reversing chronic inflammation, and repairing vascular dysfunction, metabolic dysregulation, as well as neurotoxicity. Almost all of these candidates were designed to target just one of the multiple Alzheimer’s disease pathologies, and most of these drug candidates have so far failed to demonstrate any significant benefit.

Although amyloid-beta plaques and TAU protein in the brain represent physical pathologies of the disease and are believed to cause a loss of neuronal connectivity in the brain and neuronal death, recent scientific data paints a more complex picture. Therapeutic approaches that address only one of the multiple pathologies observed in Alzheimer’s disease, for example, pathology-directed therapies that clear amyloid-beta or TAU proteins, have had limited efficacy. More efficacious therapies will require addressing additional pathologies which we believe are associated with microglial failure.

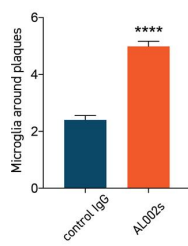
Our TREM2 Preclinical Data

AL002 binds to TREM2 on the surface of microglia and is designed to optimize microglial activity through the phosphorylation of Spleen Associated Tyrosine Kinase (Syk). With prominent academic collaborators, we have demonstrated that AL002s, an antibody that is functionally similar to AL002 but cross-reacts to the mouse TREM2, can normalize gene expression signature associated with Alzheimer’s disease and reduce pathology in a mouse model of Alzheimer’s disease. Furthermore, AL002 was shown to induce microglial proliferation, increase microglial survival and decrease dystrophic neurites associated with damaged neurons in an aggressive mouse model of Alzheimer’s disease that expresses either the normal or genetic risk variant of the human TREM2.

AL002 strongly increases a marker of microglial proliferation



AL002s recruit microglia to plaques



AL002s reduces area occupied by plaques

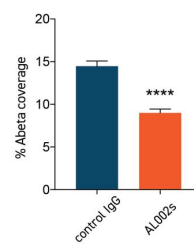


Figure 13. AL002s statistically significantly increases the number of microglia around amyloid-beta plaques (left) and reduces the area occupied by amyloid-beta plaques⁵ (right) in a mouse model of Alzheimer's disease (** indicates p<0.001 by T-test).**

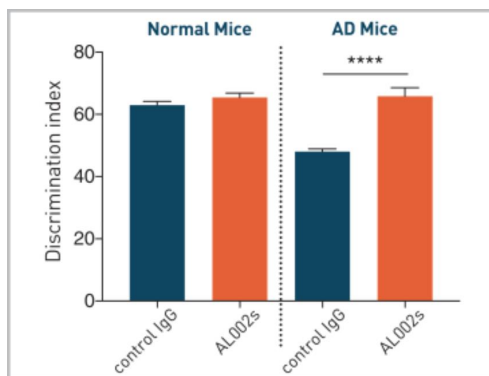


Figure 14. AL002s statistically significantly improves cognitive deficit in a mouse model of Alzheimer's disease (** indicates p<0.0001 by T-test).**

AL002 Development Plan

In the third quarter of 2019, we completed the Phase 1a portion (n=56) of a clinical trial in healthy volunteers with AL002. AL002 was generally safe and well-tolerated in the single ascending dose part of the Phase 1 study. In addition, a dose dependent and statistically significant change in both soluble TREM2 (sTREM2) and downstream biomarkers for microglia functionality in cerebrospinal fluid were observed upon treatment, indicating both target engagement and proof-of-mechanism in healthy volunteers.

⁵ Data generated by D. Wilcox, University of Kentucky.

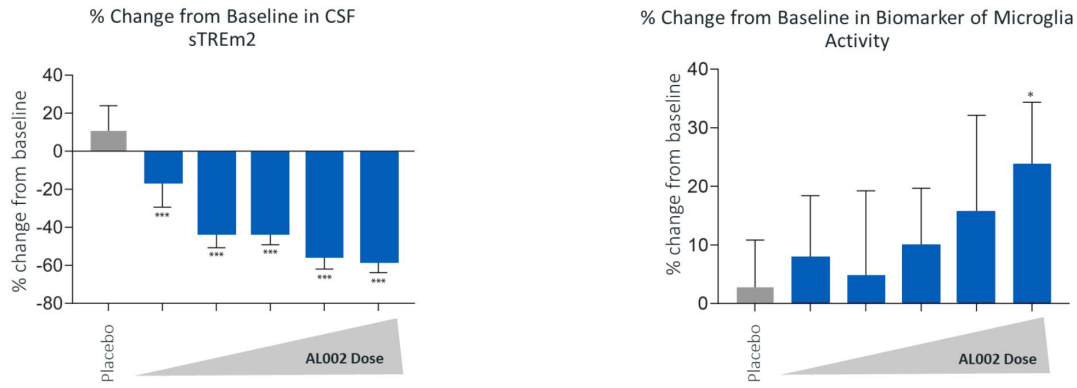


Figure 15. In healthy volunteers, a dose dependent decrease in sTREM2 and an increase in an immune activity biomarker was observed in the AL002 Phase 1a clinical study. CSF samples were taken from the five highest dose cohorts. The data shown are derived from analysis of CSF samples from 34 healthy volunteers (* denotes p<0.05 by T-test, * denotes p<0.001 by T-test).**

In the second quarter of 2019, based on the safety and tolerability observed in the Phase 1a healthy volunteer study, as well as encouraging biomarker data, we initiated the Phase 1b portion of the trial with AL002 in people with Alzheimer’s disease. Based on the data collected to date in preclinical studies as well as in healthy volunteers, and in alignment with our partner AbbVie, we have decided to close enrollment in the Phase 1b study, which was impacted by the COVID-19 pandemic.

In January 2021, initiated our Phase 2 trial in Alzheimer’s disease patients in early stages of the disease. The randomized, double-blind, placebo-controlled, dose-ranging, multi-center Phase 2 study will enroll approximately 265 participants with early AD at up to 90 sites globally. The primary endpoint of the Phase 2 study will measure disease progression utilizing the Clinical Dementia Rating Sum of Boxes (CDR-SB). The study will also measure multiple fluid and imaging biomarkers, and assess several secondary clinical, pharmacokinetic and pharmacodynamic endpoints, as well as safety to generate data enabling pivotal Phase 3 studies.

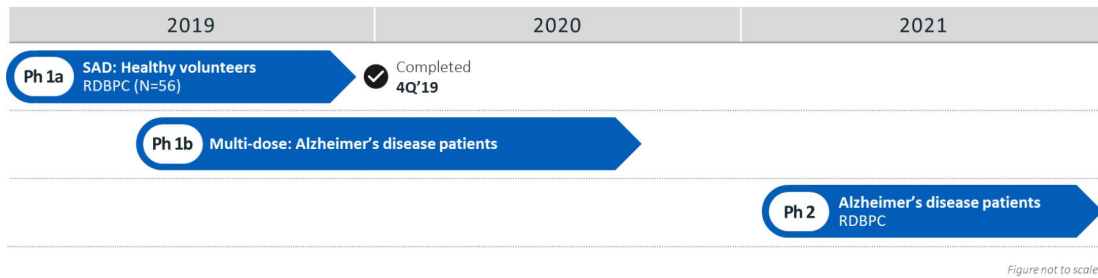


Figure 16. Clinical development plan for AL002 in Alzheimer’s disease. (Figure not to scale.)

These clinical trials have been designed in close collaboration with AbbVie. Our desired outcome is to achieve informative endpoints to enable efficient Phase 3 clinical trial design and a rapid advancement towards marketing approval. For more information on our collaboration with AbbVie see the section titled “Business—Strategic Alliance with AbbVie.”

Our SIGLEC 3 Program

Large scale genomic profiling of datasets from Alzheimer's disease patients has been used to identify the association between certain variants of SIGLEC 3, also known as CD33, and increased risk to develop Alzheimer's disease. SIGLEC 3 is an inhibitory receptor expressed on microglia and acts as the brakes of the immune system in the brain, slowing down microglial activity. Excessive inhibition of the microglia by the disease risk variant of SIGLEC 3, which increases expression of the inhibitory SIGLEC 3 receptor on microglia, leads to reduced functionality of the myeloid cells, and consequently, increased deposition of amyloid-beta plaques and accelerated loss of tissue in the brain of Alzheimer's disease patients that carry this risk variant.

Our analysis further showed that the natural inhibitory ligands for SIGLEC 3, which are required for activation of SIGLEC 3, are upregulated in the brain of Alzheimer's disease patients, further reducing the functionality of the microglia.

Consistent with the genetic findings in humans, Alzheimer's disease mouse models, in which the gene for SIGLEC 3 was genetically ablated, have microglia with improved phagocytosis of beta amyloid and displayed fewer amyloid-beta plaques compared to the same Alzheimer's disease model that expressed the mouse SIGLEC 3 gene. In line with the findings that the presence of SIGLEC 3 increased the severity of Alzheimer's disease, a reduced number of certain disease associated microglia that are thought to counteract the progression of Alzheimer's disease was observed when the human SIGLEC 3 in Alzheimer's disease mouse models was over-expressed.

Taken together, this data supports the hypothesis that blocking the function of SIGLEC 3 would increase the number of beneficial microglia and elicit a therapeutic benefit in Alzheimer's disease.

AL003 for Treatment of Alzheimer's Disease

Our product candidate, AL003, is a SIGLEC 3 blocking, monoclonal antibody (Figure 17) that is intended to be delivered by intravenous, peripheral infusion into the blood stream. The function of SIGLEC 3 on microglia is similar to the inhibitory function of PD-1 on T-cells. AL003 acts similarly to PD-1 inhibitors that have been employed successfully in immunotherapy of cancer. Both approaches aim to remove the "brakes" on the immune system to allow the system to work at its full capacity.

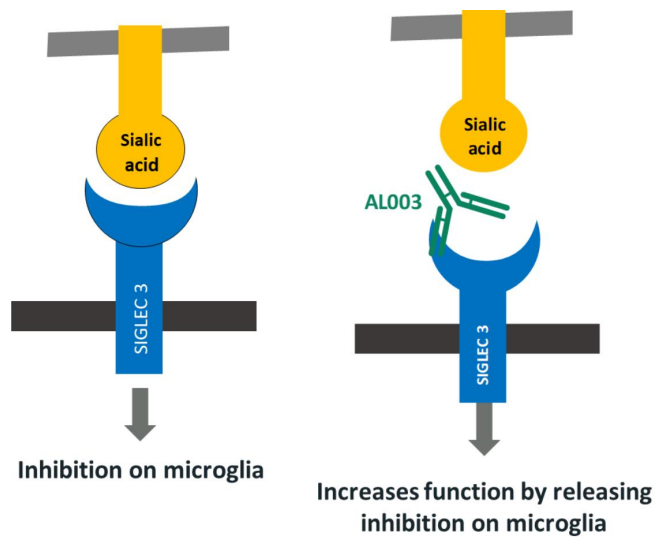


Figure 17. Mechanism of action of our SIGLEC 3 blocking product candidate AL003.

Our SIGLEC 3 Preclinical Data

The activity of AL003 in mice was assessed in immunodeficient mice containing human immune cells to recapitulate the human immune system as closely as possible. AL003 injected into the bloodstream of these mice blocks SIGLEC 3 on immune cells. In addition, a single intraperitoneal injection of AL003 into mice that express the human SIGLEC 3 in microglia leads to a long-lasting, statistically significant blockade of SIGLEC 3 on the cell surface of microglia in the brain, indicating that AL003 is potentially able to cross the blood brain barrier and exert its desired activity (Figure 18).

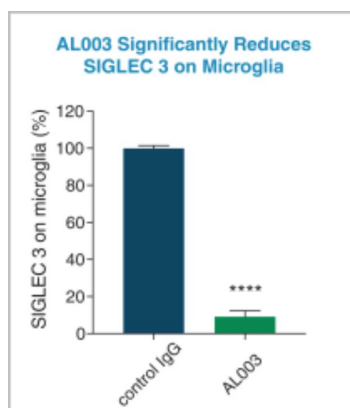


Figure 18. AL003 blocks SIGLEC 3 on microglia in mouse brain following injection to the blood stream (** indicates $p < 0.0001$ by T-test).**

AL003 Development Plan

In the fourth quarter of 2019, we completed the Phase 1a portion of our trial (n=38) in healthy volunteers with AL003 for the treatment of Alzheimer’s disease patients, and reported that the primary safety endpoint of the study

had been achieved. Additionally, secondary PK and PD endpoints were also met. In the study, 38 healthy volunteers were dosed over eight dose cohorts in the SAD portion of the AL003 Phase 1a study. A dose dependent and long-lasting change in SIGLEC 3 indicating target engagement was observed upon a single dose treatment in these healthy volunteers.

Based on the safety and tolerability observed in the Phase 1a study, we commenced dosing in January 2020 in Alzheimer’s disease patients in a Phase 1b study with AL003. We have completed enrollment of Alzheimer’s disease patients in this study which continues to progress with clinical data expected to be presented in 2021.

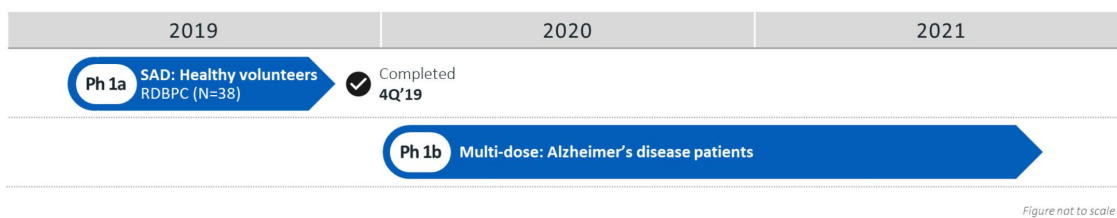


Figure 19. Clinical development plan for AL003 in Alzheimer’s disease. (Figure not to scale.)

These clinical trials have been designed in close collaboration with AbbVie. Our desired outcome is to achieve informative endpoints to enable efficient Phase 3 clinical trial design and a rapid advancement towards marketing approval. For more information on our collaboration with AbbVie see the section titled “Business—Strategic Alliance with AbbVie.”

Our MS4A4A Program

MS4A4A is among the most prominent genetic risk clusters for late-onset Alzheimer’s disease. Risk variants of *MS4A4A* are associated with an increase in the prevalence of Alzheimer’s disease and a decrease in the age of onset. *MS4A4A* is a transmembrane receptor protein that is expressed in a subset of innate immune cells, and selectively, in microglia in the brain. *MS4A4A* is thought to control microglia functionality and/or viability. Our AL044 product candidate was designed to counteract the risk variants of *MS4A4A* and to functionally convert the risk variants of *MS4A4A* to the protective variant. We expect that AL044 will mimic and exceed the beneficial activity of the protective *MS4A4A* variant, which we believe may potentially decrease the progression of Alzheimer’s disease.

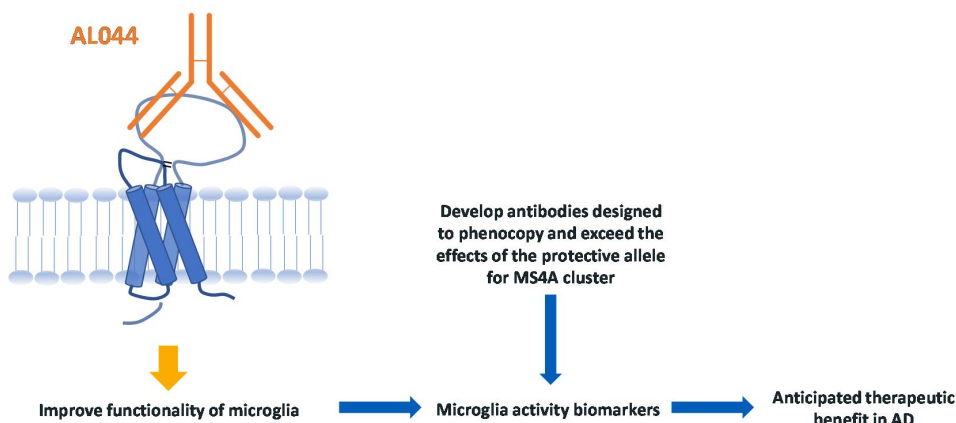


Figure 20. AL044 is designed to mimic and exceed the beneficial activity of the protective *MS4A4A* variant, which we believe may stop or slow the progression of Alzheimer’s disease.

AL044 for the Treatment of Alzheimer's Disease

AL044 is a humanized, *MS4A4A* function modulating monoclonal antibody that is intended to be delivered by intravenous, peripheral infusion into the bloodstream. AL044 was designed to mimic and exceed the beneficial activities of the protective *MS4A4A* gene variant in Alzheimer's disease, as determined by AL044's ability to partially phenocopy the gene expression signature of the protective *MS4A4A* gene variant and to increase sTREM2 levels in the CSF of non-human primates in a dose-dependent manner.

Expansion of Our Discovery Platform to Other Indications

Immuno-oncology

We are also expanding our discovery platform to other indications, such as the field of immuno-oncology. We believe that products focused on innate immune biology will complement and expand the efficacy of current immuno-oncology drugs that target the adaptive immune system. Microglia display similar gene expression signature and function to the innate cells of the peripheral immune system. These peripheral innate cells such as macrophages, NK cells, and others, likely play a significant role in multiple chronic diseases including cancer, inflammation, and autoimmune disorders. We are leveraging our expertise in the innate immune system to develop additional innate immune check-point focused programs, including programs targeting the Siglec protein family and the SIRP protein family, for peripheral disorders, particularly cancer.

We have entered into a licensing agreement with Innovent to develop and commercialize AL008, our novel antibody that non-competitively antagonizes inhibition of the CD47-SIRP-alpha (SIRP α) pathway by inducing the internalization and degradation of the inhibitory receptor on macrophages to relieve immune suppression (a "don't eat me signal") while also engaging Fc γ R2A, an activating IgG Fc receptor to promote immune-stimulatory pathways that drive anti-tumor immunity. We believe that products focused on innate, a potent immune biology will complement and expand the efficacy of current immuno-oncology drugs that target the adaptive checkpoint pathway co-opted by tumors to evade the immune system. AL008 is a potential best-in-class SIRP-alpha inhibitor with a unique dual mechanism of action that non-competitively antagonizes the CD47-SIRP-alpha pathway by inducing the internalization and degradation of the inhibitory receptor on macrophages to relieve immune suppression (a "don't eat me signal") while also engaging Fc gamma receptors to promote immuno-stimulatory pathways that drive anti-tumor immunity.

AL009, our latest prioritized investigational product candidate, is a first-in-class multi Siglec inhibitor that works to enhance both the innate and adaptive immune system response to tumors by blocking a critical glycan checkpoint pathway that drives immune inhibition. This product candidate is being developed in oncology and we believe it could also have potential therapeutic application to neurodegenerative disorders.

Combination Therapies

Our therapies are also likely to act in conjunction with each other or with other experimental drugs that are designed to remove pathological proteins. Therapies such as antibodies against amyloid-beta, the TAU filaments or misfolded alpha-synuclein protein are designed to tag the pathological proteins and recruit microglia to dispose of the drug pathological protein complex. Aging microglia are less likely to perform this function effectively, and our immuno-neurology therapies could ameliorate this deficiency. We are continuing to explore various combination strategies in preclinical models and will, in the future, consider moving this strategy into the clinic based upon results from preclinical models.

Strategic Alliance with AbbVie

Overview

In October 2017, we entered into the Co-Development and Option Agreement with AbbVie (AbbVie Agreement). The primary goal of our global strategic collaboration with AbbVie is to co-develop and commercialize therapeutics to treat Alzheimer's and other neurodegenerative diseases.

Under the AbbVie Agreement, we granted AbbVie an exclusive option to global development and commercialization for our TREM2 and SIGLEC 3 programs. The terms of the AbbVie Agreement included initial

upfront payments of \$205.0 million and \$20.0 million from the sale of shares of our stock, and if AbbVie exercises its option for both programs, we are eligible for up to an additional \$985.6 million in option exercise and milestone payments. Following AbbVie's exercise of its option, Alector and AbbVie will share the development costs and will split global profits after marketing approval. However, following AbbVie's option exercise for a program, we may opt out of sharing in development costs and profits or losses from that program and instead receive a tiered royalty on sales of products from that program. We are responsible for the design and execution of Phase 1 and Phase 2 studies, taking advantage of our significant in-house expertise in running clinical trials in Alzheimer's disease. Following its exercise of an option for a program, AbbVie will be responsible for certain development activities and global commercialization, taking advantage of its global clinical trial expertise and commercialization networks. Through this partnership, we aim to leverage the strengths of both organizations efficiently to best achieve the desired outcome.

Exercise of options. AbbVie may exercise its option for a program at any time until the expiration of an option term for that program. For each program, the option term ends following a fixed period after AbbVie's receipt of the data package after completion of Phase 2 clinical trials that includes certain information relating to the applicable program's research and development activities. If AbbVie fails to exercise its option during the option term for a product candidate, we will retain all rights to that program. If AbbVie exercises its option for a program, then AbbVie will lead development and commercialization activities worldwide. Once AbbVie opts in with respect to a given product candidate, AbbVie must use commercially reasonable efforts to develop and commercialize the corresponding product globally.

Governance. The collaboration is governed by a joint steering committee (JSC). The JSC may establish additional subcommittees to oversee particular projects or activities. Subject to limitations specified in the AbbVie Agreement, if the applicable governance committee is unable to make a decision by consensus and the parties are unable to resolve the issue through escalation to specified senior executive officers of the parties, then the issue is escalated to an alternative dispute resolution subject to final decision-making rights retained by each party.

Exclusivity. During the term of the AbbVie Agreement, each of Alector and AbbVie are subject to exclusivity requirements prohibiting certain activities outside of the AbbVie Agreement directed to targets under the AbbVie Agreement.

Intellectual Property. Ownership of intellectual property created in connection with the AbbVie Agreement is generally determined on the basis of inventorship. Generally, each party has the first right to prosecute and maintain its own patents. We generally have the first right to prosecute and maintain joint patents prior to AbbVie's exercise of its option for the program relating to such patent, and AbbVie has the right following its exercise of such option. AbbVie has the first right to prosecute any infringement of jointly held patents developed under the AbbVie Agreement and our patents that are licensed under the AbbVie Agreement. Additionally, AbbVie has the sole right to prosecute its own patents. AbbVie has the first right to defend against claims that a product developed under either of the programs that are the subject of the AbbVie Agreement infringe third-party intellectual property rights.

Term and Termination. At any point during the term of the AbbVie Agreement, including during the research, development, and clinical trial process, AbbVie can terminate the AbbVie Agreement in its entirety, or with respect to either program under the AbbVie Agreement, for convenience. In that event, all rights related to the applicable program revert to us. Additionally, AbbVie or we and can terminate the AbbVie Agreement in connection with a material breach of the AbbVie Agreement by the other party that remains uncured for a specified period of time.

Adimab Collaboration Agreements

Overview

In 2014, we entered into the 2014 Adimab Collaboration Agreement. Under the 2014 Adimab Agreement, we are required to fund, and we and Adimab LLC (Adimab) are required to use commercially reasonable efforts to conduct, certain research to discover and optimize antibodies directed against targets selected by us. We are developing antibodies discovered by Adimab in our AL001 and AL101 product candidates, and we are developing antibodies optimized by Adimab in our AL002 and AL003 product candidates.

Governance. Our collaboration with Adimab is governed by a research committee consisting of at least two representatives from each party. The research committee prioritizes among research programs and prepares and finalizes new proposed research plans, among other activities. If the research committee is unable to make a decision by consensus and the parties are unable to resolve the issue through escalation to specified senior executive officers of the parties, then either party may seek arbitration of the matter.

Exclusivity. Pursuant to the 2014 Adimab Agreement, each party is subject to limitations on its ability to use information or material provided by the other outside the scope of the collaboration.

Intellectual Property. Ownership of intellectual property arising from the research is generally owned by the party that invents or creates the applicable intellectual property, although certain categories of intellectual property are specifically assigned to one party or the other. For example, patent rights relating to improvements to Adimab's background platform technology that are invented in the course of the research are assigned to Adimab. Prior to our exercise of the option described below, we and Adimab each grant the other a non-exclusive license to the relevant intellectual property we own to allow each party to carry out its rights and obligations in connection with the research; and except for Adimab's retained rights to continue using and licensing its own libraries, each party agrees not to practice or license the patents arising out of the research that it owns for any purpose other than to carry out its rights and obligations in connection with the research. Generally, each party has the obligation to prosecute, maintain, defend, and enforce its own patents, but we are subject to certain contractual restrictions on our ability to prosecute, practice, and license certain of our patents that arose out of the research. These restrictions are lifted once we exercise the option described below as to such patents.

Exercise of Options. The 2014 Adimab Agreement granted us an exclusive option to obtain certain rights relating to a specified number of antibodies discovered or optimized by Adimab directed against the targets we selected. The option extended to ownership of patent rights specifically covering the sequences of such antibodies, and the right to obtain worldwide, royalty-bearing, sublicensable licenses under certain technology owned or developed by Adimab to research, develop, make, have made, use, sell, offer to sell, import and export such antibodies and products based on such antibodies for all human therapeutic, prophylactic and diagnostic uses. These licenses are exclusive, except as to Adimab background and platform technology and Adimab's retained rights to continue using and licensing its own libraries, as to which the licenses are non-exclusive. We have confirmed with Adimab in writing that key patents we have filed relating to the programs partnered with AbbVie claim inventions owned solely by us, and do not include any such background or platform technology of Adimab. All of our options under the 2014 Adimab Agreement have either expired, are in the process of being exercised, or, with respect to multiple targets and hundreds of antibodies (including the target programs partnered with AbbVie), have already been exercised. Upon our exercise of the option with respect to a target, we are subject to an obligation to devote commercially reasonable efforts to commercialize products using the optioned rights to such target. The assigned and licensed patent rights we obtained from these option exercises are described in more detail above under the section titled "Business—Intellectual Property."

Financial terms. We fund Adimab's research in connection with our collaboration, in accordance with the terms and limitations described in the 2014 Adimab Agreement. We also have potential milestone payments per program for use of antibodies and low- to mid-single digit royalty payments for commercial sales of products incorporating such antibodies. However, if we enter into any transaction granting rights to the inventions or sell products created as a result of a collaboration with a third party, we have a choice to pay a share of the resulting revenue instead of royalties from such sales.

Term and Termination. We are able to terminate the 2014 Adimab Agreement, in its entirety or with respect to a products or antibodies directed to particular targets, on three months prior written notice to Adimab. In addition, either party can terminate the 2014 Adimab Agreement in its entirety, or, subject to certain limitations, with respect to specific optioned rights, for material breaches that remain uncured after 90 days' notice to the breaching party. In the case of a termination before expiration of the 2014 Adimab Agreement, we would have certain continuing payment obligations to Adimab, or would be required to adhere to certain restrictions as to the fruits of the collaboration. The 2014 Adimab Agreement expires on the twelfth anniversary of the first commercial sale of the products created under the collaboration, on a product-by-product and country-by-country basis. The licenses we and Adimab granted to each other do not survive, subject to certain limitations.

Overview—2019 Adimab Collaboration Agreement (2019 Adimab Agreement)

In 2019, we entered into another Adimab collaboration agreement. Under the 2019 Adimab Agreement, we are required to fund, and we and Adimab are required to use commercially reasonable efforts to conduct, certain research to discover and optimize antibodies directed against targets selected by us. We have not yet identified any research programs under the 2019 Adimab Agreement.

Governance. Our collaboration with Adimab is governed by a research committee consisting of at least two representatives from each party. The research committee facilitates communication regarding research under the 2019 Adimab Agreement and has the limited authority to amend a research plan in a manner not substantially affecting the resources required from a party. If the research committee is unable to make a decision by consensus, no decision will be taken.

Exclusivity. Pursuant to the 2019 Adimab Agreement, each party is subject to limitations on its ability to use information or material provided by the other outside the scope of the collaboration.

Intellectual Property. Ownership of intellectual property arising from the research is generally owned by the party that invents or creates the applicable intellectual property, although certain categories of intellectual property are specifically assigned to one party or the other. Certain intellectual property relating to Adimab's background platform technology including any improvements thereto that are invented in the course of the research are assigned to Adimab. Patents covering antibodies that are the subject of the collaboration are owned by us; however, prior to our exercise of the option described below, we are prohibited from practicing such patents for any purpose other than to perform our research obligations under the 2019 Adimab Agreement. Upon the expiration of the option term described below, in the event we elect not to exercise our option right with respect to an antibody, ownership of such patents is transferred to Adimab. Prior to our exercise of the option described below, we and Adimab each grant the other a non-exclusive license to the relevant intellectual property we own to allow each party to carry out its rights and obligations in connection with the research. Generally, each party has the obligation to prosecute, maintain, defend, and enforce its own patents, but we are subject to certain contractual restrictions on our ability to prosecute, practice, and license certain of our patents that arose out of the research. These restrictions are lifted once we exercise the option described below as to such patents.

Exercise of Options. The 2019 Adimab Agreement granted us an exclusive option to obtain certain rights relating to a specified number of antibodies discovered or optimized by Adimab directed against the targets we selected. The option extends to ownership of the applicable optioned antibody, and the right to obtain worldwide, royalty-bearing, sublicensable non-exclusive licenses under certain technology owned or developed by Adimab to research, develop, make, have made, use, sell, offer to sell, import and export such antibodies and products based on such antibodies for all human therapeutic, prophylactic and diagnostic uses. Upon our exercise of the option with respect to a target, we are subject to an obligation to devote commercially reasonable efforts to commercialize products using the optioned rights to such target.

Financial terms. We fund Adimab's research in connection with our collaboration, in accordance with the terms and limitations described in the 2019 Adimab Agreement. We are also responsible for certain development fees and, in the event we exercise the option right, we are obligated to pay an option fee. We also have potential milestone payments per product for use of antibodies, subject to certain limitations on total payments owed on any given target, and low-single digit royalty payments for commercial sales of products incorporating such antibodies.

Term and Termination. We are able to terminate the 2019 Adimab Agreement, in its entirety or with respect to a products or antibodies directed to particular targets, on 60 days' prior written notice to Adimab. In addition, either party can terminate the 2019 Adimab Agreement in its entirety for material breaches that remain uncured after 90 days' notice to the breaching party. In the case of a termination before expiration of the 2019 Adimab Agreement, we would be prohibited from using the fruits of the collaboration. The 2019 Adimab Agreement expires, on a product-by-product and country-by-country basis, on the later of the twelfth anniversary of the first commercial sale of such product in such country and expiration of the last patent covering such product in such country, or, in the event no product is optioned under the 2019 Adimab Agreement, upon the last to expire option period. Upon expiration, the licenses Adimab granted to us with respect to products for which we have exercised our option will continue on a non-exclusive, royalty-free basis.

Manufacturing

We must manufacture our product candidates for clinical trial use in compliance with cGMP regulations. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. The manufacturing facilities for our product candidates must meet cGMP requirements and FDA or comparable foreign regulatory authority's satisfaction before any product is approved for human clinical trial use. Our third-party manufacturers will also be subject to periodic inspections of their respective facilities for general cGMP compliance by the FDA and other foreign authorities. These inspections may include review of procedures and operations used in the testing and manufacture of our products to assess compliance with applicable regulations.

We do not currently have the infrastructure or internal capability to manufacture our product candidates for use in clinical trials and commercialization. We rely, and expect to continue to rely, on third-party cGMP manufacturers for the production of our products for human clinical trials in compliance with FDA and other foreign authority regulations for such products. We rely on CDMOs to manufacture and supply our preclinical and clinical materials to be used during the preclinical and clinical development of our product candidates. As part of our broad manufacturing strategy to expedite the manufacturing of our product candidates and minimize manufacturing risk, we currently have established relationships with several CDMOs for the manufacturing of our drug substance or product candidates.

We do not have long-term supply agreements and we purchase our required drug product on a development manufacturing services agreement or purchase order basis. We expect to continue to rely on third-party manufacturers for the commercial supply of any of our product candidates for which we obtain marketing approval. We have personnel with significant technical, manufacturing, analytical, quality, regulatory, including cGMP, and project management experience to oversee our third-party manufacturers and to manage manufacturing and quality data and information for regulatory compliance purposes.

Failure to comply with statutory and regulatory requirements subjects a manufacturer to possible legal or regulatory action, including warning letters, the seizure or recall of products, injunctions, consent decrees placing significant restrictions on or suspending manufacturing operations and civil and criminal penalties. Contract manufacturers often encounter difficulties involving production yields, quality control and quality assurance, as well as shortages of qualified personnel. Any of these actions or events could have a material impact on the availability of our products.

Commercialization Plan

We do not currently have any approved drugs and we do not expect to have any approved drugs in the near term. Therefore, we have no sales, marketing or commercial product distribution capabilities and have no experience as a company in marketing drugs. When, and if any of our product candidates are approved for commercialization, we intend to develop a commercialization infrastructure for those products in the United States, Europe, Asia, and potentially in certain other key markets. We may also rely on partnerships, such as our AbbVie collaboration, to provide commercialization infrastructure, including sales and marketing and commercial distribution.

Intellectual Property

Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. Our strategy is to seek to protect our proprietary position by, among other methods, pursuing and obtaining patent protection in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements and product candidates that are important to the development and implementation of our business. Our patent portfolio is intended to cover our product candidates and related components, their methods of use and processes for their manufacture, our proprietary reagents and assays and any other inventions that are commercially important to our business. We also rely on trademarks as well as trade secret protection of our confidential information and know-how relating to our

proprietary technology, platforms and product candidates. We believe that we have substantial know-how and trade secrets relating to our technology and product candidates.

Our patent portfolio contains over 40 families, and as of December 31, 2020, our patent portfolio includes 11 issued patents and over 300 pending patent applications, directed to over 20 different targets and/or technologies, that are solely owned or we have rights to exclusive licenses by us. For our product candidates, we generally pursue multilayered patent protection covering the composition of matter based on binding epitopes of the product candidates on the target protein, functional characteristics of the product candidates, degenerative sequence of the product candidates, and/or specific sequence of the product candidates. In addition to composition of matter coverage, we also generally pursue claims directed to methods of making, nucleic acids, formulations, and methods of use of the product candidates. The method of use claims further include claims directed to patient selection criteria, biomarkers, disease subgroups, pharmacodynamic and clinical end-points, and dosage regimes. As further described below, we intend to strengthen the patent protection of our product candidates and technologies through additional patent application filings.

PGRN Programs

We own five patent families directed to our PGRN programs, AL001 and AL101, which include three issued U.S. patents, covering the compositions and uses of our PGRN program product candidates. The first two patent families are expected to expire in 2036, the third patent family is expected to expire in 2039, the fourth patent family is expected to expire in 2040, and the fifth patent family, assuming that the necessary non-provisional patent applications are timely filed and all other applicable requirements are satisfied for the U.S. provisional patent application, is expected to expire in 2041, in all cases excluding any patent term adjustments and any patent term extensions.

TREM2 Program

We own six patent families directed to the TREM2 program covering the compositions and uses of our TREM2 program product candidates. Four patent families are expected to expire in 2035, 2036, 2038, 2040, respectively, and two patent families, assuming that the necessary non-provisional patent applications are timely filed and all other applicable requirements are satisfied for the U.S. provisional patent application, are expected to expire in 2041, in all cases excluding any patent term adjustments and any patent term extensions.

SIGLEC 3 Program

We own five patent families directed to the SIGLEC 3 program covering the compositions and uses of our SIGLEC 3 program product candidates. Two patent families are expected to expire in 2036, the third patent family in 2038, the fourth patent family in 2039, and the fifth patent family in 2040, in all cases excluding any patent term adjustments and any patent term extensions.

MS4A4A Program

We own two patent families directed to the MS4A4A program covering the compositions and uses of our MS4A4A program product candidates. The first patent family is expected to expire in 2039 and the second patent family in 2040.

The term of individual patents depends upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, the patent term is generally 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country. In the United States, a patent's term may, in certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over a commonly owned patent or a patent naming a common inventor and having an earlier expiration date. The Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Act) permits a patent term extension of up to five years beyond the expiration date of a U.S. patent as partial compensation for the length of time the drug is under regulatory review while the patent is in force. A patent

term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it, may be extended.

Similar provisions are available in the European Union and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our product candidates receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those products, depending upon the length of the clinical trials for each drug and other factors. Expiration dates referred to above are without regard to potential patent term extension or other market exclusivity that may be available to us.

We also rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

Competition

The biotechnology and pharmaceutical industries, including in the neurodegenerative disease field, are characterized by rapidly advancing technologies, strong competition and an emphasis on intellectual property. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, governmental agencies and public and private research institutions. Some of the pharmaceutical and biotechnology companies that are currently pursuing the development of products for the treatment of the neurodegenerative disease indications for which we have research programs, including FTD, Alzheimer's disease, Parkinson's disease, and ALS, include large companies with significant financial resources, such as Biogen, Eli Lilly, GlaxoSmithKline, Merck and Roche Holding AG. We believe that the key competitive factors affecting the success of any of our product candidates will include efficacy, safety profile, method of administration, cost, level of promotional activity and intellectual property protection.

Our product candidates will compete with current therapies approved for the treatment of neurodegenerative diseases, which to date have been primarily targeted at treating the symptoms of such diseases rather than halting or slowing the progression of the disease. However, in addition to such currently approved therapies, we believe that our product candidates, if approved, may also compete with other potential therapies intended to halt or slow the progression of neurodegenerative disease that are being developed by a number of companies and institutions.

Government Regulation

Government authorities in the United States at the federal, state and local level and in other countries regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug and biological products. Generally, before a new drug or biologic can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority.

U.S. Drug Development

In the United States, the FDA regulates drugs under the Food, Drug, and Cosmetic Act (FDCA) and biologics under the FDCA and the Public Health Service Act (PHSA). Both drugs and biologics also are subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or post-market may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or market

withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Any future product candidates must be approved by the FDA through either a biologics license application (BLA) or new drug application (NDA) process before they may be legally marketed in the United States. The process generally involves the following:

- Completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with GLP;
- Submission to the FDA of an investigational new drug application (IND), which must become effective before human clinical trials may begin;
- Approval by an independent Institutional Review Board (IRB), or ethics committee at each clinical trial site before each trial may be initiated;
- Performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, good clinical practice (GCP), requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- Submission to the FDA of a NDA or BLA;
- A determination by the FDA within 60 days of its receipt of an NDA or Biologics License Application (BLA) to accept the filing for review;
- Satisfactory completion of a FDA pre-approval inspection of the manufacturing facility or facilities where the drug or biologic will be produced to assess compliance with cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the drug or biologic's identity, strength, quality, and purity;
- Potential FDA audit of the preclinical study and/or clinical trial sites that generated the data in support of the NDA or BLA;
- FDA review and approval of the NDA or BLA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug or biologic in the United States; and
- Compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy (REMS), and the potential requirement to conduct post-approval studies.

The data required to support an NDA or BLA are generated in two distinct developmental stages: preclinical and clinical. The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for any future product candidates will be granted on a timely basis, or at all.

The preclinical developmental stage generally involves laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which support subsequent clinical testing. The sponsor must submit the results of the preclinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational product to humans, and must become effective before human clinical trials may begin.

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as *in vitro* and animal studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically

becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

The clinical stage of development involves the administration of the investigational product to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative, and must monitor the clinical trial until completed. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

A sponsor who wishes to conduct a clinical trial outside of the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA or BLA. The FDA will accept a well-designed and well-conducted foreign clinical trial not conducted under an IND if the trial was conducted in accordance with GCP requirements and the FDA is able to validate the data through an onsite inspection if deemed necessary.

Clinical trials in the United States generally are conducted in three sequential phases, known as Phase 1, Phase 2, and Phase 3, and may overlap.

- Phase 1 clinical trials generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, tolerability and safety of the drug.
- Phase 2 clinical trials involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, possible adverse effects and safety risks are identified, and a preliminary evaluation of efficacy is conducted.
- Phase 3 clinical trials generally involve a large number of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. These trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA or BLA.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the drug or biologic, findings from animal or *in vitro* testing that suggest a significant risk for human

volunteers and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

Phase 1, Phase 2, and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug or biologic has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether a trial may move forward at designated check-points based on access to certain data from the trial. Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the chemistry and physical characteristics of the drug or biologic as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product and, among other things, companies must develop methods for testing the identity, strength, quality, and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that our product candidates do not undergo unacceptable deterioration over their shelf life.

As a result of the consequences of the COVID-19 pandemic, the FDA has issued various COVID-19 related guidance documents applicable to biopharmaceutical manufacturers and clinical trial sponsors. For example, in March 2020, the FDA issued a guidance, which the FDA subsequently updated, on conducting clinical trials during the pandemic, which describes a number of considerations for sponsors of clinical trials impacted by the pandemic, including the requirement to include in the clinical trial report contingency measures implemented to manage the clinical trial, and any disruption of the clinical trial as a result of the COVID-19 pandemic; a list of all subjects affected by the COVID-19-pandemic related study disruption by unique subject identifier and by investigational site and a description of how the individual's participation was altered; and analyses and corresponding discussions that address the impact of implemented contingency measures (e.g., participant discontinuation from investigational product and/or study, alternative procedures used to collect critical safety and/or efficacy data) on the safety and efficacy results reported for the clinical trial. The FDA also issued a guidance on good manufacturing practice considerations for responding to COVID-19 infection in employees in drug products manufacturing, including recommendations for manufacturing controls to prevent contamination of drugs; guidance on recommendations for reducing the risk of human immunodeficiency virus transmission by blood and blood products; a guidance on drug and biologics manufacturing operations during the COVID-19 public health emergency; and a guidance on review timelines for applicant responses to Complete Response Letters when a facility assessment is needed during the COVID-19 public health emergency. These and future guidance documents and regulatory requirements, including future legislation, may require us to develop and implement new policies and procedures, make significant adjustments to our clinical trials, or increase the amount time and resources needed for regulatory compliance, which may impact our clinical development plans and timelines. The extent to which the COVID-19 public health emergency impacts our business, including non-clinical studies and clinical trials, will depend on future developments, which are highly uncertain and cannot be predicted with confidence.

NDA/BLA Review Process

Following completion of the clinical trials, data is analyzed to assess whether the investigational product is safe and effective for the proposed indicated use or uses. The results of preclinical studies and clinical trials are then submitted to the FDA as part of an NDA or BLA, along with proposed labeling, chemistry and manufacturing information to ensure product quality and other relevant data. In short, the NDA or BLA is a request for approval to market the drug or biologic for one or more specified indications and must contain proof of safety and efficacy for a drug or safety, purity, and potency for a biologic. The application may include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of FDA. FDA approval of an NDA or BLA must be obtained before a drug or biologic may be marketed in the United States.

Under the Prescription Drug User Fee Act (PDUFA), as amended, each NDA or BLA must be accompanied by a user fee. FDA adjusts the PDUFA user fees on an annual basis. According to the FDA's 2021 fee schedule for prescription drug user fees, which became effective on October 1, 2020, and will remain in effect through September 30, 2021, the user fee for an application requiring clinical data, such as an NDA or BLA, is approximately \$2.9 million. PDUFA also imposes an annual program fee for each marketed human drug or biologic (\$336,432 in 2021) and an annual establishment fee on facilities used to manufacture prescription drugs and biologics. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs or BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews all submitted NDAs and BLAs before it accepts them for filing, and may request additional information rather than accepting the NDA or BLA for filing. The FDA must make a decision on accepting an NDA or BLA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA or BLA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has 10 months, from the filing date, in which to complete its initial review of a new molecular-entity NDA or original BLA and respond to the applicant, and six months from the filing date of a new molecular-entity NDA or original BLA designated for priority review. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs or BLAs, and the review process is often extended by FDA requests for additional information or clarification.

Before approving an NDA or BLA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMP requirements. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA also may audit data from clinical trials to ensure compliance with GCP requirements. Additionally, the FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions, if any. The FDA is not bound by recommendations of an advisory committee, but it considers such recommendations when making decisions on approval. The FDA likely will reanalyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. After the FDA evaluates an NDA or BLA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the NDA or BLA identified by the FDA. The Complete Response Letter may require additional clinical data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA or BLA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA or BLA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for this type of disease or condition will be recovered from sales of the product.

Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity by means of greater effectiveness, greater safety or providing a major contribution to patient care or in instances of drug supply issues. However, competitors may receive approval of either a different product for the same indication or the same product for a different indication but that could be used off-label in the orphan indication. Orphan drug exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval before we do for the same product, as defined by the FDA, for the same indication we are seeking approval, or if a product candidate is determined to be contained within the scope of the competitor's product for the same indication or disease. If one of our products designated as an orphan drug receives marketing approval for an indication broader than that which is designated, it may not be entitled to orphan drug exclusivity. Orphan drug status in the European Union has similar, but not identical, requirements and benefits.

Expedited Development and Review Programs

The FDA has a fast track program that is intended to expedite or facilitate the process for reviewing new drugs and biologics that meet certain criteria. Specifically, new drugs and biologics are eligible for fast track designation if they are intended to treat a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to both the product and the specific indication for which it is being studied. The sponsor can request the FDA to designate the product for fast track status any time before receiving NDA or BLA approval, but ideally no later than the pre-NDA or pre-BLA meeting.

Any product submitted to the FDA for marketing, including under a fast track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies.

A product may also be eligible for accelerated approval, if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality (IMM), which is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA may require that a sponsor of a drug or biologic receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. If the FDA concludes that a drug or biologic shown to be effective can be safely used only if distribution or use is restricted, it may require such post-marketing restrictions as it deems necessary to assure safe use of the product.

Additionally, a drug or biologic may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints. The benefits of breakthrough therapy designation include the same benefits as fast track designation, plus intensive guidance from the FDA to ensure an efficient drug development program. Fast track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval, but may expedite the development or approval process.

Abbreviated Licensure Pathway of Biological Products as Biosimilar or Interchangeable

The Patient Protection and Affordable Care Act, or ACA, signed into law in 2010, includes the BPCIA, which created an abbreviated approval pathway for biological products shown to be highly similar to an FDA-licensed reference biological product. The BPCIA attempts to minimize duplicative testing, and thereby lower development costs and increase patient access to affordable treatments. An application for licensure of a biosimilar product must include information demonstrating biosimilarity based upon the following, unless the FDA determines otherwise:

- analytical studies demonstrating that the proposed biosimilar product is highly similar to the approved product notwithstanding minor differences in clinically inactive components;
- animal studies (including the assessment of toxicity); and
- a clinical trial or trials (including the assessment of immunogenicity and pharmacokinetic or pharmacodynamic) sufficient to demonstrate safety, purity, and potency in one or more conditions for which the reference product is licensed and intended to be used.

In addition, an application must include information demonstrating that:

- the proposed biosimilar product and reference product utilize the same mechanism of action for the condition(s) of use prescribed, recommended or suggested in the proposed labeling, but only to the extent the mechanism(s) of action are known for the reference product;
- the condition or conditions of use prescribed, recommended or suggested in the labeling for the proposed biosimilar product have been previously approved for the reference product;
- the route of administration, the dosage form and the strength of the proposed biosimilar product are the same as those for the reference product; and
- the facility in which the biological product is manufactured, processed, packed or held meets standards designed to assure that the biological product continues to be safe, pure, and potent.

Biosimilarity means that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and that there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product. In addition, the law provides for a designation of “interchangeability” between the reference and biosimilar products, whereby the biosimilar may be substituted for the reference product without the intervention of the healthcare provider who prescribed the reference product. The higher standard of interchangeability must be demonstrated by information sufficient to show that:

- the proposed product is biosimilar to the reference product;
- the proposed product is expected to produce the same clinical result as the reference product in any given patient; and
- for a product that is administered more than once to an individual, the risk to the patient in terms of safety or diminished efficacy of alternating or switching between the biosimilar and the reference product is no greater than the risk of using the reference product without such alternation or switch.

FDA approval is required before a biosimilar may be marketed in the United States. However, complexities associated with the large and intricate structures of biological products and the process by which such products are manufactured pose significant hurdles to the FDA’s implementation of the law that are still being worked out by the FDA. For example, the FDA has discretion over the kind and amount of scientific evidence—laboratory, preclinical and/or clinical—required to demonstrate biosimilarity to a licensed biological product.

The FDA intends to consider the totality of the evidence provided by a sponsor to support a demonstration of biosimilarity, and recommends that sponsors use a stepwise approach in the development of their biosimilar products. Biosimilar product applications thus may not be required to duplicate the entirety of preclinical and clinical testing used to establish the underlying safety and effectiveness of the reference product. However, the FDA may refuse to approve a biosimilar application if there is insufficient information to show that the active ingredients are the same or to demonstrate that any impurities or differences in active ingredients do not affect the safety, purity,

or potency of the biosimilar product. In addition, as with BLAs, biosimilar product applications will not be approved unless the product is manufactured in facilities designed to assure and preserve the biological product's safety, purity, and potency.

The submission of a biosimilar application does not guarantee that the FDA will accept the application for filing and review, as the FDA may refuse to accept applications that it finds are insufficiently complete. The FDA will treat a biosimilar application or supplement as incomplete if, among other reasons, any applicable user fees assessed under the Biosimilar User Fee Act of 2012 have not been paid. In addition, the FDA may accept an application for filing but deny approval on the basis that the sponsor has not demonstrated biosimilarity, in which case the sponsor may choose to conduct further analytical, preclinical or clinical studies and submit a BLA for licensure as a new biological product.

The timing of final FDA approval of a biosimilar for commercial distribution depends on a variety of factors, including whether the manufacturer of the branded product is entitled to one or more statutory exclusivity periods, during which time the FDA is prohibited from approving any products that are biosimilar to the branded product. The FDA cannot approve a biosimilar application for 12 years from the date of first licensure of the reference product. Additionally, a biosimilar product sponsor may not submit an application for four years from the date of first licensure of the reference product. A reference product may also be entitled to exclusivity under other statutory provisions. For example, a reference product designated for a rare disease or condition (an orphan drug) may be entitled to seven years of exclusivity, in which case no product that is biosimilar to the reference product may be approved until either the end of the twelve-year period provided under the biosimilarity statute or the end of the seven-year orphan drug exclusivity period, whichever occurs later. In certain circumstances, a regulatory exclusivity period can extend beyond the life of a patent, and thus block biosimilarity applications from being approved on or after the patent expiration date. In addition, the FDA may under certain circumstances extend the exclusivity period for the reference product by an additional six months if the FDA requests, and the manufacturer undertakes, studies on the effect of its product in children, a so-called pediatric extension.

The first biological product determined to be interchangeable with a branded product for any condition of use is also entitled to a period of exclusivity, during which time the FDA may not determine that another product is interchangeable with the reference product for any condition of use. This exclusivity period extends until the earlier of: one year after the first commercial marketing of the first interchangeable product; 18 months after resolution of a patent infringement against the applicant that submitted the application for the first interchangeable product, based on a final court decision regarding all of the patents in the litigation or dismissal of the litigation with or without prejudice; 42 months after approval of the first interchangeable product, if a patent infringement suit against the applicant that submitted the application for the first interchangeable product is still ongoing; or 18 months after approval of the first interchangeable product if the applicant that submitted the application for the first interchangeable product has not been sued.

Post-Approval Requirements

Following approval of a new product, the manufacturer and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and record-keeping requirements, requirements to report adverse experiences and comply with promotion and advertising requirements, which include restrictions on promoting drugs for unapproved uses or patient populations, known as "off-label use", and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such uses. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Further, if there are any modifications to the drug or biologic, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA/BLA or NDA/BLA supplement, which may require the development of additional data or preclinical studies and clinical trials.

The FDA may also place other conditions on approvals including the requirement for REMS, to assure the safe use of the product. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or

dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market, or product recalls;
- fines, warning letters, or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications;
- applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs and biologics may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Other U.S. Regulatory Matters

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in the United States in addition to the FDA, including the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency, and state and local governments.

For example, in the United States, sales, marketing and scientific and educational programs also must comply with state and federal fraud and abuse laws. These laws include the federal Anti-Kickback Statute, which makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Violations of this law are punishable by up to five years in prison, criminal fines, administrative civil money penalties and exclusion from participation in federal healthcare programs. Moreover, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the ACA. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws.

The distribution of biologic and pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals or refusal to allow a firm to enter into supply contracts, including government contracts. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: changes to our manufacturing arrangements; additions or modifications to product labeling; the recall or discontinuation of our products; or additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

U.S. Patent-Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of any future product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act permits restoration of the patent term of up to five years as compensation for patent term lost during product development and FDA regulatory review process. Patent-term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent-term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA or BLA plus the time between the submission date of an NDA or BLA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The United States Patent and Trademark Office (USPTO), in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA or BLA.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of a NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application (ANDA), or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for a NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

A reference biological product is granted 12 years of data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. "First

licensure” typically means the initial date the particular product at issue was licensed in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a biological product if the licensure is for a supplement for the biological product or for a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength or for a modification to the structure of the biological product that does not result in a change in safety, purity, or potency. Therefore, one must determine whether a new product includes a modification to the structure of a previously licensed product that results in a change in safety, purity, or potency to assess whether the licensure of the new product is a first licensure that triggers its own period of exclusivity. Whether a subsequent application, if approved, warrants exclusivity as the “first licensure” of a biological product is determined on a case-by-case basis with data submitted by the sponsor.

European Union Drug Development

Similar to the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the National Competent Authority (NCA), and one or more Ethics Committees (ECs). Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

The EU clinical trials legislation currently is undergoing a transition process mainly aimed at harmonizing and streamlining clinical-trial authorization, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. Recently enacted Clinical Trials Regulation EU No 536/2014 ensures that the rules for conducting clinical trials in the EU will be identical. In the meantime, Clinical Trials Directive 2001/20/EC continues to govern all clinical trials performed in the EU.

European Union Drug Review and Approval

In the European Economic Area (EEA), which is comprised of the 27 Member States of the European Union (including Norway and excluding Croatia), Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a Marketing Authorization (MA). There are two types of marketing authorizations.

- The Community MA is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use (CHMP), of the European Medicines Agency (EMA), and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicines such as gene-therapy, somatic cell-therapy or tissue-engineered medicines and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.
- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State (RMS). The competent authority of the RMS prepares a draft

assessment report, a draft summary of the product characteristics (SPC), and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the Member States Concerned).

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Coverage and Reimbursement

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health programs, commercial insurance, and managed healthcare organizations. In the United States, no uniform policy of coverage and reimbursement for drug or biological products exists. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor-by-payor basis. As a result, the coverage determination process is often a time-consuming and costly process that will 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 obtained.

The United States government, state legislatures, and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs, including price-controls, restrictions on reimbursement, and requirements for substitution of generic products for branded prescription drugs. For example, the ACA contains provisions that may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Adoption of general controls and measures, coupled with the tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceutical drugs.

The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. The ACA made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs from 15.1% of average manufacturer price (AMP), to 23.1% of AMP and adding a new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. The ACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization and by enlarging the population potentially eligible for Medicaid drug benefits. The Centers for Medicare & Medicaid Services (CMS), have proposed to expand Medicaid rebate liability to the territories of the United States as well.

The Trump administration announced several executive orders designed to reduce prescription drug pricing. The FDA also released a final rule in September 2020 providing guidance for states to build and submit importation plans for drugs from Canada. In November 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturer. In December 2020, the CMS issued a final rule implementing significant manufacturer price reporting changes under the Medicaid Drug Rebate Program, including regulations that affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value-based purchasing arrangements. It is unclear to what extent the new administration and these new regulations will impact our business.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Part A and B, Part D coverage is not standardized. While all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan likely will be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

For a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer.

As noted above, the marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. An increasing emphasis on cost containment measures in the United States has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In addition, in most foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower.

Scientific Advisory Board

We have assembled a highly qualified scientific advisory board comprised of advisors who have, collectively, deep expertise in neurodegenerative diseases, genomics, protein engineering, drug development, and drug discovery as well as translational medicine. Our scientists work in collaboration with these advisors to identify new disease targets, develop a biomarker strategy, and accelerate discovery and development.

Name	Affiliated Entity
Adam Boxer, M.D., Ph.D.	Director of UCSF Neurosciences Clinical Research Unit
Stephen Hauser, M.D.	Chair of the Department of Neurology at UCSF
Michael Heneka, M.D.	Director of the Department of Neurodegenerative Diseases and Gerontopsychiatry at the University of Bonn
Lewis Lanier, Ph.D.	Chair of the Department of Microbiology and Immunology at UCSF

Name	<u>Affiliated Entity</u>
Liqun Luo, Ph.D.	Member of National Academy of Sciences, Stanford University
Richard Scheller, Ph.D.	Member of National Academy of Sciences
Thomas Christian Südhof, M.D., Ph.D.	Nobel Laureate, Stanford University
Robert Vassar, Ph.D.	Northwestern University Feinberg School of Medicine
Berislav Zlokovic, M.D., Ph.D.	Chair of the Department of Physiology & Neuroscience at USC Keck School of Medicine

Employees and Human Capital

As of December 31, 2020, we had 171 full-time employees, over 75% of whom were engaged in research and development activities. None of our employees are represented by a labor union or covered under a collective bargaining agreement.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing, and integrating our existing and new employees, advisors, and consultants. The principal purposes of our equity and cash incentive plans are to attract, retain and reward personnel through the granting of stock-based and cash-based compensation awards, in order to increase stockholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

In response to the COVID-19 pandemic, we focused our health and safety efforts on protecting our employees and their families. We swiftly implemented changes that we determined were in the best interest of our employees and the communities in which we operate, and which are aligned with guidance from the Centers for Disease Control and Prevention and in compliance with state and local regulations. This includes having some of our employees work from home, while implementing additional safety measures for employees continuing critical on-site work.

Corporate Information

We were initially formed as a limited liability company in Delaware in May 2013 under the name Alector LLC and completed our restructuring to a Delaware corporation in October 2017 under the name Alector, Inc. Our principal executive offices are located at 131 Oyster Point Boulevard, Suite 600, South San Francisco, California 94080. Our telephone number is 415-231-5660. Our website address is www.alector.com. Information contained on, or that can be accessed through, our website is not incorporated by reference in this Annual Report on Form 10-K or in any other filings we make with the SEC.

We make available on or through our website certain reports and amendments to those reports that we file with or furnish to the SEC in accordance with the Securities Exchange Act of 1934, as amended (Exchange Act). These include our annual reports on Form 10-K, our quarterly reports on Form 10-Q, and our current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make this information available on or through our website free of charge as soon as reasonably practicable after we electronically file the information with, or furnish it to, the SEC.

We use Alector, the Alector logo, and other marks as trademarks in the United States and other countries. This report contains references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this report, including logos, artwork, and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights, or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other entities' trade names, trademarks, or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

Item 1A. Risk Factors.

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.

Summary Risk Factors

Our business is subject to numerous risks and uncertainties that you should consider before investing in our company, as fully described below. The principal factors and uncertainties that make investing in our company risky include, among others:

- We are in the early stages of clinical drug development and have a limited operating history and no products approved for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability.
- We have incurred significant net losses in each period since our inception and anticipate that we will continue to incur net losses for the foreseeable future.
- The market price of our common stock may continue to be volatile, which could result in substantial losses for investors.
- Drug development is a highly uncertain undertaking and involves a substantial degree of risk.
- We will need to obtain substantial additional financing to complete the development and any commercialization of our product candidates, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce, or terminate our commercialization efforts, product development, or other operations.
- Due to the significant resources required for the development of our programs, and depending on our ability to access capital, we must prioritize development of certain product candidates. Moreover, we may expend our limited resources on programs that do not yield a successful product candidate or fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.
- Research and development of biopharmaceutical products is inherently risky, and our business is heavily dependent on the successful development of our product candidates, which are in the early stages of preclinical and clinical development, so 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 may not be successful in our efforts to continue to create a pipeline of product candidates from our Discovery Platform or to develop commercially successful products. If we fail to successfully identify and develop additional product candidates from our Discovery Platform, our commercial opportunity may be limited.
- We may not be successful in our efforts to expand indications for approved product candidates.

- We have concentrated a substantial portion of our research and development efforts on the treatment of neurodegenerative diseases, a field that has seen limited success in drug development. Further, our product candidates are based on new approaches and novel technology, and we must be able to identify and develop new biomarkers that are signs of a disease or condition and that can measure impact on disease progression of our product candidates, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval.
- We may encounter substantial delays in our clinical trials, or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all.
- Our clinical trials may reveal significant adverse events, toxicities, or other side effects and may fail to demonstrate substantial evidence of the safety and efficacy of our product candidates, which would prevent, delay, or limit the scope of regulatory approval and commercialization.
- 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 operations and financial results could be adversely impacted by the COVID-19 pandemic in the United States and the rest of the world.

Risks Related to Our Business, Financial Condition, and Capital Requirements

We are in the early stages of clinical drug development and have a limited operating history and no products approved for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability.

We are a clinical stage biopharmaceutical company with a limited operating history, focused initially on developing therapeutics for neurodegenerative diseases, including FTD, Alzheimer’s disease, Parkinson’s disease, and ALS. We commenced operations in May 2013. To date, we have only generated revenue from our collaboration arrangements and a government grant. We have no products approved for commercial sale and have not generated any revenue from product sales. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We are in Phase 2 and Phase 3 clinical trials for one product candidate, AL001, are in Phase 2 clinical trials for one product candidate, AL002, and are in Phase 1 clinical trials for two product candidates, AL003 and AL101. 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 short operating history as a company makes any assessment of our future success and viability subject to significant uncertainty.

We will encounter risks and difficulties frequently experienced by clinical-stage biopharmaceutical companies in rapidly evolving fields, and we have not yet demonstrated an ability to successfully overcome such risks and difficulties. If we do not address these risks and difficulties successfully, our business will suffer.

We have incurred significant net losses in each period since our inception and anticipate that we will continue to incur net losses for the foreseeable future.

We have incurred net losses in each reporting period since our inception, including net losses of \$190.2 million, \$105.4 million, and \$52.2 million for the years ended December 31, 2020, 2019, and 2018, respectively. As of December 31, 2020, we had an accumulated deficit of \$410.0 million.

We have invested significant financial resources in research and development activities, including for our preclinical and clinical product candidates. We do not expect to generate revenue from product sales for several years, if at all. The revenue we currently generate from our collaboration arrangement with AbbVie is variable and limited in amount. For our collaboration with AbbVie, we recognize collaboration revenue by measuring the progress towards complete satisfaction of the performance of obligation measured as the program costs are incurred. The amount of our future net losses will depend, in part, on the level of our future expenditures and revenue.

Moreover, our net losses may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

We expect to continue to incur significant expenses and increasingly higher operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue our research and discovery activities;
- advance our Discovery Platform, including our target, patient, and biomarker selections;
- progress our current and any future product candidates through preclinical and clinical development;
- initiate and conduct additional preclinical, clinical, or other studies for our product candidates;
- work with our contract development and manufacturing organizations (CDMOs) to scale up the manufacturing processes for our product candidates or, in the future, establish and operate a manufacturing facility;
- change or add 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;
- make milestone, royalty, or other payments due under any license or collaboration agreements;
- take steps to seek protection of our intellectual property and defend our intellectual property against challenges from third parties;
- obtain, maintain, protect, and enforce our intellectual property portfolio, including intellectual property obtained through license agreements, including as a result of the arbitration proceeding that we have initiated against our former consulting co-founder;
- attract, hire, and retain qualified personnel;
- provide additional internal infrastructure to support our continued research and development operations and any planned commercialization efforts in the future;
- experience any delays or encounter other issues related to our operations;
- implement additional internal systems and infrastructure related to cybersecurity;
- meet the requirements and demands of being a public company; and
- defend against any product liability claims or other lawsuits related to our products.

Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

Drug development is a highly uncertain undertaking and involves a substantial degree of risk.

We have no products approved for commercial sale. To obtain revenues from the sales of our product candidates that are significant or large enough to achieve profitability, we must succeed, either alone or with third parties, in developing, obtaining regulatory approval for, manufacturing, and marketing therapies with significant commercial success. Our ability to generate revenue and achieve profitability depends on many factors, including:

- completing research and preclinical and clinical development of our product candidates;
- addressing any delays in our clinical trials or other impacts resulting from factors related to the COVID-19 pandemic;
- obtaining regulatory approvals and marketing authorizations for product candidates for which we successfully complete clinical development and clinical trials;

- developing a sustainable and scalable manufacturing process for our product candidates, as well as establishing and maintaining commercially viable supply relationships with third parties that can provide adequate products and services to support clinical activities and commercial demand of our product candidates;
- identifying, assessing, acquiring, and/or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter;
- launching and successfully commercializing product candidates for which we obtain regulatory and marketing approval, either 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 milestones and other payments under our current and any future collaboration arrangements;
- maintaining, protecting, expanding, and enforcing our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and
- attracting, hiring, and retaining qualified personnel.

Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of our expenses, or when we will be able to generate any meaningful revenue or achieve or maintain profitability, if ever. In addition, our expenses could increase beyond our current expectations if we are required by the FDA or foreign regulatory agencies, to perform studies in addition to those that we currently anticipate, or if there are any delays in any of our or our future collaborators' clinical trials or the development of any of our product candidates. Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs associated with launching and commercializing any approved product candidate and ongoing compliance efforts.

We will need to obtain substantial additional financing to complete the development and any commercialization of our product candidates, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce, or terminate our commercialization efforts, product development, or other operations.

Our operations have required substantial amounts of cash since inception, and we expect our expenses to increase significantly in the foreseeable future. To date, we have financed our operations primarily through the sale of equity securities and upfront payments received in connection with our collaboration arrangement with AbbVie. Developing our product candidates and conducting clinical trials for the treatment of neurodegenerative diseases, including FTD, Alzheimer's disease, and Parkinson's disease, will require substantial amounts of capital. We will also require a significant amount of capital to commercialize any approved products.

As of December 31, 2020, we had cash, cash equivalents, and marketable securities of \$413.3 million. In February 2019, we received \$168.2 million of net proceeds from the issuance of common stock upon the completion of our initial public offering (IPO), net of underwriting discounts and commissions and offering expenses. In January 2020, we received \$224.5 million of net proceeds from the issuance of common stock upon the completion of a follow-on offering, net of underwriting discounts and commissions and offering expenses. In May 2020, we established an "at-the-market" facility for the sale of up to \$150 million worth of shares of common stock from time to time by entering into an equity distribution agreement with Morgan Stanley & Co. LLC and Goldman Sachs & Co. LLC, as sales agents. We have not issued any shares pursuant to any at-the-market offerings but may at a future date.

Based on our current operating plan, we believe that our existing cash, cash equivalents, and marketable securities will be sufficient to fund our projected operations through at least the next 12 months, subsequent to the filing date of this Annual Report on Form 10-K. 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 proved inaccurate, and we could use our available capital resources sooner than we currently expect. In addition, changing circumstances may cause us to increase our spending significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We may need to raise additional funds sooner than we anticipate if we choose to expand more rapidly than we presently anticipate.

We will require additional capital for the further development and, if approved, commercialization of our product candidates. In recent months, global markets have experienced volatility in connection with continued concerns over the global impact of a novel strain of coronavirus, COVID-19. Our ability to raise money in the public markets may be severely impacted for the foreseeable future due to the impact of COVID-19. Additional capital may not be available when we need it, on terms acceptable to us or at all. 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, as desired, which could materially affect our business, financial condition, results of operations, and growth prospects and cause the price of our common stock to decline.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends. If we raise additional funds through collaborations, strategic alliances, or licensing arrangements with pharmaceutical partners, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, or product candidates, or grant licenses on terms that may not be favorable to us.

Due to the significant resources required for the development of our 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 or fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

As a result, we have identified over 100 immune system targets, have advanced four product candidates, AL001, AL002, AL003, and AL101 into clinical development, and continue to develop our research pipeline. We currently have four product candidates in clinical trials. Together, the development of these programs and product candidates require significant capital investment. Due to the significant resources required for the development of our programs and product candidates, we must focus our programs and product candidates on specific diseases and disease pathways and decide which product candidates to pursue and advance and the amount of resources to allocate to each. Our drug development strategy is to clinically test and seek regulatory approval for our product candidates in indications in which we believe there is the most evidence that we will be able to quickly generate proof-of-concept data. We then intend to expand to clinical testing and seek regulatory approvals in other neurodegenerative indications based on genetic and mechanistic overlap with the primary indication. However, even if our product candidates are able to gain regulatory approval in one indication, there is no guarantee that we will be able to expand to other indications, and we may expend significant resources in seeking such approvals. In addition, we may focus resources on pursuing indications outside of neurodegeneration based on the same genetic and mechanistic rationale we utilize in determining on which of our discovery programs to focus. Our decisions concerning the allocation of research, development, collaboration, management, and financial resources toward particular product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities. Similarly, our potential decisions to delay, terminate, or collaborate with third parties in respect of certain programs may subsequently also prove to be suboptimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the viability or market potential of any of our programs or product candidates or misread trends in the biopharmaceutical industry, in particular for neurodegenerative diseases, our business, financial condition, and results of operations could be

materially adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases and disease pathways that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing, or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights.

Risks Related to the Discovery, Development, and Commercialization of Our Product Candidates

Research and development of biopharmaceutical products is inherently risky. Our business is heavily dependent on the successful development of our product candidates, which are in various stages of preclinical and clinical development. We cannot give any assurance that any of our product candidates will receive regulatory, including marketing, approval, which is necessary before they can be commercialized.

We are at the early stages of development of many of the product candidates currently in our programs. To date, we have invested substantially in our efforts and financial resources to identify, procure intellectual property for, and develop our programs, including conducting preclinical studies and clinical trials in our programs for our product candidates, AL001, AL002, AL003, AL101, and AL044, 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;
- a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- our competitors may develop therapeutics that render our product candidates obsolete or less attractive;
- the product candidates that we develop may not be sufficiently covered by intellectual property for which we hold exclusive rights;
- the product candidates that we develop may be covered by third parties' patents or other intellectual property or exclusive rights;
- the market for a product candidate may change so that the continued development of that product candidate is no longer reasonable or commercially attractive;
- a product candidate may not be capable of being produced in 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, to gain market acceptance; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors, if applicable.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

We may not be successful in our efforts to further develop our current product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. Most of our product candidates are in the early stages of development and 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 currently have one product candidate, AL001, in a pivotal Phase 3 clinical trial, one product candidate, AL002 in a Phase 2 clinical trial, and two product candidates, AL003 and AL101, in Phase 1 clinical trials. Further, we cannot be certain that any of our product candidates will be successful in clinical trials. 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 European Union, and in additional foreign countries where we believe there is a viable commercial opportunity. We have never commenced, compiled or submitted an application seeking regulatory approval to market any product candidate. We may never receive regulatory approval to market any product candidates even if such product candidates successfully complete clinical trials, which would adversely affect our viability. To obtain regulatory approval in countries outside the United States, we must comply with numerous and varying regulatory requirements of such other countries regarding safety, efficacy, manufacturing and controls, clinical trials, commercial sales, pricing, and distribution of our product candidates. We may also rely on our collaborators or partners to conduct the required activities to support an application for regulatory approval, and to seek approval, for one or more of our product candidates. For example, for our AL002 and AL003 product candidates, our collaboration arrangement with AbbVie provides that we are responsible for the execution of the Phase 1 and Phase 2 studies. We cannot be sure that our collaborators or partners will conduct these activities or do so within the timeframe we desire. Even if we (or our collaborators or partners) are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. If we are unable to obtain approval for our product candidates in multiple jurisdictions, our business, financial condition, results of operations, and our growth prospects could be negatively affected.

Even if we receive regulatory approval to market any of our product candidates, whether for the treatment of neurodegenerative diseases or other diseases, we cannot 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 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 from our Discovery Platform or to develop commercially successful products. If we fail to successfully identify and develop additional product candidates from our Discovery Platform, our commercial opportunity may be limited.

One of our strategies is to identify and pursue clinical development of additional product candidates. Identifying, developing, obtaining regulatory approval, and commercializing additional product candidates for the treatment of neurodegenerative 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 are unable to successfully identify, acquire, develop, and commercialize additional product candidates, our commercial opportunity may be limited.

We may not be successful in our efforts to expand indications for approved product candidates.

Our drug development strategy is to clinically test and seek regulatory approval for our product candidates in indications in which we believe there is the most evidence that we will be able to quickly generate proof-of-concept data. We then intend to expand to clinical testing and seek regulatory approvals in other neurodegenerative indications based on genetic and mechanistic overlap with the primary indication. Conducting clinical trials for additional indications for our product candidates requires substantial technical, financial, and human resources and is prone to the risks of failure inherent in drug development. We cannot provide you any assurance that we will be

successful in our effort to obtain regulatory approval for our product candidates for additional indications even if we obtain approval for an initial indication.

For example, our product candidate AL001 is initially targeting FTD-GRN patients. In the third quarter of 2019, we advanced AL001 into a Phase 2, which also includes an additional genetic subset of FTD patients (FTD-*C9orf72*) and we will evaluate AL001 in patients with amyotrophic lateral sclerosis (ALS) caused by *C9orf72* repeats, which share TDP-43 pathology with FTD-GRN. If we are unable to expand indications for our product candidates, our commercial opportunity may be limited.

We have concentrated a substantial portion of our research and development efforts on the treatment of neurodegenerative diseases, a field that has seen limited success in drug development. Further, our product candidates are based on new approaches and novel technology, and we must be able to identify and develop new biomarkers that are signs of a disease or condition and that can measure impact on disease progression of our product candidates, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval.

We have focused a substantial portion of our research and development efforts on addressing neurodegenerative diseases. Collectively, efforts by biopharmaceutical companies in the field of neurodegenerative diseases have seen limited success in drug development. There are few effective therapeutic options available for patients with FTD, Alzheimer's disease, Parkinson's disease, and other neurodegenerative diseases. Our future success is highly dependent on the successful development of our product candidates for treating neurodegenerative diseases. Developing and, if approved, commercializing our product candidates for treatment of neurodegenerative diseases subjects us to a number of challenges, including obtaining disease modifying activity and efficacious dose in target tissue and obtaining regulatory approval from the FDA and other regulatory authorities who have only a limited set of precedents to rely on.

Our approach to the treatment of neurodegenerative diseases aims to identify and select targets enriched in microglia and other myeloid immune cells which are genetically associated with neurodegenerative diseases. We identify and develop product candidates that are designed to cross the blood brain barrier in sufficient quantity and potency to enable efficacious dosing in the brain and engage the intended target, and we must be able to identify and develop biomarkers and biomarker assays that can accurately identify signs of a disease or condition, assist us in selecting the right patient population, and demonstrate target engagement, pathway engagement, and measure the impact on disease progression of our product candidates. This strategy may not prove to be successful. We cannot be sure that our approach will yield satisfactory therapeutic products that are safe and effective, scalable, or profitable.

We may encounter substantial delays in our clinical trials, or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all.

Clinical testing is expensive, time consuming, and subject to uncertainty. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. We cannot be sure that submission of an IND or a clinical trial application (CTA) will result in the FDA or EMA, as applicable, allowing clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could suspend or terminate such clinical trials. A failure of one or more clinical trials can occur at any stage of testing, and our future clinical trials may not be successful. Events that may prevent successful or timely initiation or completion of clinical trials include:

- inability to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of clinical trials;
- delays in confirming target engagement, patient selection, or other relevant biomarkers to be utilized in preclinical and clinical product candidate development;
- delays in reaching a consensus with regulatory agencies on study design;
- delays in reaching agreement on acceptable terms with prospective contract research organizations (CROs) and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;

- delays in identifying, recruiting, and training suitable clinical investigators;
- delays in obtaining required IRB approval at each clinical trial site;
- imposition of delays to clinical trials, including as a result of temporary or permanent clinical hold by regulatory agencies for a number of reasons, including:
 - after review of an IND or amendment, CTA or amendment, or equivalent application or amendment;
 - as a result of a new safety finding that presents unreasonable risk to clinical trial participants;
 - as a result of modifications to clinical trial protocols or related documentation;
 - a negative finding from an inspection of our clinical trial operations or study sites; or
 - the finding that the investigational protocol or plan is clearly deficient to meet its stated objectives;
- delays in identifying, recruiting, and enrolling suitable patients to participate in our clinical trials, and delays caused by patients withdrawing from clinical trials, or failing to return for post-treatment follow-up;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties, or us to adhere to clinical trial requirements;
- failure to perform in accordance with the FDA's or any other regulatory authority's current good clinical practices (cGCPs) requirements, or applicable EMA or other regulatory guidelines in other countries;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- the cost of clinical trials of our product candidates being greater than we anticipate;
- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon product development programs; and
- delays in manufacturing, testing, releasing, validating, or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing.

Any and all of the events described above may be caused or exacerbated by factors related to the ongoing COVID-19 pandemic.

Any inability to successfully initiate or complete clinical trials could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, we may be required to or we may elect to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which our products have patent protection and may allow our competitors to bring products to market before we do, 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, by the data safety monitoring board for such trial or by the FDA, EMA, or any other regulatory authority, or if the IRBs of the institutions in which such trials are being conducted suspend or terminate the participation of their clinical investigators and sites subject to their review. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our

clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA, or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions, or lack of adequate funding to continue the clinical trial.

We may in the future advance product candidates into clinical trials and terminate such trials prior to their completion, which could adversely affect our business.

Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process and delay, or potentially jeopardize our ability to commence product sales and generate revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

We may encounter difficulties enrolling patients in our clinical trials, and our clinical development activities could thereby be delayed or otherwise adversely affected.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons, including:

- the size and nature of the patient population;
- the patient eligibility criteria defined in the protocol, including biomarker-driven identification and/or certain highly-specific criteria related to stage of disease progression, which may limit the patient populations eligible for our clinical trials to a greater extent than competing clinical trials for the same indication that do not have biomarker-driven patient eligibility criteria;
- the size of the study population required for analysis of the trial's primary endpoints;
- the proximity of patients to a trial site;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- 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.

Enrollment of patients in our clinical trials and maintaining patients in our ongoing clinical trials have been, and may continue to be, delayed or limited as certain of our clinical trial sites limit their onsite staff or temporarily close as a result of the COVID-19 pandemic. In addition, patients may not be able or willing to visit clinical trial sites for dosing or data collection purposes due to limitations on travel and physical distancing imposed or recommended by federal or state governments or patients' reluctance to visit the clinical trial sites during the pandemic. These factors resulting from the COVID-19 pandemic could delay or prevent the anticipated readouts from our clinical trials.

Our clinical trials may reveal significant adverse events, toxicities, or other side effects and may fail to demonstrate substantial evidence of the safety and efficacy of our product candidates, which would prevent, delay, or limit the scope of regulatory approval and commercialization.

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 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 cost of a clinical test substantially. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. This is particularly true in neurodegenerative diseases, where failure rates historically have been higher than in many other disease areas. Most product candidates that begin clinical trials are never approved by regulatory authorities for commercialization.

We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. We cannot be certain that our current clinical trials or any other future clinical trials will be successful. Additionally, any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications, which could have a material adverse effect on our business, financial condition, and results of operations.

In addition, even if such clinical trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates. Even if regulatory approval is secured for any of our product candidates, the terms of such approval may limit the scope and use of our product candidates, which may also limit its commercial potential.

Our operations and financial results could be adversely impacted by the COVID-19 pandemic in the United States and the rest of the world.

In January 2020, the World Health Organization declared the outbreak of COVID-19 as a “Public Health Emergency of International Concern,” which continues to spread throughout the world and has adversely impacted global commercial activity and contributed to significant declines and volatility in financial markets. The COVID-19 pandemic and government responses are creating disruption in global supply chains and adversely impacting many industries. The pandemic could have a continued material adverse impact on economic and market conditions and trigger a period of global economic slowdown. We continue to monitor the impact of the COVID-19 pandemic closely. The extent to which the COVID-19 pandemic will impact its operations or financial results is uncertain.

The pandemic and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. In response to the spread of COVID-19 and in compliance with local shelter-in-place regulations, we reduced the number of employees operating at our headquarters, which has altered our operations and processes. While the extent of the impact of the COVID-19 pandemic on our business and financial results is uncertain, a continued and prolonged public health crisis such as the COVID-19 pandemic could have a material adverse effect on our business, financial condition and results of operations. As the COVID-19 pandemic continues to spread around the globe, we may experience disruptions that could severely impact our business and clinical trials, including:

- the size and nature of the patient population;
- delays or difficulties in recruiting, enrolling, and maintaining patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others;
- limitations in resources that would otherwise be focused on the conduct of our business or our clinical trials, including because of sickness or the desire to avoid contact with large groups of people or as a result of government-imposed “shelter in place” or similar working restrictions;
- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials;
- interruption in global shipping that may affect the transport of clinical trial materials, such as investigational drug product used in our clinical trials;
- changes in regulations as part of a response to the COVID-19 pandemic which may require us to change the ways in which our clinical trials are conducted, or to discontinue the clinical trials altogether, or which may result in unexpected costs;
- delays in necessary interactions with regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government or contractor personnel; and
- refusal of the FDA to accept data from clinical trials in affected geographies outside the United States.

We may be required to develop and implement additional clinical trial policies and procedures designed to help protect subjects from the COVID-19 virus, which may delay our anticipated timelines for clinical studies and regulatory approval and increase our costs for clinical studies. For example, in March 2020, the FDA issued a guidance, which the FDA subsequently updated, on conducting clinical trials during the pandemic, that describes a number of considerations for sponsors of clinical trials impacted by the pandemic. In this guidance, pharmaceutical companies would be required to include in the clinical trial report contingency measures implemented to manage the clinical trial, and any disruption of the clinical trial as a result of the COVID-19 pandemic; a list of all subjects affected by the COVID-19 pandemic related study disruption (by unique subject identifier and by investigational site and a description of how the individual’s participation was altered); and analyses and corresponding discussions that address the impact of implemented contingency measures (e.g., participant discontinuation from investigational product and/or study, alternative procedures used to collect critical safety and/or efficacy data) on the safety and efficacy results reported for the clinical trial. In June 2020, the FDA also issued a guidance on good manufacturing practice considerations for responding to COVID-19 infection in employees in drug and biological products manufacturing, including recommendations for manufacturing controls to prevent contamination of drugs and a guidance on resuming normal drug and biologics manufacturing operations during the COVID-19 public health emergency. To the extent our clinical studies are delayed or data from our clinical studies become compromised due to COVID-19 related factors, we may be required to expend additional resources to conduct additional studies and/or enroll more participants, which could adversely affect our business operations and delay regulatory approval.

The COVID-19 pandemic continues to evolve rapidly, with the status of operations and government restrictions evolving weekly. The extent to which the outbreak impacts our business, preclinical studies, and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the pandemic, travel restrictions, and social distancing in the United States and other countries, business closures or business disruptions, and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

Additionally, certain third parties with whom we engage, including our collaborators, contract organizations, third party manufacturers, suppliers, clinical trial sites, regulators and other third parties with whom

we conduct business are similarly adjusting their operations and assessing their capacity in light of the COVID-19 pandemic. If these third parties experience shutdowns or continued business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively impacted.

For example, certain of our clinical trial sites have experienced clinical trial visit delays, and we are aware that for a period of time, some participants in each of our ongoing trials did not receive scheduled doses on time. These events could negatively impact the integrity, reliability, or robustness of the data from our clinical trials. We and our CROs have also made certain adjustments to the operation of such trials in an effort to ensure the monitoring and safety of patients and minimize risks to trial integrity during the pandemic in accordance with the guidance issued by the FDA, and we may be required to make further adjustments in the future. Many of these adjustments are new and untested, may not be effective, and may have unforeseen effects on the enrollment, progress and completion of these trials and the findings from these trials. In addition, notwithstanding any adjustments, some trial participants may decline to visit clinical trial sites for dosing or data collection purposes due to limitations on travel and physical distancing imposed or recommended by federal or state governments or patients' reluctance to visit the clinical trial sites during the pandemic. We may not be successful in adding clinical trial sites, may experience delays in patient enrollment or in the progression of our clinical trials and collection and analysis of patient data, may need to suspend or abandon our clinical trials, and may encounter other negative impacts to our trials, due to the effects of the COVID-19 pandemic.

The global outbreak of COVID-19 continues to rapidly evolve, with particularly significant case increases in the United States. While the extent of the impact of the current COVID-19 pandemic on our business and financial results is uncertain, a continued and prolonged public health crisis such as the COVID-19 pandemic could have a material negative impact on our business, financial condition and operating results. To the extent the COVID-19 pandemic adversely affects our operations and financial results, it may also have the effect of heightening many of the other risks described in this "Risk Factors" section.

We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer, more advanced, or more effective than ours, which may negatively impact our ability to successfully market or commercialize any product candidates we may develop and ultimately harm our financial condition.

The development and commercialization of new drug products is highly competitive. Moreover, the neurodegenerative field is characterized by strong and increasing competition, and a strong emphasis on intellectual property. We may face competition with respect to any of our product candidates that we seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

There are a number of large pharmaceutical and biotechnology companies that are currently pursuing the development of products for the treatment of neurodegenerative diseases, including FTD and Alzheimer's disease. Many of these current or potential competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop. Furthermore, currently approved products could be discovered to have application for treatment of neurodegenerative disease indications, which could give such products significant regulatory and market timing advantages over any of our product candidates. Our competitors also may obtain FDA, EMA, or other regulatory approval for their products more rapidly than we may obtain approval for ours and may obtain orphan drug exclusivity from the FDA for indications our product candidates are targeting, which could result in our competitors establishing a strong market position

before we are able to enter the market. Additionally, products or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, we could face litigation or other proceedings with respect to the scope, ownership, validity, and/or enforceability of our patents relating to our competitors' products and our competitors may allege that our products infringe, misappropriate, or otherwise violate their intellectual property. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

The manufacture of our product candidates is complex, and we may encounter difficulties in production. If we or any of our third-party manufacturers encounter such difficulties, or fail to meet rigorously enforced regulatory standards, our ability to provide supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.

The processes involved in manufacturing our drug and biological product candidates are complex, expensive, highly-regulated, and subject to multiple risks. Further, as product candidates are developed through preclinical studies to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials.

In order to conduct clinical trials of our product candidates, or supply commercial products, if approved, we will need to manufacture them in large quantities. Our CDMOs may be unable to successfully 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 CDMOs 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 risk would apply to our internal manufacturing facilities, should we in the future decide to build internal manufacturing capacity. In addition, building internal manufacturing capacity would carry significant risks in terms of being able to plan, design, and execute on a complex project to build manufacturing facilities in a timely and cost-efficient manner.

In addition, the manufacturing process for any products that we may develop is subject to FDA, EMA, and foreign regulatory authority approval processes, and continuous oversight, and we will need to contract with manufacturers who can meet all applicable FDA, EMA, and foreign regulatory authority requirements, including complying with current good manufacturing practices (cGMPs) on an ongoing basis. If we or our third-party manufacturers are unable to reliably produce products to specifications acceptable to the FDA, EMA, or other regulatory authorities, including recent FDA guidance on good manufacturing practice considerations for responding to COVID-19 infection in employees in drug and biological products manufacturing, as well as any future guidance and regulations, we may not obtain or maintain the approvals we need to commercialize such products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our CDMOs will be able to manufacture the approved product to specifications acceptable to the FDA, EMA, or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product 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 a sales or marketing infrastructure and have no experience in the sale, marketing, or distribution of pharmaceutical products. To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing, and commercial support infrastructure to sell, or participate in 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 and safety of such product candidates as demonstrated in clinical trials and published in peer-reviewed journals;
- the potential and perceived advantages compared to alternative treatments;
- the ability to offer our products for sale at competitive prices;
- sufficient third-party coverage or reimbursement;
- the ability to offer appropriate patient access programs, such as co-pay assistance;
- the extent to which physicians recommend our products to their patients;
- convenience and ease of dosing and administration compared to alternative treatments;
- the clinical indications for which the product candidate is approved by FDA, EMA, or other regulatory agencies;
- product labeling or product insert requirements of the FDA, EMA, or other comparable foreign regulatory authorities, including any limitations, contraindications, or warnings contained in a product's approved labeling;
- restrictions on how the product is distributed;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- the strength of marketing and distribution support; and
- the prevalence and severity of any side effects.

If any product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenue, and we may not become profitable.

Any products we commercialize may become subject to unfavorable pricing regulations, third-party reimbursement practices, or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing, and reimbursement for new drugs vary widely from country to country. In the United States, recently enacted or potential future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing 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 hospitals, and may seek to increase such discounts at any time. Future regulation may negatively impact the price of our products, if approved.

Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. In order to get reimbursement, physicians may need to show that patients have superior treatment outcomes with our products compared to standard of care drugs, including lower-priced generic versions of standard of care drugs. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the medicine is approved by the FDA, EMA, or other comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize product candidates, and our overall financial condition.

Our 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 ahead of our competitors, our product candidates may face competition from biosimilar products. In the United States, our product candidates are regulated by the FDA as biologic products and we intend to seek approval for these product candidates pursuant to the BLA pathway. The Biologics Price Competition and Innovation Act of 2009 (BPCIA) created an abbreviated pathway for the approval of biosimilar and interchangeable biologic products. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as “interchangeable” based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our product candidates.

We believe that any of our product candidates approved as a biologic product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, 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, the European Commission has granted marketing authorizations for several biosimilar products pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In Europe, a competitor may reference data supporting approval of an innovative biological product, but will not be able to get it on the market until 10 years after the time of approval of the innovative product. This 10-year marketing exclusivity period will be extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. In addition, companies may be developing biosimilar products in other countries that could compete with our products, if approved.

If competitors are able to obtain marketing approval for biosimilars referencing our product candidates, if approved, such products 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 product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk when and if we commercialize any products. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing, or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, or a breach of warranties. Claims could also be asserted under state consumer protection acts. 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 financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased or interrupted demand for our products;
- injury to our reputation;
- withdrawal of clinical trial participants and inability to continue clinical trials;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing, or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources; and
- the inability to commercialize any product candidate.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with collaborators. Our insurance policies may have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

The regulatory approval processes of the FDA, EMA, and comparable foreign regulatory authorities are lengthy, time consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.

The time required to obtain approval by the FDA, EMA, and comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials, and depends upon numerous factors, including the type, complexity, and novelty of the product candidates involved. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical, or other studies. We have not submitted for, or obtained regulatory approval for any product candidate, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Further, development of our product candidates and/or regulatory approval may be delayed for reasons beyond our control. For example, the U.S. federal government has experienced and may in the future experience shutdown or budget sequestration, which could result in significant reductions to the FDA's budget, employees, and operations, which may lead to slower response times and longer review periods, potentially affecting our ability to progress development of our product candidates or obtain regulatory approval for our product candidates. To the extent FDA and other regulatory authorities experience any delays or limited resources in reviewing our regulatory applications or requests for meetings and/or guidance, and inspection of manufacturing facilities prior to regulatory approval due to the COVID-19 pandemic or other reasons, we may experience significant delays in our anticipated timelines for our clinical studies and/or seeking regulatory approvals, which could adversely affect our business.

Applications for our product candidates could fail to receive regulatory approval in an initial or subsequent indication for many reasons, including but not limited to the following:

- the FDA, EMA, or comparable foreign regulatory authorities may disagree with the design, implementation, or results of our clinical trials;
- the FDA, EMA, or comparable foreign regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities, or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;
- the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- we may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio when compared to the standard of care is acceptable;
- the FDA, EMA, or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a NDA, BLA, or other submission or to obtain regulatory approval in the United States or elsewhere;
- we may be unable to demonstrate to the FDA, EMA, or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio for a proposed indication is acceptable;
- the FDA, EMA, or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures, and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA, EMA, or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

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 side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences.

Adverse events or other undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay, or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, EMA, or other comparable foreign regulatory authorities.

Drug-related side effects could affect patient recruitment, the ability of enrolled patients to complete the study, and/or result in potential product liability claims. We are required to maintain product liability insurance pursuant to certain of our development and commercialization agreements. We may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. A successful product liability claim or series of claims brought against us could adversely affect our results of operations, business, and reputation. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, withdrawal of clinical trial participants, costs due to related litigation, distraction of management's attention from our primary business, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our product candidates, and decreased demand for our product candidates, if approved for commercial sale.

Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects or adverse events caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may withdraw approvals of such product and cause us to recall our products;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way the product is administered or conduct additional clinical trials or post-approval studies;
- we may be required to create a Risk Evaluation and Mitigation Strategy plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers, and/or other elements, such as boxed warning on the packaging, to assure safe use;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, financial condition, results of operations, and growth prospects.

We currently are and may continue in the future to conduct clinical trials for our product candidates outside the United States, and the FDA, EMA, and applicable foreign regulatory authorities may not accept data from such trials.

We currently are and may continue in the future choose to conduct one or more of our clinical trials outside the United States, including in Europe or Australia. The acceptance of study data from clinical trials conducted outside the United States or another jurisdiction by the FDA, EMA, or applicable foreign regulatory authority may be subject to certain conditions. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to cGCP regulations.

Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, EMA, or any applicable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. 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, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA or EMA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing, and promotion of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the United States, including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to 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 for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers' facilities are required to comply with extensive requirements imposed by the FDA, EMA, and comparable foreign regulatory authorities, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA, BLA, or marketing authorization application (MAA). Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

Any regulatory approvals that we receive for our product candidates will be subject to limitations on the approved indicated uses for which the product may be marketed and promoted or to the conditions of approval (including 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. As such, we may not promote our products for indications or uses for which they do not have approval. The holder of an approved NDA, BLA, or MAA must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process. We could also be asked to conduct post-marketing clinical trials to verify the safety and efficacy of our products in general or in specific patient subsets. If original marketing approval was obtained via the accelerated approval pathway, we could be required to conduct a successful post-marketing clinical trial to confirm clinical benefit for our products. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning letters that would result in adverse publicity;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approvals;
- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities;
- seize or detain products; or
- require a product recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

We have received orphan drug designation from the FDA for AL001 and AL101 for treatment of FTD and plan to seek orphan drug designation for some of our other product candidates, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug status, including market exclusivity, which may cause our revenue, if any, to be reduced.

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting an NDA or BLA. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. While we have obtained orphan drug designation from the FDA for AL001 and AL101 for treatment of FTD, we may be unable to reap the benefits associated with orphan drug status. In addition, we plan to seek orphan drug designations for some of our other product candidates in the future but may be unable to obtain an orphan drug designation for any additional product candidates.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product

exclusivity, which means that the FDA may not approve any other NDA or BLA applications to market the same drug or biologic for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan exclusivity or if FDA finds that the holder of the orphan exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan product to meet the needs of patients with the disease or condition for which the drug was designated. As a result, even though the FDA has approved orphan drug status for AL001 and AL101 for treatment of FTD, the FDA can still approve other drugs that have a different active ingredient for use in treating the same indication or disease. Furthermore, the FDA can waive orphan exclusivity if we are unable to manufacture sufficient supply of our product.

We have received Fast Track designation from the FDA for AL001 and AL101 for the treatment of patients with frontotemporal dementia carrying specific genetic mutation in the granulin gene, but we may be unable to obtain or maintain the benefits associated with the Fast Track designation.

Fast Track designation is designed to facilitate the development and expedite the review of therapies which treat serious conditions and fill an unmet medical need. Programs with Fast Track designation may benefit from early and frequent communications with the FDA, potential priority review, and the ability to submit a rolling application for regulatory review. Fast Track designation applies to both the product and the specific indication for which it is being studied.

In December 2019, the FDA granted Fast Track designation for AL001 and in January 2020, the FDA granted Fast Track designation for AL101 for the treatment of patients with FTD carrying specific genetic mutations in the granulin gene. If our clinical development program does not continue to meet the criteria for Fast Track designation, or if our clinical trials are 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.

Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations.

Third-party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could impact our ability to sell our products profitably. In particular, in 2010, the ACA was enacted, which, among other things, subjected biologic products to potential competition by lower-cost biosimilars, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjected manufacturers to new annual fees and taxes for certain branded prescription drugs, and provided incentives to programs that increase the federal government's comparative effectiveness research. The ACA has been subject to litigation and other efforts to repeal and replace the ACA. It is unclear how such efforts, including the Supreme Court's ruling on the constitutionality of the ACA, and healthcare measures of the new administration will impact the ACA and our business. Complying with any new legislation or reversing changes implemented under the Trump administration could be time-intensive and expensive, resulting in a material adverse effect on our business. Until the ACA is fully implemented or there is more certainty concerning the future of the ACA, it will be difficult to predict its full impact and influence on our business.

There have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. In 2020, the Trump administration announced several executive orders related to prescription drug pricing. The FDA also released a final rule in September 2020 providing guidance for states to build and submit importation plans for drugs from Canada. Further, in November 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price

reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturer. It is unclear to what extent these new regulations and those of the new administration will affect these policies and what the effects will be on our business. In December 2020, the CMS issued a final rule implementing significant manufacturer price reporting changes under the Medicaid Drug Rebate Program, including regulations that affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value-based purchasing arrangements.

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 our product candidates, if we obtain regulatory approval;
- our ability to receive or set a price that we believe is fair for our products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

We expect that the ACA, 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. Further, the governmental may take further action to address the COVID-19 pandemic. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. This could lower the price that we receive for any approved product. The new administration and the states may pass further legislation and regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures. Any denial in coverage or reduction in reimbursement from Medicare or other government-funded programs may result in a similar denial or reduction in payments from private payors, which may prevent us from being able to generate sufficient revenue, attain profitability, or commercialize our product candidates, if approved. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Our employees, independent contractors, consultants, commercial partners, and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of fraud, misconduct, or other illegal activity by our employees, independent contractors, consultants, commercial partners, and vendors. Misconduct by these parties could include intentional, reckless, and negligent conduct that fails to:

- comply with the laws of the FDA, EMA, and other comparable foreign regulatory authorities;
- provide true, complete, and accurate information to the FDA, EMA, and other comparable foreign regulatory authorities;
- comply with 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.

If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. In particular, research, sales, marketing, education, and other business arrangements in the healthcare industry are subject to extensive laws designed to prevent fraud, kickbacks,

self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, educating, marketing and promotion, sales and commission, certain customer incentive programs, and other business arrangements generally. 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. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

If we fail to comply with healthcare laws, we could face substantial penalties and our business, operations, and financial conditions could be adversely affected.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations will be subject to various federal and state fraud and abuse laws. The laws that may impact our operations include the following:

- The federal Anti-Kickback Statute, prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering, or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order, or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.
- Federal civil and criminal false claims laws and civil monetary penalty laws, including the False Claims Act, impose criminal and civil penalties, including through civil “qui tam” or “whistleblower” actions, against individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other third-party payors that are false or fraudulent or knowingly making a false statement to improperly avoid, decrease, or conceal an obligation to pay money to the federal government. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation.
- The federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing, or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH) and their respective implementing regulations, impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security, and transmission of individually identifiable health information without appropriate authorization.
- The federal Physician Payment Sunshine Act, created under the ACA, and its implementing regulations, require manufacturers of drugs, devices, biologicals, and medical supplies for which payment is available under Medicare, Medicaid, or the Children’s Health Insurance Program to report

annually to the U.S. Department of Health and Human Services under the Open Payments Program, information related to payments or other transfers of value made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include payments and transfers of value made during the previous year to certain non-physician providers, such as physician assistants and nurse practitioners.

- Federal consumer protection and unfair competition laws broadly regulate marketplace activities and activities that potentially harm consumers.
- Analogous state and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection, and unfair competition laws may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales, and marketing arrangements, as well as submitting claims involving healthcare items or services reimbursed by any third-party payer, including commercial insurers.
- State laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines, and the relevant compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to healthcare providers and other potential referral sources.
- State laws also require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration, and items of value provided to healthcare professionals and entities.
- State and foreign laws also govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could, despite our efforts to comply, be subject to challenge under one or more of such laws. Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal, and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid, and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our product candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.

We and any contract manufacturers and suppliers we engage are subject to numerous federal, state, and local environmental, health, and safety laws, regulations, and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air, and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our

current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research, product development, and manufacturing efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty, and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Our business is subject to complex and evolving U.S. and foreign laws and regulations relating to security, privacy and data protection. These laws and regulations are subject to change and uncertain interpretation, and could result in claims, changes to our business practices, or monetary penalties, and otherwise may harm our business.

A wide variety of state, national, and international laws and regulations apply to security and cybersecurity requirements and the collection, use, retention, protection, disclosure, transfer, and other processing of personal data. These security and data protection and privacy-related laws and regulations are evolving and may result in ever-increasing regulatory and public scrutiny and escalating levels of enforcement and sanctions. We are working to comply with these laws, and we anticipate needing to devote significant additional resources to our compliance efforts. It is possible that the new legislation may impose new obligations and requirements on similarly situated companies, and these laws may be interpreted and applied in a manner that is inconsistent from jurisdiction to jurisdiction or inconsistent with our current policies and practices. Our actual or perceived failure to adequately comply with applicable laws and regulations relating to security, privacy and data protection, or to protect our systems, personal data and other data we process or maintain, could result in regulatory fines, investigations and enforcement actions, penalties and other liabilities, claims for damages by affected individuals, and damage to our reputation, any of which could materially affect our business, financial condition, results of operations and prospects.

Inadequate funding for the FDA and other government agencies could hinder our ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. In the past, the U.S. government has experienced budgetary shutdowns and certain regulatory agencies, such as the FDA, have had to furlough critical FDA and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Our business activities may be subject to the Foreign Corrupt Practices Act (FCPA) and similar anti-bribery and anti-corruption laws.

Our business activities may be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate, including the U.K. Bribery Act. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the healthcare providers who 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 SEC and Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of our facilities, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition.

Risks Related to Our Reliance on Third Parties

We expect to depend on collaborations with third parties for the research, development, and commercialization of certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates.

We currently use and expect to continue to use third-party collaborators for the research, development, and commercialization of certain of the product candidates we may develop, including our previously disclosed arrangements with AbbVie and Adimab. We have entered into a licensing agreement with Innovent Biologics to develop and commercialize our AL008 product, an anti-SIRP-alpha antibody for the treatment of oncology indications in China. 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. Such arrangements with any third parties, generally provide us with shared or limited control over the amount and timing of resources that our collaborators dedicate to the development or potential commercialization of any product candidates we may seek to develop with them. Our ability to generate revenue from these arrangements with commercial entities will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of 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 and development programs that results from our collaboration with them, and in such cases, we may not

have the exclusive right to commercialize such intellectual property or such product candidates or research programs;

- we may need the cooperation of our collaborators to enforce or defend any intellectual property we contribute to or that arises out of our collaborations, which may not be provided to us;
- collaborators may control certain interactions with regulatory authorities, which may impact our ability to obtain and maintain regulatory approval of our product candidates;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of our product candidates or research programs or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborators may decide to not pursue development and commercialization of any product candidates we develop or may elect not to continue or renew development or commercialization programs 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 or collaborators may elect to fund or commercialize a competing product;
- 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 collaborations, including if we undergo a change of control;
- collaborators may grant sublicenses to our technology or product candidates or undergo a change of control, and the sublicensees or new owners may decide to take the collaboration in a direction which is not in our best interest;
- collaborators may become bankrupt, which may significantly delay our research or development programs, or may cause us to lose access to valuable technology, know-how, or intellectual property of the collaborator relating to our products, product candidates, or research programs;
- key personnel at our collaborators may leave, which could negatively impact our ability to productively work with our collaborators;
- collaborations may require us to incur short and long-term expenditures, issue securities that dilute our stockholders, or disrupt our management and business;
- if our collaborators do not satisfy their obligations under our agreements with them, or if they terminate our collaborations with them, we may not be able to develop or commercialize product candidates as planned;
- 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; 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.

We may not realize the benefit of collaborations if we or our collaborator elects not to exercise the rights granted under the agreement or if we or our collaborator are unable to successfully integrate a product candidate into existing operations and company culture. In addition, if our agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator's technology or intellectual property or require us to stop development of those product candidates completely. We may also find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. Many of the risks relating to product development, regulatory approval, and commercialization described in this "Risk Factors" section also apply to the activities of our collaborators and any negative impact on our collaborators may adversely affect us.

We expect to rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research, or testing.

We currently rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators, to conduct some aspects of our research and preclinical testing and our clinical trials. Any of these third parties may terminate their engagements with us or be unable to fulfill their contractual obligations. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. 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 timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, 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.

We contract with third parties for the manufacture of materials for our research programs, preclinical studies, clinical trials, and for commercialization of any product candidates that we may develop. This reliance on third parties carries and may increase the risk that we will not have sufficient quantities of such materials, product candidates, or any medicines that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.

We do not have any manufacturing facilities. We currently rely on CDMOs for the manufacture of our materials for preclinical studies and clinical trials and expect to continue to do so for preclinical studies, clinical trials, and for commercial supply of any product candidates that we may develop. We currently have established relationships with several CDMOs for the manufacturing of our product candidates. We may be unable to establish any further agreements with CDMOs or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on CDMOs entails additional risks, including:

- the possible breach of the manufacturing agreement by the third party;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- reliance on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting; and
- the inability to produce required volume in a timely manner and to quality standards.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our CDMOs, to comply with applicable regulations could result in clinical holds on our trials, sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures, or recalls of product candidates or medicines, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business, financial condition, results of operations, and prospects.

Any medicines that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future third-party manufacturers could delay clinical development or marketing approval. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer and may incur added costs and delays in identifying and qualifying any such replacement. Furthermore, securing and reserving production capacity with contract manufacturers may result in significant costs.

Our current and anticipated future dependence upon others for the manufacture of any product candidates we may develop or medicines may adversely affect our future profit margins and our ability to commercialize any medicines that receive marketing approval on a timely and competitive basis.

We 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 supply of the raw materials required for the production of our product candidates, and we expect to continue to rely on third-party manufacturers for the commercial supply of any of our product candidates for which we obtain marketing approval. 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 competitors who are larger than we are. We do not have long-term supply agreements, and we purchase our required drug product on a development manufacturing services

agreement or purchase order basis. We cannot be certain that 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. Any supply interruption in limited or sole sourced raw materials could materially harm our ability to manufacture our product candidates until a new source of supply, if any, could be identified and qualified. 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.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for any product candidates we develop, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize any product candidates we may develop may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary product candidates and other technologies we may develop. We seek to protect our proprietary position by filing patent applications in the United States and abroad relating to our core programs and product candidates, as well as other technologies that are important to our business. Given that the development of many of our product candidates is at an early stage, our intellectual property portfolio with respect to certain aspects of many of our product candidates is also at an early stage. For example, we have filed or intend to file patent applications on aspects of our technology and core product candidates; however, there can be no assurance that any such patent applications will issue as granted patents. Furthermore, in 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 12 months of the filing date of the applicable provisional patent application. Any failure to file a non-provisional patent application within this timeline could cause us to lose the ability to obtain patent protection for the inventions disclosed in the associated provisional patent applications. Furthermore, in some cases, we may not be able to obtain issued claims covering compositions relating to our core programs and product candidates, as well as other technologies that are important to our business, and instead may need to rely on filing patent applications with claims covering a method of use and/or method of manufacture for protection of such core programs, product candidates, and other technologies. There can be no assurance that any such patent applications will issue as granted patents, and even if they do issue, such patent claims may be insufficient to prevent third parties, such as our competitors, from utilizing our technology. Any failure to obtain or maintain patent protection with respect to our core programs and product candidates could have a material adverse effect on our business, financial condition, results of operations, and prospects.

If any of our patent applications, or those of our collaborators, do not issue as patents in any jurisdiction, we may not be able to compete effectively.

Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our patents or those of our collaborators with respect to our product candidates. With respect to both our intellectual property and that of our collaborators related to our product candidates, we cannot predict whether the patent applications we and our collaborators are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors or other third parties.

The patent prosecution process is expensive, time-consuming, and complex, and we or our collaborators may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into nondisclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, CDMOs, consultants, advisors, and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In

addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we or our collaborators were the first to make the inventions claimed in any of our or our collaborators' patents or pending patent applications, or that we or our collaborators 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 or our collaborators' pending and future patent applications may not result in patents being issued which protect our product candidates or other technologies or which effectively prevent others from commercializing competitive technologies and product candidates.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we or our collaborators license or own currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents to which we or our collaborators have rights may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether product candidates or other technologies will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner which could materially adversely affect our business, financial condition, results of operations and prospects.

The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. We or our collaborators may be subject to a third-party 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 or our collaborators' patent rights. An adverse determination in any such submission, proceeding, or litigation could reduce the scope of, or invalidate or render unenforceable, such patent rights, allow third parties to commercialize our product candidates or other technologies and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, we, or one of our collaborators, 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 collaborators' priority of invention or other features of patentability with respect to our or our collaborators' patents and patent applications. Such challenges may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our product candidates and other technologies. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. If we or our collaborators are unsuccessful in any such proceeding or other 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 patents and patent applications may in the future be co-owned with third parties. In addition, collaborators or future licensors may co-own their patents and patent applications with other third parties with whom we do not have a direct relationship. Our rights to certain of these patents and patent applications may be dependent, in part, on inter-institutional or other operating agreements between the joint owners of such patents and patent applications, who are not parties to our license agreements. If our collaborators or future licensors do not have exclusive control of the grant of licenses under any such third-party co-owners' interest in such patents or patent applications or we are otherwise unable to secure such exclusive rights, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology to the extent such products and technology are not also covered by our intellectual property. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Our rights to develop and commercialize our product candidates are subject, in part, to the terms and conditions of agreements with others.

We are heavily reliant upon option rights to certain patent rights and proprietary technology from third parties that are important or necessary to the development of our product candidates and are subject to the terms and conditions of certain collaboration agreements with third parties. For example, in 2014 we entered into the Adimab Collaboration Agreement with Adimab. Under the Adimab Collaboration Agreement, we are developing antibodies discovered by Adimab in our AL001 and AL101 product candidates, and we are developing antibodies optimized by Adimab in our AL002 and AL003 product candidates. Additionally, in October 2017, we entered into the AbbVie Agreement to co-develop and commercialize medicines with AbbVie to treat Alzheimer's disease and other neurodegenerative diseases. In August 2019, we entered into a new Adimab collaboration agreement for development of antibodies for use in future programs. For additional information on the Adimab Collaboration Agreement and the AbbVie Agreement, see the sections titled "Business—Adimab Collaboration Agreements" and "Business—Strategic Alliance with AbbVie."

Our agreements with Adimab and AbbVie and other agreements we enter into in the future may not provide exclusive rights to use certain intellectual property and technology retained by the collaborator in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future. As a result, we may not be able to prevent competitors or other third parties from developing and commercializing competitive products that utilizes technology retained by such collaborators to the extent such products are not also covered by our intellectual property.

In addition, subject to the terms of any such agreements, we 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 certain patents and patent applications retained by the collaborator and provided to us under a limited license. For example, under the Adimab Collaboration Agreements, patent rights relating to improvements to Adimab's background platform technology that are invented in the course of the research under the Adimab Collaboration Agreements are assigned to Adimab. We also have an exclusive option under the Adimab Collaboration Agreements to obtain with respect to a specified number of antibodies directed against such target and discovered or optimized by Adimab, ownership of certain patent rights relating to such antibodies, including certain patent rights. Until we exercise such option, we and Adimab each grant each other a non-exclusive license to the relevant intellectual property. We cannot be certain that patents and patent applications that are controlled by our collaborators will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If our collaborators fail to prosecute, maintain, enforce, and defend such patents, or lose rights to those patents or patent applications, the limited rights we have licensed may be reduced or eliminated, our right to develop and commercialize any of our product candidates that are subject of such licensed rights could be adversely affected, and we may have a reduced ability to prevent competitors from making, using, and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications we have

licensed to and from collaborators, we may still be adversely affected or prejudiced by actions or inactions of our collaborators that took place prior to the date upon which we assumed control over patent prosecution.

Furthermore, our or our collaborators' patents may be subject to a reservation of rights by one or more third parties. For example, we received an award from the National Institute of Health in support of our research into the production and characterization of novel therapeutic antibodies against SORT1. As a result, the U.S. government may have certain rights to resulting intellectual property. When new technologies are developed with U.S. government funding, the U.S. government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the U.S. government to use the invention or to have others use the invention on its behalf. The U.S. government's rights may also permit it to disclose the funded inventions and technology to third parties and to exercise march-in rights to use or allow third parties to use the technology developed using U.S. government funding. The U.S. government may exercise its march-in rights if it determines that action is necessary because we fail to achieve the practical application of the government funded technology, or because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in facilities in the United States in certain circumstances and if this requirement is not waived. Any exercise by the U.S. government of such rights or by any third party of its reserved rights could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects.

If we fail to comply with our obligations in the agreements under which we option or license intellectual property rights from our collaborators or future licensors or otherwise experience disruptions to our business relationships with our collaborators or future licensors, we could lose intellectual property rights that are important to our business.

We have entered into agreements with our collaborators to option or license certain intellectual property and may need to obtain additional intellectual property rights from others to advance our research or allow commercialization of product candidates we may develop. It is possible that we may be unable to obtain additional intellectual property rights at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, manufacturing methods, product candidates, or future methods or products resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

In addition, each of our agreements with collaborators do, and we expect our future agreements will, impose various economic, development, diligence, commercialization, and other obligations on us. Certain of our collaboration agreements also require us to meet development timelines, or to exercise commercially reasonable efforts to develop and commercialize licensed products. In spite of our efforts, our collaborators might conclude that we have materially breached our obligations under such agreements and might therefore terminate or seek damages under the agreements, thereby removing or limiting our ability to develop and commercialize products and technology covered by these agreements. If termination of these agreements causes us to lose the rights to certain patents or other intellectual property, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties may have the freedom to seek regulatory approval of, and to market, products similar to or identical to ours and we may be required to cease our development and commercialization of certain of our product candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and growth prospects.

Moreover, disputes may arise regarding intellectual property subject to a collaboration agreement, including:

- the scope of the option or license rights granted under the agreement and other interpretation-related issues;

- the extent to which our technology and processes infringe on intellectual property of the collaborator that is not subject to the option or license rights granted under the agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our collaborators and us and our other partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently have rights to option or license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and growth prospects. Moreover, if disputes over intellectual property that we have optioned or licensed prevent or impair our ability to maintain our current arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and growth prospects.

We may not be able to protect our intellectual property and proprietary rights throughout the world.

Filing, prosecuting, and defending patents on our product candidates and other technologies in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States.

Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in 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. 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.

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, our collaborators or any of our future licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees, and various other government fees on patents and applications will be due to 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 collaborators or licensing partners to pay these fees due to U.S. and non-U.S. patent agencies. The USPTO and various non-U.S. government agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. We also are dependent on our collaborators or licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

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 were the first to either (i) file any patent application related to our product candidates or other technologies or (ii) invent any of the inventions claimed in our patents or patent 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 patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, the patent positions of companies in the development and commercialization of pharmaceuticals are particularly uncertain. 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. 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.

Issued patents covering our product candidates and other technologies could be found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad.

If we initiated legal proceedings against a third party to enforce a patent covering our product candidates or other technologies, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, 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. Third parties may raise claims challenging the validity or enforceability of our patents before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, 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 product candidates or other technologies. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we or our licensing partners and the patent examiner were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates or other technologies. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations, and growth prospects.

If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration, and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent term extension of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar extensions as compensation for patent term lost during regulatory review processes are also available in certain foreign countries and territories, such as in Europe under a Supplementary Patent Certificate. However, we may not be granted an extension in the United States and/or foreign countries and territories because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is shorter than what we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and growth prospects could be materially harmed.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of employees, consultants, or others who are involved in developing our product candidates or other technologies. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership of our patents, trade secrets, or other intellectual property. If the defense of any such claims fails, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates and other technologies. Even if we are successful in defending against such claims, litigation could result

in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for our product candidates and other technologies, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology, and other proprietary information and to maintain our competitive position. We consider trade secrets and know-how to be one of our primary sources of intellectual property. Trade secrets and know-how can be difficult to protect. We expect our trade secrets and know-how to over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel from academic to industry scientific positions.

We seek to protect these trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, CROs, CDMOs, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants, train our employees not to bring or use proprietary information or technology from former employers to us or in their work, and remind former employees when they leave their employment of their confidentiality obligations. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. Despite our efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. For example, on June 18, 2019, we initiated a confidential arbitration proceeding against Dr. Asa Abeliovich, our former consulting co-founder, related to alleged breaches of his consulting agreement and the improper use of our confidential information learned during the course of rendering services to us as our consulting Chief Scientific Officer/Chief Innovation Officer. Although an independent arbitrator issued a confidential decision in favor of the Company and which found Dr. Abeliovich liable for breach of his confidentiality agreement and for spoliation based on his destruction of documents relevant to the proceeding, asserting and maintaining such proceeding was difficult, expensive, and time-consuming. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

We may not be successful in obtaining, through acquisitions or otherwise, necessary rights to our product candidates or other technologies.

Many pharmaceutical companies, biotechnology companies, and academic institutions are competing with us in the field of neurodegeneration therapy may have patents and have filed and are likely filing patent applications potentially relevant to our business. In order to avoid infringing these third-party patents, we may find it necessary or prudent to obtain licenses to such patents from such third-party intellectual property holders. We may also require licenses from third parties for certain technologies for use with future product candidates. In addition, with respect to any patents we co-own with third parties, we may wish to obtain licenses to such co-owners' interest to such patents. However, we may be unable to secure such licenses or otherwise acquire any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for our future product candidates. The licensing or acquisition of third-party intellectual property rights is a competitive area, and 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 competitors and potential competitors. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

Third-party claims of intellectual property infringement, misappropriation, or other violation against us or our collaborators may prevent or delay the development and commercialization of our product candidates and other technologies.

The field of discovering treatments for neurodegenerative diseases is highly competitive and dynamic. Due to the focused research and development that is taking place by several companies, including us and our competitors, in this field, the intellectual property landscape is in flux, and it may remain uncertain in the future. Additionally, the technology used in our product candidates is still in its infancy and no products utilizing similar technology have yet reached the market. As such, there may be significant intellectual property related litigation and proceedings relating to our, and other third party, intellectual property and proprietary rights in the future.

Our commercial success depends in part on our and our collaborators' ability to develop, manufacture, market, and sell any product candidates that we develop and to use our proprietary technologies without infringing, misappropriating, and otherwise violating the patents and other intellectual property rights of third parties. There is a substantial amount of complex litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, 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. We may become party to, or threatened with, such actions in the future, regardless of their merit. 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 in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates and other technologies may give rise to claims of infringement of the patent rights of others. We cannot assure you that our product candidates and other technologies that we have developed, are developing, or may develop in the future will not infringe existing or future patents owned by third parties. We may not be aware of patents that have already been issued and that a third party, for example, a competitor in the fields in which we are developing product candidates, and other technologies might assert are infringed by our current or future product candidates or other technologies, including claims to

compositions, formulations, methods of manufacture or methods of use or treatment that cover our product candidates or other technologies. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our product candidates or other technologies, could be found to be infringed by our product candidates or other technologies. In addition, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates or other technologies may infringe.

Third parties may have patents or obtain patents in the future and claim that the manufacture, use or sale of our product candidates or other technologies infringes upon these patents. In the event that any third-party claims that we infringe their patents or that we are otherwise employing their proprietary technology without authorization and initiates litigation against us, even if we believe such claims are without merit, a court of competent jurisdiction could hold that such patents are valid, enforceable and infringed by our product candidates or other technologies. In this case, the holders of such patents may be able to block our ability to commercialize the applicable product candidate or technology unless we obtain a license under the applicable patents, or until such patents expire or are finally determined to be held invalid or unenforceable. Such a license may not be available on commercially reasonable terms or at all. Even if we are able to obtain a license, the license would likely obligate us to pay license fees or royalties or both, and the rights granted to us might be nonexclusive, which could result in our competitors gaining access to the same intellectual property. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, we may be unable to commercialize our product candidates or other technologies, or such commercialization efforts may be significantly delayed, which could in turn significantly harm our business.

Defense of infringement claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and other employee resources from our business, and may impact our reputation. In the event of a successful claim of infringement against us, we may be enjoined from further developing or commercializing our infringing product candidates or other technologies. In addition, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties, and/or redesign our infringing product candidates or technologies, which may be impossible or require substantial time and monetary expenditure. In that event, we would be unable to further develop and commercialize our product candidates or other technologies, which could harm our business significantly.

Engaging in litigation to defend against third parties alleging that we have infringed, misappropriated, or otherwise violated their patents or other intellectual property rights is very expensive, particularly for a company of our size, and time-consuming. Some of our competitors may be able to sustain the costs of litigation or administrative proceedings more effectively than we can because of greater financial resources. Patent litigation and other proceedings may also absorb significant management time. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings against us could impair our ability to compete in the marketplace. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, 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 patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented, or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations, and growth prospects.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products that are similar to our product candidates or utilize similar technology but that are not covered by the claims of the patents that we license or may own;
- we, or our current or future licensors or collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or own now or in the future;
- we, or our current or future licensors or collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our current or future pending owned or licensed patent applications will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties;
- our competitors or other third parties might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and

- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

Risks Related to Our Operations

We are highly dependent on our key personnel, and if we are not successful in attracting, motivating, and retaining highly qualified personnel, 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. Arnon Rosenthal, 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 conduct our operations at our facility in South San Francisco, California, in 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 and will continue to provide restricted stock, stock option grants, and other equity awards that vest over time. The value to employees of these equity grants that vest over time may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Although we have employment agreements with our key employees, these employment agreements provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. If we are unable to attract and incentivize quality personnel on acceptable terms, or at all, it may cause our business and operating results to suffer.

We will need to grow the size and capabilities of our organization, and we may experience difficulties in managing this growth.

As of December 31, 2020, we had 171 full-time employees. As our development plans and strategies develop, and as we continue to implement the requirements applicable to operating as a public company, 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:

- identifying, recruiting, integrating, retaining, and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and FDA review process for our current and future product candidates, while complying with our contractual obligations to contractors and other third parties;
- expanding our operational, financial and management controls, reporting systems, and procedures; and
- managing increasing operational and managerial complexity.

Our future financial performance and our ability to continue to develop and, if approved, commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth. Our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to manage these growth activities.

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 expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop our product candidates and, accordingly, may not achieve our research, development, and commercialization goals.

We have engaged in strategic collaborations and may in the future engage in acquisitions, collaborations, or strategic partnerships, which may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

We have engaged in strategic collaborations in the past, such as our strategic collaboration with AbbVie, and we may engage in various acquisitions, collaborations, and strategic partnerships in the future, including licensing or acquiring complementary products, intellectual property rights, technologies, or businesses. Any acquisition, collaboration, or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- volatility with respect to the financial reporting related to such arrangements, such as our expected variability in the recognition of revenue each quarter from the AbbVie Agreement based on the percentage-of-completion basis under the applicable accounting rules;
- assumption of indebtedness or contingent liabilities;
- 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;
- diversion of our management's attention from our existing product programs and initiatives in pursuing such an acquisition or strategic partnership;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and
- our inability to generate revenue from acquired intellectual property, technology, and/or products sufficient to meet our objectives or even to offset the associated transaction and maintenance costs.

In addition, if we undertake such a transaction, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses, and acquire intangible assets that could result in significant future amortization expense.

Our 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 that could compromise the confidentiality, integrity, and availability of such systems and data, result in material disruptions of our development programs and business operations, risk disclosure of confidential, financial, or proprietary information, and affect our reputation.

Despite the implementation of security measures, our internal computer systems and those of our future CROs and other contractors and consultants may be vulnerable to damage from computer viruses and unauthorized access. As the cyber-threat landscape evolves, these attacks are growing in frequency, sophistication, and intensity, and are becoming increasingly difficult to detect. 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. If a breakdown, cyberattack, or other information security breach were to occur and cause interruptions in our operations, it could result in a misappropriation of confidential information, including our intellectual property or financial information, and a material disruption of our development programs and our business operations. For example, the loss 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. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or systems, or inappropriate disclosure of confidential, financial, or proprietary information, including data related to our personnel, we could incur liability or risk disclosure of confidential, financial, or proprietary information, and the further development and commercialization of our product candidates could be delayed. There can be no assurance that we and our business counterparties will be successful in efforts to detect, prevent, or fully recover systems or data from all breakdowns, service interruptions, attacks, or breaches of systems that could adversely affect our business and operations and/or result in the loss of critical or sensitive data, which 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, and other contractors and consultants, could be subject to pandemic events and the spread of disease, earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, political unrest, and other natural or man-made disasters or business interruptions, for which we are partly uninsured. In addition, we rely on our third-party research institution collaborators for conducting research and development of our product candidates, and they may be affected by government shutdowns or withdrawn funding. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce and process our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster, global pandemics, or other business interruption.

The majority of our operations including our corporate headquarters are located in a facility in South San Francisco, California. Damage or extended periods of interruption to our corporate, development, or research facilities due to fire, natural disaster, global pandemics, power loss, communications failure, unauthorized entry, or other events could cause us to cease or delay development of some or all of our product candidates. Although we maintain property damage and business interruption insurance coverage on these facilities, our insurance might not cover all losses under such circumstances and our business may be seriously harmed by such delays and interruption.

Our business is subject to economic, political, regulatory, and other risks associated with international operations.

Our business is subject to risks associated with conducting business internationally. Some of our CDMOs are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- differing and changing regulatory requirements in non-U.S. countries;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- difficulties in compliance with non-U.S. laws and regulations;

- changes in non-U.S. regulations and customs, tariffs, and trade barriers;
- changes in non-U.S. currency exchange rates and currency controls;
- changes in a specific country's or region's political or economic environment;
- shipping of biologics/drugs;
- trade protection measures, import or export licensing requirements, or other restrictive actions by U.S. or non-U.S. governments;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration, and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- potential liability under the FCPA, UK Bribery Act, or comparable foreign laws; and
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods, and fires.

These and other risks associated with our planned international operations may materially adversely affect our ability to attain profitable operations.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

As of December 31, 2020, we had federal and state net operating loss (NOL) carryforwards of approximately \$195.3 million and \$191.4 million, respectively, some of which have an indefinite life. Pursuant to Internal Revenue Code Sections 382 and 383, annual use of the Company's net operating loss and research and development credit carryforwards may be limited in the event that a cumulative change in ownership of more than 50% occurs within a three-year period. As a result of our initial public offering in February 2019 and follow-on public offering in January 2020, and other transactions that have occurred since our incorporation, we may have experienced such an ownership change. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which are outside our control. As a result, our ability to use our pre-change net operating loss carryforwards and other pre-change tax attributes to offset post-change taxable income or taxes may be subject to limitation. In addition, the enacted legislation commonly referred to as the Tax Cuts and Jobs Act of 2017 (the Tax Act) imposes certain limitations on the deduction of NOLs. The Tax Act, as amended by the Coronavirus Aid, Relief, and Economic Security Act of 2020 (CARES Act), also provides that NOLs from tax years that began after December 31, 2017 may offset no more than 80% of current taxable income annually for taxable years beginning after December 31, 2020. Our NOLs may also be subject to limitations under state law. For example, California enacted legislation suspending the use of NOLs for taxable years 2020, 2021 and 2022 for many taxpayers.

General Risk Factors

An active trading market for our common stock may not be sustained.

Prior to our initial public offering in February 2019, there was no public trading market for our common stock. Although our common stock is listed on the NASDAQ Global Select Market, the market for our shares has demonstrated varying levels of trading activity. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations and progression of our product pipeline may not meet the expectations of public market analysts and investors, and, as a result of these and other factors, the price of our common stock may fall.

The market price of our common stock may continue to be volatile, which could result in substantial losses for investors.

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. Some of the factors that may cause the market price of our common stock to fluctuate include:

- the success of existing or new competitive products or technologies;
- the timing and results of clinical trials for our current product candidates and any future product candidates that we may develop;
- commencement or termination of collaborations for our product development and research programs;
- failure to achieve development, regulatory, or commercialization milestones under our collaborations;
- failure or discontinuation of any of our product development and research programs;
- results of preclinical studies, clinical trials, or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents, or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our research programs, clinical development programs, or product candidates that we may develop;
- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders, or other stockholders, such as if we use our at-the-market facility;
- expiration of market standoff or lock-up agreements;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry, and market conditions; and
- the other factors described in this “Risk Factors” section.

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. Following periods of such volatility in the market price of a company’s securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management’s attention and resources from our business.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. If one or more of the analysts covering our business cease to cover us or downgrade their evaluations of our stock or if we fail to meet their operating results estimates for us, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

Sales of substantial amounts of our common stock in the public markets, or the perception that such sales might occur, could cause the market price of our common stock to decline significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. If our stockholders sell, or the market perceives that our stockholders intend to sell, substantial amount of our common stock in the public market, the market price of our common stock could decline significantly.

Certain holders of shares of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. Registration of these shares under the Securities Act would result in the shares becoming freely tradeable in the public market, subject to the restrictions of Rule 144 in the case of our affiliates. Any sales of securities by these stockholders could have a material adverse effect on the market price for our common stock.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances, and licensing arrangements. We, and indirectly, our stockholders, will bear the cost of issuing and servicing such securities. Because our decision to issue debt or equity securities in any future offering will depend on market conditions and other factors beyond our control, we cannot predict or estimate the amount, timing, or nature of any future offerings. To the extent that we raise additional capital through the sale of equity or debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell, or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. On May 13, 2020, we filed a shelf registration statement on Form S-3 with the SEC that automatically became effective and permits us to use our at-the-market facility for sales of up to \$150 million worth of shares of common stock from time to time. Additionally, any future collaborations we enter into with third parties may provide capital in the near term but limit our potential cash flow and revenue in the future. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms unfavorable to us.

Our principal stockholders and management own a significant percentage of our stock and will be able to exercise significant influence over matters subject to stockholder approval.

Our directors, executive officers, holders of more than 5% of our outstanding stock and their respective affiliates beneficially owned 42.1% of our outstanding common stock as of February 15, 2021. As a result, these stockholders, if they act together, may significantly influence all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company that our other stockholders may believe is in their best interests. This in turn could have a material adverse effect on our stock price and may prevent attempts by our stockholders to replace or remove the board of directors or management.

We have incurred and will continue to incur significant additional costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, we have incurred and will continue to incur significant legal, accounting, and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform, and Consumer Protection Act, the listing requirements of NASDAQ, and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We have hired, and expect that we will need to continue to hire, additional accounting, finance, and other personnel in connection with our becoming, and our efforts to comply with the requirements of being, a public company, and our management and other personnel have devoted and will continue to devote a substantial amount of time towards maintaining compliance with these requirements. These requirements have increased and will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that the rules and regulations applicable to us as a public company may make it more difficult and more expensive for us to maintain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We are currently evaluating these rules and regulations and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

If we are unable to maintain effective internal controls, our business, financial position, and results of operations could be adversely affected.

As a public company, we are subject to reporting and other obligations under the Exchange Act, including the requirements of Sarbanes-Oxley Act 404(a) of the Sarbanes-Oxley Act, which require annual management assessments of the effectiveness of our internal control over financial reporting. Section 404(b) of the Sarbanes-Oxley Act also requires our independent auditors to attest to, and report on, this management assessment.

The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes-Oxley Act of 2002. These reporting and other obligations place significant demands on our management and administrative and operational resources, including accounting resources. If we are not able to comply with the requirements of Section 404 or if we or our independent registered public accounting firm are unable to attest to the effectiveness of our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC, or other regulatory authorities, which would require additional financial and management resources.

We do not expect to pay any dividends for the foreseeable future. Investors may never obtain a return on their investment.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. In addition, any future credit facility may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

Delaware law and provisions in our amended and restated certificate of incorporation and bylaws might discourage, delay, or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock.

Provisions in our amended and restated certificate of incorporation and bylaws may discourage, delay, or prevent a merger, acquisition, or other change in control that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares of our common stock. These provisions may also prevent or frustrate attempts by our stockholders to replace or remove our management. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our charter documents:

- establish that our board of directors is divided into three classes, Class I, Class II, and Class III, with each class serving staggered three-year terms;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- provide that our directors may only be removed for cause;
- eliminate cumulative voting in the election of directors;
- authorize our board of directors to issue shares of preferred stock and determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval;
- provide our board of directors with the exclusive right to elect a director to fill a vacancy or newly created directorship;
- permit stockholders to only take actions at a duly called annual or special meeting and not by written consent;
- prohibit stockholders from calling a special meeting of stockholders;
- require that stockholders give advance notice to nominate directors or submit proposals for consideration at stockholder meetings;
- authorize our board of directors, by a majority vote, to amend the bylaws; and
- require the affirmative vote of at least 66 2/3% or more of the outstanding shares of common stock to amend many of the provisions described above.

In addition, Section 203 of the General Corporation Law of the State of Delaware (DGCL), prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, amended and restated bylaws, or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.

Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, another State court in Delaware or the federal district court for the District of Delaware) is the exclusive forum for the following (except for any claim as to which such court determines that there is an indispensable party not subject to the jurisdiction of such court (and the indispensable party does not consent to the personal jurisdiction of such court within 10 days following such determination), which is vested in

the exclusive jurisdiction of a court or forum other than such court, or for which such court does not have subject matter jurisdiction).

- any derivative action or proceeding brought on our behalf;
- any action asserting a claim of breach of fiduciary duty;
- any action asserting a claim against us arising under the DGCL, our amended- and restated certificate of incorporation or our amended and restated bylaws; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine.

This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act or any other claim for which the U.S. federal courts have exclusive jurisdiction.

Our amended and restated bylaws further provide that the federal district courts of the United States 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. Any person or entity purchasing or otherwise acquiring any interest in any of our securities shall be deemed to have notice of and consented to these provisions. There is uncertainty as to whether a court would enforce such provisions, and the enforceability of similar choice of forum provisions in other companies' charter documents has been challenged in legal proceedings. It is possible that a court could find these types of provisions to be inapplicable or unenforceable, and if a court were to find either exclusive-forum provision in our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters are currently located in South San Francisco, California, where we lease approximately 105,000 square feet of office and laboratory space. The term of the lease agreement expires in May 2029, with an option to extend the term of the lease for an additional 10 years. The lease agreement also provides us a right of first offer to expand into available office space in the building. We sublease approximately 23,600 square feet of our corporate headquarters with a lease term that expires in November 2021. We lease approximately 18,700 square feet of additional office and laboratory space in Newark, California. We believe that these facilities will be adequate for our near-term needs. If required, we believe that suitable additional or alternative space would be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings.

From time to time, we may become involved in litigation or other legal proceedings. We are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are likely to have a material adverse effect on our business. We have been engaged in an arbitration against a third party as set forth below. Regardless of outcome, litigation, or other legal proceedings can have an adverse impact on us because of legal fees and settlement costs, diversion of management resources, and other factors.

On June 18, 2019, we initiated a confidential arbitration proceeding against Dr. Asa Abeliovich, our former consulting co-founder, related to alleged breaches of his consulting agreement and the improper use of our confidential information that he learned during the course of rendering services to us as our consulting Chief Scientific Officer/Chief Innovation Officer.

On November 2, 2020, we provided an update on our confidential arbitration proceedings against Dr. Asa Abeliovich, co-founder and CEO of Prevail Therapeutics. An independent arbitrator issued a confidential decision in

our favor, finding Dr. Abeliovich liable for breach of his confidentiality agreement and for spoliation based on his destruction of documents relevant to the proceeding. The arbitrator awarded damages for breach of the agreement and sanctions for the spoliation, as well as violation of orders during the proceeding, and the amount of such damages will be determined in a pending proceeding.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information for Common Stock

Our common stock is publicly traded on the Nasdaq Global Select Market under the symbol "ALEC."

Holders of Record

As of February 15, 2021, there were approximately 17 stockholders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees.

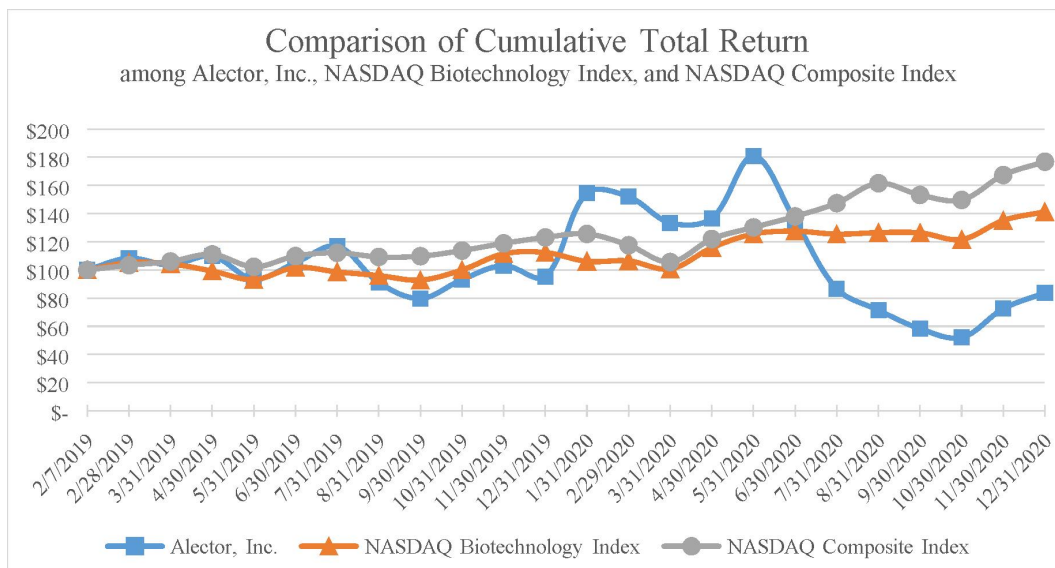
Dividend Policy

We have not declared or paid any cash dividends on our capital stock since our inception. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Payment of future cash dividends, if any, will be at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results, current and anticipated cash needs, the requirements and contractual restrictions of then-existing debt instruments, and other factors that our board of directors deems relevant.

Stock Performance Graph

This graph is not "soliciting material" or deemed "filed" with the SEC for purposes of Section 18 of the Exchange Act, or otherwise subject to liabilities under that Section, and shall not be deemed incorporated by reference into any filing of Alector, Inc. under the Securities Act of 1933, as amended (the "Securities Act"), whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

The following graph compares the cumulative total return to stockholder return on our common stock relative to the cumulative total returns of the NASDAQ Composite Index and the NASDAQ Biotechnology Index. An investment of \$100 is assumed to have been made in our common stock and each index on February 7, 2019 (the first day of trading of our common stock) and its relative performance is tracked through December 31, 2020. Pursuant to applicable Securities and Exchange Commission rules, all values assume reinvestment of the full amount of all dividends, however no dividends have been declared on our common stock to date. The stockholder returns shown on the graph below are based on historical results and are not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.



Use of Proceeds

The Registration Statement on Form S-1 (File No. 333-229152) was declared effective by the SEC for our initial public offering of common stock on February 6, 2019. We started trading on the Nasdaq Global Select Market on February 7, 2019. In connection with our initial public offering, we sold an aggregate of 9,739,541 shares of common stock at a public offering price of \$19.00 per share, including 489,541 shares sold pursuant to the underwriters' partial exercise of their option to purchase additional shares. The aggregate offering price for shares sold in the offering was \$185.1 million. The underwriters for our initial public offering were Morgan Stanley & Co. LLC, Merrill Lynch, Pierce, Fenner & Smith Incorporated, and Cowen and Company, LLC. The aggregate net proceeds received by the Company from the offering, net of underwriting discounts and commissions and estimated offering expenses, were \$168.2 million. No offering expenses were paid or are payable, directly or indirectly, to our directors or officers, to persons owning 10% or more of any class of our equity securities or to any of our affiliates.

We filed the Registration Statement on Form S-1 (File No. 333-236094) for issuing additional shares as part of a secondary public offering. The Registration Statement was declared effective by the SEC on January 29, 2020. We sold an aggregate of 9,602,500 shares of common stock at a public offering price of \$25.00 per share, including 1,252,500 shares sold pursuant to the underwriters' full exercise of their option to purchase additional shares. The aggregate offering price for shares sold in the offering was \$240.1 million. The underwriters for our secondary public offering were Morgan Stanley & Co. LLC, Goldman Sachs & Co. LLC, BofA Securities, Inc., and Cowen and Company, LLC. The aggregate net proceeds received by the Company from the offering, net of underwriting discounts and commissions and estimated offering expenses, were \$224.5 million. No offering expenses were paid or are payable, directly or indirectly, to our directors or officers, to persons owning 10% or more of any class of our equity securities or to any of our affiliates.

There has been no material change in the planned use of proceeds from our public offerings as described in our final prospectuses filed with the SEC on February 7, 2019 and January 30, 2020, respectively, pursuant to Rule 424(b)(4). We invested the funds received in interest-bearing, investment-grade securities and government securities, corporate bonds, and commercial paper.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve risks and uncertainties, including those described in the section titled “Special Note Regarding Forward Looking Statements.” Our actual results and the timing of selected events could differ materially from those discussed below. Factors that could cause or contribute to such differences include, but are not limited to, those identified below and those set forth under the section titled “Risk Factors” included elsewhere in this report.

Overview

We are a clinical stage biopharmaceutical company pioneering immuno-neurology, a novel therapeutic approach for the treatment of neurodegeneration. Immuno-neurology targets immune dysfunction as a root cause of multiple pathologies that are drivers of degenerative brain disorders. We are developing therapies designed to simultaneously counteract these pathologies by restoring healthy immune function to the brain. Supporting our scientific approach, our Discovery Platform enables us to advance a broad portfolio of product candidates, validated by human genetics, which we believe will improve the probability of technical success over shorter development timelines. As a result we have identified over 100 immune system targets, have advanced four product candidates, AL001, AL002, AL003, and AL101 into clinical development, and continue to develop our research pipeline.

Our operations have been financed primarily through the issuance and sale of convertible preferred stock, our collaboration with AbbVie, and issuance of common stock upon the completion of our IPO. We completed our IPO in February 2019, and received \$168.2 million net proceeds, after deducting underwriting discounts and commissions and offering expenses. We completed a follow-on offering in January 2020 and received \$224.5 million net proceeds, after deducting underwriting discounts and commissions and estimated offering expenses.

To date, we have not had any products approved for sale and have not generated any revenue from product sales nor been profitable. Further, we do not expect to generate revenue from product sales until such time, if ever, that we are able to successfully complete the development and obtain marketing approval for one of our product candidates. We will continue to require additional capital to develop our product candidates and fund operations for the foreseeable future. We have incurred net losses in each year since inception and expect to continue to incur net losses for the foreseeable future. Our ability to generate product revenue will depend on the successful development and eventual commercialization of one or more of our product candidates. Our net losses were \$190.2 million, \$105.4 million, and \$52.2 million for the years ended December 31, 2020, 2019, and 2018, respectively. As of December 31, 2020, we had an accumulated deficit of \$410.0 million. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect our expenses will increase substantially in connection with our ongoing activities, as we:

- advance product candidates through preclinical studies and clinical trials;
- pursue regulatory approval of product candidates;
- hire additional personnel;
- continue to operate as a public company;
- acquire, discover, validate, and develop additional product candidates;
- require the manufacture of supplies for our preclinical studies and clinical trials; and
- obtain, maintain, expand, and protect our intellectual property portfolio.

Components of Results of Operations

Revenue

We have not generated any revenue from product sales and do not expect to do so in the near future. Our revenue to date has been primarily related to the AbbVie Agreement to co-develop product candidates in two

programs in clinical development with AbbVie. We recognize revenue related to our research and development grant as the related research services are performed. We recognize revenue from the upfront payments under the AbbVie Agreement over time as the services are provided. Revenues are recognized as the program costs are incurred by measuring actual costs incurred to date compared to the overall total expected costs to satisfy the performance obligation. In addition to receiving the upfront payments, we may also be entitled to development and regulatory milestone payments, opt-in payments for continued development after proof-of-concept for AL002 and AL003, and other future payments from profit sharing or royalties after commercialization of product candidates from such programs.

We expect that our revenue for the next several years will be derived primarily from the AbbVie Agreement. The balance of deferred revenue was \$132.3 million as of December 31, 2020. The deferred revenue is expected to be recognized over the research and development period of the programs through the completion of proof-of-concept for AL002 and AL003.

Research and Development Expenses

Research and development expenses account for a significant portion of our operating expenses. We record research and development expenses as incurred. Research and development expenses consist primarily of costs incurred for the discovery and development of our product candidates, which include:

- expenses incurred under agreements with third-party contract organizations, preclinical testing organizations, and consultants;
- costs related to production of clinical materials, including fees paid to contract manufacturers;
- laboratory and vendor expenses related to the execution of preclinical studies and clinical trials;
- personnel-related expenses, including salaries, benefits, and stock-based compensation for personnel engaged in research and development functions;
- costs related to the preparation of regulatory submissions;
- third-party license fees; and
- facilities and other expenses, which include expenses for rent and maintenance of facilities, depreciation and amortization expense, and other supplies.

We expense all research and development costs in the periods in which they are incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors, collaborators, and third-party service providers. Nonrefundable advance payments for goods or services to be received in future periods for use in research and development activities are deferred and capitalized. The capitalized amounts are then expensed as the related goods are delivered and as services are performed.

Specific program expenses include expenses associated with the development of our most advanced product candidates, AL001 which commenced dosing of the first patient in a pivotal Phase 3 clinical trial, INFRONT-3, and remains in an ongoing Phase 2 clinical trial, AL002, which commenced dosing of the first patient in a Phase 2 clinical trial, and AL003 and AL101, which are in Phase 1 clinical trials. We also have expenses related to the discovery and development of future product candidates and separately tracked expenses related to programs that we expect to move out of preclinical studies and into Phase 1 clinical trials. We do not track personnel or other operating expenses incurred for our research and development programs on a program-specific basis. These expenses primarily relate to salaries and benefits, stock-based compensation, facility expenses, including depreciation, and lab consumables.

At this time, we cannot reasonably estimate or know the nature, timing, and estimated costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, any of our product candidates. We expect our research and development expenses to increase substantially for the foreseeable future as we continue to invest in research and development activities related to developing our product candidates, as our product candidates advance into later stages of development, as we begin to conduct larger clinical trials, as we seek

regulatory approvals for any product candidates that successfully complete clinical trials, and incur expenses associated with hiring additional personnel to support our research and development efforts. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and the successful development of our product candidates is highly uncertain.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel-related costs, including stock-based compensation, for our personnel in executive, legal, finance and accounting, information technology, human resources, and other administrative functions. General and administrative expenses also include legal fees relating to intellectual property and corporate matters, professional fees paid for accounting, auditing, consulting, and tax services, insurance costs, and facility costs not otherwise included in research and development expenses.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research activities and development of our programs. We also anticipate that we will continue to incur expenses as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the SEC and those of the NASDAQ Stock Market on which our securities are traded, legal, auditing, additional insurance expenses, investor relations activities, and other administrative and professional services. In connection with our arbitration proceeding against Dr. Asa Abeliovich, our former consulting co-founder, an independent arbitrator issued a confidential decision in favor of the Company and the amount of damages will be determined in a pending proceeding. We expect these arbitration related expenses to decrease.

Other Income, Net

Other income, net consists of interest earned on our cash equivalents and marketable securities and foreign currency transaction gains and losses incurred during the period.

Results of Operations

Comparison of the Years Ended December 31, 2020 and 2019

	Year Ended December 31,		Dollar Change
	2020	2019	
	(In thousands)		
Collaboration revenue	\$ 21,098	\$ 21,219	\$ (121)
Operating expenses:			
Research and development	156,869	100,528	56,341
General and administrative	59,403	35,095	24,308
Total operating expenses	<u>216,272</u>	<u>135,623</u>	<u>80,649</u>
Loss from operations	(195,174)	(114,404)	(80,770)
Other income, net	4,946	9,019	(4,073)
Net loss	<u>\$ (190,228)</u>	<u>\$ (105,385)</u>	<u>\$ (84,843)</u>

Revenue

Collaboration revenue was \$21.1 million for the year ended December 31, 2020, compared to \$21.2 million for the year ended December 31, 2019. We recognize revenue from the upfront payments under the AbbVie Agreement over time as the services are provided. Revenues are recognized as the program costs are incurred by measuring actual costs incurred to date compared to the overall total expected costs to satisfy the performance obligation. Changes in estimates for revenue recognized over time are recognized on a cumulative basis. Revenue decreased by \$0.1 million, reflecting the level of our estimated cumulative research activities on the AL002 and AL003 programs under the AbbVie Agreement.

Research and Development Expenses

Research and development expenses were \$156.9 million for the year ended December 31, 2020, compared to \$100.5 million for the year ended December 31, 2019. The increase of \$56.3 million was driven by a \$23.3 million increase in AL001 related to manufacturing runs and continued progression through clinical trials. We had a \$15.6 million increase in personnel-related expenses, including stock-based compensation, due to an increase in headcount and issuance of option grants to employees. In addition, expenses increased by \$9.9 million for AL044, a recent program to progress to preclinical trials, and increased by \$6.6 million for other early stage programs as we continue to invest in developing our pipeline.

	Year Ended December 31,		Dollar Change
	2020	2019	
	(In thousands)		
<i>Direct research and development expenses</i>			
AL001	\$ 40,398	\$ 17,067	\$ 23,331
AL101	4,911	8,203	(3,292)
AL002	19,219	17,359	1,860
AL003	8,748	8,386	362
AL044	11,148	1,246	9,902
Other early stage programs	19,983	13,423	6,560
<i>Indirect research and development expenses</i>			
Personnel related (including stock-based compensation)	40,539	24,902	15,637
Facilities and other unallocated research and development expenses	11,923	9,942	1,981
Total research and development expenses	<u>\$ 156,869</u>	<u>\$ 100,528</u>	<u>\$ 56,341</u>

General and Administrative Expenses

General and administrative expenses were \$59.4 million for the year ended December 31, 2020, compared to \$35.1 million for the year ended December 31, 2019. The increase of \$24.3 million was driven by a \$12.2 million increase in personnel-related expenses, including stock-based compensation, due to an increase in headcount and issuance of option grants to employees. In addition, there was an \$8.2 million increase in legal expense due mainly to our arbitration proceeding that we commenced in June 2019 with decision issued in November 2020. We also had a \$3.4 million increase in consulting expense to support the growth of the business related to information technology, accounting, human resources, and other administrative functions.

Other Income, Net

Other income, net was \$4.9 million for the year ended December 31, 2020, compared to \$9.0 million for the year ended December 31, 2019. The decrease of \$4.1 million was due to due lower investment yields on our marketable securities.

Comparison of the Years Ended December 31, 2019 and 2018

	Year Ended December 31,		Dollar Change
	2019	2018	
	(In thousands)		
Revenue:			
Collaboration revenue	\$ 21,219	\$ 27,508	\$ (6,289)
Grant revenue	—	169	(169)
Total revenue	21,219	27,677	(6,458)
Operating expenses:			
Research and development	100,528	73,031	27,497
General and administrative	35,095	11,934	23,161
Total operating expenses	135,623	84,965	50,658
Loss from operations	(114,404)	(57,288)	(57,116)
Other income, net	9,019	5,040	3,979
Net loss	<u>\$ (105,385)</u>	<u>\$ (52,248)</u>	<u>\$ (53,137)</u>

Revenue

Total revenue was \$21.2 million for the year ended December 31, 2019, compared to \$27.7 million for the year ended December 31, 2018. We recognize revenue from the upfront payments under the AbbVie Agreement over time as the services are provided. Revenues are recognized as the program costs are incurred by measuring actual costs incurred to date compared to the overall total expected costs to satisfy the performance obligation. Changes in estimates for revenue recognized over time are recognized on a cumulative basis. Revenue decreased by \$6.5 million, primarily due to an increase in total expected costs for the AL002 and AL003 programs through the completion of proof-of-concept.

Research and Development Expenses

Research and development expenses were \$100.5 million for the year ended December 31, 2019, compared to \$73.0 million for the year ended December 31, 2018. The increase of \$27.5 million was driven by an \$11.8 million increase in personnel related expenses, including stock-based compensation, due to an increase in headcount and issuance of option grants to employees. There was a \$6.3 million increase in facilities and other unallocated research and development related to the lease expense for the new headquarters and higher depreciation expense due to purchase of property and equipment. Expenses for AL101 increased by \$5.0 million as we did not incur any expenses for AL101 until the second quarter of 2018 and this year we began clinical trials in the fourth quarter of 2019. In addition, expenses increased by \$3.7 million for other early stage programs, including AL044, as we continue to invest in developing our pipeline.

	Year Ended December 31,		Dollar Change
	2019	2018	
	(In thousands)		
<i>Direct research and development expenses</i>			
AL001	\$ 17,067	\$ 14,531	\$ 2,536
AL101	8,203	3,159	5,044
AL002	17,359	15,500	1,859
AL003	8,386	12,174	(3,788)
AL044	1,246	—	1,246
Other early stage programs	13,423	10,980	2,443
<i>Indirect research and development expenses</i>			
Personnel related (including stock-based compensation)	24,902	13,066	11,836
Facilities and other unallocated research and development expenses	9,942	3,621	6,321
Total research and development expenses	\$ 100,528	\$ 73,031	\$ 27,497

General and Administrative Expenses

General and administrative expenses were \$35.1 million for the year ended December 31, 2019, compared to \$11.9 million for the year ended December 31, 2018. The increase of \$23.2 million was primarily due to an \$10.1 million increase in personnel-related expenses, including stock-based compensation, as a result of an increase in headcount and issuance of option grants to employees. Facilities and general overhead expenses increased by \$6.6 million due to additional lease expense related to the lease for the new headquarters, impairment loss on the right-of-use asset related to the sublease, higher depreciation expense due to purchase of property and equipment, directors and officers insurance necessary to operate a public company, and other allocated costs from the increased headcount. The increase is also due to a \$4.5 million increase in legal expense due to increased costs of operating as a public company, increased patent costs, and our arbitration proceeding that we commenced in June 2019.

Other Income, Net

Other income, net was \$9.0 million for the year ended December 31, 2019, compared to \$5.0 million for the year ended December 31, 2018. The increase of \$4.0 million was due to interest income earned after we invested the proceeds from the issuance of common stock upon completion of the IPO into marketable securities.

Liquidity and Capital Resources

Since our inception through December 31, 2020, our operations have been financed primarily by net proceeds of \$210.5 million from sales of our convertible preferred stock and through the \$205.0 million in upfront payments from the AbbVie Agreement. In addition, on February 7, 2019, we completed our IPO through issuing and selling 9,739,541 shares of common stock at a public offering price of \$19.00 per share, including 489,541 shares sold pursuant to the underwriters' partial exercise of their option to purchase additional shares, resulting in aggregate net proceeds from the offering of \$168.2 million, after deducting underwriting discounts and commissions and offering costs. On January 30, 2020, we completed a follow-on offering through issuing and selling 9,602,500 shares of common stock at a public offering price of \$25.00 per share, including 1,252,500 shares sold pursuant to the underwriters' full exercise of their option to purchase additional shares, resulting in aggregate net proceeds of \$224.5 million, after deducting underwriting discounts and commissions and estimated offering costs. As of December 31, 2020, we had \$413.3 million of cash, cash equivalents, and marketable securities. As of December 31, 2020, we had an accumulated deficit of \$410.0 million.

Future Funding Requirements

Our primary uses of cash are to fund our operations, which consist primarily of research and development expenditures related to our programs, and to a lesser extent, general and administrative expenditures. We expect our expenses to continue to increase in connection with our ongoing activities, in particular as we continue to advance our product candidates and our discovery programs. In addition, we expect to incur additional costs associated with operating as a public company.

Based on our current operating plan, we believe that our existing cash, cash equivalents, and marketable securities will enable us to fund our operating expenses and capital expenditure requirements through at least mid-2022. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. We may also choose to seek additional financing opportunistically. We expect to need to obtain substantial additional funding in the future for our research and development activities and continuing operations. If we were unable to raise capital when needed or on favorable terms, we would be forced to delay, reduce, or eliminate our research and development programs or future commercialization efforts.

Our future capital requirements will depend on many factors, including:

- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- successful enrollment in and completion of clinical trials;
- our ability to establish agreements with third-party manufacturers for clinical supply for our clinical trials and, if our product candidates are approved, commercial manufacturing;
- our ability to maintain our current research and development programs and establish new research and development programs;
- addition and retention of key research and development personnel;
- our efforts to enhance operational, financial, and information management systems, and hire additional personnel, including personnel to support development of our product candidates;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter and performing our obligations in such collaborations;
- the timing and amount of milestone and other payments we may receive under our collaboration arrangements;
- our eventual commercialization plans for our product candidates;
- the costs involved in prosecuting, defending, and enforcing patent claims and other intellectual property claims, including related to the ongoing arbitration proceeding that we commenced in June 2019; and
- the costs and timing of regulatory approvals.

A change in the outcome of any of these or other variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of that product candidate. Furthermore, our operating plans may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such operating plans.

Cash Flows

The following table summarizes our cash flows for the periods indicated (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Cash provided by (used in) operating activities	\$ (166,734)	\$ (99,308)	\$ 127,464
Cash used in investing activities	(105,051)	(48,874)	(224,119)
Cash provided by financing activities	232,113	172,353	131,146

Operating Activities

For the year ended December 31, 2020, cash used in operating activities was \$166.7 million. This was mainly due to the net loss of \$190.2 million and the decrease in deferred revenue of \$21.1 million as revenue was recognized related to the AbbVie Agreement. This was partially offset by a non-cash charges of \$30.5 million for stock-based compensation and \$5.9 million for depreciation and amortization expense. We also had an increase of \$12.2 million in accrued liabilities and accrued clinical supply costs, which offset the cash used in operating activities.

For the year ended December 31, 2019, cash used in operating activities was \$99.3 million. This was mainly due to the net loss of \$105.4 million and the decrease in deferred revenue of \$21.2 million as revenue was recognized related to the AbbVie Agreement. This was offset by a non-cash charges of \$16.3 million for stock-based compensation and \$3.8 million for depreciation and amortization expense. We also had an increase of \$9.2 million in accrued liabilities and accrued clinical supply costs.

For the year ended December 31, 2018, cash provided by operating activities was \$127.5 million. The net cash inflow from operations primarily resulted from the receipt of \$200.0 million upfront payment from AbbVie in January 2018, that was reflected as a net increase in deferred revenue of \$172.5 million during the period. This was mainly offset by net loss of \$52.2 million. In addition, the company had a non-cash charge of \$6.9 million for stock-based compensation.

Investing Activities

For the year ended December 31, 2020, cash used in investing activities of \$105.1 million was primarily related to the purchase of marketable securities of \$506.8 million offset by the proceeds from maturities of marketable securities of \$406.8 million. In addition, we used cash for the purchase of \$5.0 million of property and equipment.

For the year ended December 31, 2019, cash used in investing activities of \$48.9 million was primarily related to the purchase of marketable securities of \$529.6 million offset by the proceeds from maturities of marketable securities of \$496.0 million. In addition, we used cash for the purchase of \$15.3 million of property and equipment.

For the year ended December 31, 2018, cash used in investing activities of \$224.1 million was primarily related to the purchase of short-term marketable securities of \$472.2 million offset by the proceeds from maturities of marketable securities of \$250.0 million. In addition, we used cash for the purchase of \$1.9 million of property and equipment.

Financing Activities

For the year ended December 31, 2020, cash provided by financing activities of \$232.1 million was primarily from net proceeds of the issuance of 9,602,500 shares of our common stock upon the completion of a follow-on public offering. In addition, we received \$6.3 million cash from the exercise of options to purchase common stock.

For the year ended December 31, 2019, cash provided by financing activities of \$172.4 million was primarily from net proceeds of the issuance of 9,739,541 shares of our common stock upon the completion of our IPO.

For the year ended December 31, 2018, cash provided by financing activities of \$131.1 million was from net proceeds of the issuance of 9,373,633 shares of our Series E convertible preferred stock in April 2018, July, and October 2018, offset by payment of \$1.9 million of deferred offering costs for our IPO.

Critical Accounting Policies and Estimates

Management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States (GAAP). The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenue generated and expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions and any such differences may be material. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Revenue Recognition

We recognize revenue from the upfront payments under the AbbVie Agreement over time as the services are provided. We recognize collaboration revenue by measuring the progress toward complete satisfaction of the performance obligation using an input measure. In order to recognize revenue over the research and development period, the Company measures actual costs incurred to date compared to the overall total expected costs to satisfy the performance obligation. Revenues are recognized as the program costs are incurred. We re-evaluate the estimate of expected costs to satisfy the performance obligation each reporting period and make adjustments for any significant changes. Clinical trials are expensive and can take many years to complete, and the outcome is inherently uncertain. Changes in our forecasted costs are likely to occur over time based upon changes in clinical trial procedures set forth in protocols, changes in estimates of manufacturing costs, or feedback from regulators on the design or operation of our clinical trials. We have had changes to the overall expected costs to satisfy the performance obligations from period to period. For the year ended December 31, 2020, we had a 7% increase in the forecast of the total expected costs. For the year ended December 31, 2020, the increase in the overall expected costs to satisfy the performance obligation resulted in an approximately \$6.7 million reduction in revenue compared to if the expected costs had remained the same, as a result of the cumulative catch up for the change in estimate. The balance of deferred revenue was \$132.3 million as of December 31, 2020. The deferred revenue is expected to be recognized over the research and development period of the programs through the completion of Phase 2 clinical trials.

Accrued Research and Development Expenses

We record accrued expenses for estimated preclinical study and clinical trial expenses. Estimates are based on the services performed pursuant to contracts with research institutions, contract research organizations in connection with clinical studies, investigative sites in connection with clinical studies, vendors in connection with preclinical development activities, and contract manufacturing organizations in connection with the production of materials for clinical trials. Further, we accrue expenses related to clinical trials based on the level of patient enrollment and activity according to the related agreement. We monitor patient enrollment levels and related activity to the extent reasonably possible and make judgments and estimates in determining the accrued balance in each reporting period. If we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. To date, we have not experienced significant changes in our estimates of preclinical studies and clinical trial accruals.

Stock-based Compensation

Stock-based compensation is measured at the date of grant, based on the estimated fair value of the award and recognized as an expense over the employee's requisite service period (usually the vesting period) on a straight-line

basis. We estimate the grant date fair value, and the resulting stock-based compensation, using the Black-Scholes option-pricing model.

The Black-Scholes option-pricing model requires the use of highly subjective assumptions which determine the fair value of stock-based awards. These assumptions include:

Expected Term—The expected term represents the period that stock-based awards are expected to be outstanding. The expected term was derived by using the simplified method which uses the midpoint between the average vesting term and the contractual expiration period of the stock-based award.

Expected Volatility—We have limited information on the volatility of our stock as shares of our common stock were not actively traded on any public markets prior to February 7, 2019. The expected volatility was derived from the historical stock volatilities of comparable peer public companies within our industry. These companies are considered to be comparable to our business over a period equivalent to the expected term of the stock-based awards. In 2020, we began giving weight to our own historical volatility in the determination of expected volatility.

Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the measurement date with maturities approximately equal to the expected term.

Expected Dividend—The expected dividend rate is zero because we have not historically paid and do not expect for the foreseeable future to pay a dividend on our common stock.

Recent Accounting Pronouncements

Effective January 1, 2020, we adopted Accounting Standards Update (ASU) No. 2016-13, *Financial Instruments—Credit Losses (Topic 326)*. This ASU implements an impairment model, known as the current expected credit loss model that is based on expected losses rather than incurred losses. For available-for-sale debt securities, entities are required to recognize an allowance for credit losses rather than an other-than-temporary impairment that reduces the cost basis of the investment. Further, an entity will recognize any changes in estimated credit losses immediately in earnings. There was no material impact to our consolidated financial statements from the adoption of ASU No. 2016-13.

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740) Simplifying the Accounting for Income Taxes*. This ASU modifies ASC 740 to simplify several aspects of accounting for income taxes, including eliminating certain exceptions to the guidance in ASC 740 related to the approach for intraperiod tax allocation, and the methodology for calculating income taxes in an interim period. We early adopted this ASU as of January 1, 2020. There was no material impact to our consolidated financial statements from the adoption of ASU No. 2019-12.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Interest Rate Risk

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. The primary objective of our investment activities is to preserve capital to fund our operations. We also seek to maximize income from our investments without assuming significant risk. To achieve our objectives, we maintain a portfolio of investments in a variety of securities of high credit quality and short-term duration, invested in compliance with our policy.

We had cash, cash equivalents, and marketable securities of \$413.3 million as of December 31, 2020, which consisted primarily of bank deposits, money market funds, and short-term government marketable securities. Such interest-earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been significant for us. Due to the short-term maturities of our cash equivalents and marketable securities, and the low risk profile of our marketable securities, an immediate 100 basis point increase or decrease in interest rates would cause a change in fair value of approximately \$2.3 million.

Foreign Currency Risk

Our expenses are generally denominated in U.S. dollars. However, we have entered into a limited number of contracts with vendors for research and development services with payments denominated in foreign currencies, including the Euro. We are subject to foreign currency transaction gains or losses on our contracts denominated in foreign currencies. To date, foreign currency transaction gains and losses have not been material to our financial statements, and we have not had a formal hedging program with respect to foreign currency. A 10% increase or decrease in current exchange rates would not have a material effect on our financial results.

Item 8. Financial Statements and Supplementary Data.

ALECTOR, INC.
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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Alector, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Alector, Inc. (the Company) as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2020, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2020, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 25, 2021, expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Revenue Recognition

Description of the Matter

The Company recorded collaboration revenue of \$21.1 million for the year ended December 31, 2020. As described in Note 2, collaboration revenue is recognized by measuring the progress toward complete satisfaction of the performance obligations using an input measure. In order to recognize collaboration revenue over the research and development period, the Company measures actual costs incurred to date compared to the overall total expected costs to satisfy the performance obligations. Revenues are recognized as the program costs are incurred.

Auditing collaboration revenue was challenging as it involves assessing highly judgmental estimates with respect to the Company's determination of the total expected costs to satisfy the performance obligations.

How We Addressed the Matter in Our Audit We obtained an understanding, evaluated the design and tested the operating effectiveness of internal controls that address the identified risks related to the Company's process used to determine total expected costs to satisfy the performance obligations, including management's controls over updates to the budget for the relevant research and development programs.

To test collaboration revenue, our audit procedures included, among others, obtaining an understanding of the Company's estimated costs to satisfy the performance obligations, as well as assessing management's updates to the budget for the relevant research and development programs. We also tested a sample of expenses recorded to the development program, evaluated the historical accuracy of management's budget estimates for the relevant research and development programs, and inquired of Company personnel directly involved with supervising the development programs.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2017.

San Jose, California
February 25, 2021

ALECTOR, INC.

Consolidated Balance Sheets
(In thousands, except share and per share data)

	December 31,	
	2020	2019
Assets		
Current assets:		
Cash and cash equivalents	\$ 49,969	\$ 89,641
Marketable securities	363,339	263,432
Prepaid expenses and other current assets	8,203	4,364
Total current assets	421,511	357,437
Property and equipment, net	30,181	33,852
Operating lease right-of-use assets	32,470	28,476
Restricted cash	1,472	1,472
Other assets	2,617	676
Total assets	\$ 488,251	\$ 421,913
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	\$ 3,004	\$ 278
Accrued clinical supply costs	11,148	6,706
Accrued liabilities	22,538	18,256
Deferred revenue, current portion	23,886	30,165
Operating lease liabilities, current portion	7,512	6,565
Total current liabilities	68,088	61,970
Deferred revenue, long-term portion	108,417	123,236
Operating lease liabilities, long-term portion	43,744	41,471
Other long-term liabilities	472	493
Total liabilities	220,721	227,170
Commitments and contingencies (Note 5)		
Stockholders' equity:		
Common stock, \$0.0001 par value; 200,000,000 shares authorized; 79,316,261 and 69,052,873 shares issued and outstanding as of December 31, 2020 and 2019, respectively	8	7
Additional paid-in capital	676,956	414,414
Accumulated other comprehensive income	614	142
Accumulated deficit	(410,048)	(219,820)
Total stockholders' equity	267,530	194,743
Total liabilities and stockholders' equity	\$ 488,251	\$ 421,913

The accompanying notes are an integral part of these consolidated financial statements.

Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share data)

	Year Ended December 31,		
	2020	2019	2018
Revenue:			
Collaboration revenue	\$ 21,098	\$ 21,219	\$ 27,508
Grant revenue	—	—	169
Total revenue	21,098	21,219	27,677
Operating expenses:			
Research and development	156,869	100,528	73,031
General and administrative	59,403	35,095	11,934
Total operating expenses	216,272	135,623	84,965
Loss from operations	(195,174)	(114,404)	(57,288)
Other income, net	4,946	9,019	5,040
Net loss	(190,228)	(105,385)	(52,248)
Unrealized gain (loss) on marketable securities	472	184	(42)
Comprehensive loss	\$ (189,756)	\$ (105,201)	\$ (52,290)
Net loss per share, basic and diluted	\$ (2.45)	\$ (1.71)	\$ (4.62)
Shares used in computing net loss per share, basic and diluted	77,758,806	61,734,492	11,302,788

The accompanying notes are an integral part of these consolidated financial statements.

ALECTOR, INC.

Consolidated Statement of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(In thousands, except member unit and share data)

	Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balance — December 31, 2017	36,001,203	\$ 77,485	13,776,153	\$ 1	\$ 10,153	\$ —	\$ (62,187)	\$ (52,033)
Issuance of Series E convertible preferred stock, net of issuance costs of \$214	9,373,633	133,035	—	—	—	—	—	—
Cancellation of restricted common stock	—	—	(11,324)	—	—	—	—	—
Stock-based compensation	—	—	—	—	6,925	—	—	6,925
Unrealized loss on marketable securities	—	—	—	—	—	(42)	—	(42)
Net loss	—	—	—	—	—	—	(52,248)	(52,248)
Balance — December 31, 2018	45,374,836	210,520	13,764,829	1	17,078	(42)	(114,435)	(97,398)
Conversion of convertible preferred stock into common stock	(45,374,836)	(210,520)	45,374,836	5	210,516	—	—	210,521
Issuance of common stock upon initial public offering, net of issuance costs of \$3,874	—	—	9,739,541	1	168,222	—	—	168,223
Exercise of stock options	—	—	180,287	—	1,519	—	—	1,519
Purchase of common stock under employee stock purchase plan	—	—	50,353	—	798	—	—	798
Forfeiture of restricted common stock	—	—	(56,973)	—	—	—	—	—
Stock-based compensation	—	—	—	—	16,281	—	—	16,281
Unrealized gain on marketable securities	—	—	—	—	—	184	—	184
Net loss	—	—	—	—	—	—	(105,385)	(105,385)
Balance — December 31, 2019	—	—	69,052,873	7	414,414	142	(219,820)	194,743
Issuance of common stock upon follow-on public offering, net of issuance costs of \$1,148	—	—	9,602,500	1	224,510	—	—	224,511
Exercise of stock options	—	—	655,772	—	6,331	—	—	6,331
Purchase of common stock under employee stock purchase plan	—	—	86,870	—	1,179	—	—	1,179
Forfeiture of restricted common stock	—	—	(81,754)	—	—	—	—	—
Stock-based compensation	—	—	—	—	30,522	—	—	30,522
Unrealized gain on marketable securities	—	—	—	—	—	472	—	472
Net loss	—	—	—	—	—	—	(190,228)	(190,228)
Balance — December 31, 2020	—	\$ —	79,316,261	\$ 8	\$ 676,956	\$ 614	\$ (410,048)	\$ 267,530

The accompanying notes are an integral part of these consolidated financial statements.

ALECTOR, INC.

Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,		
	2020	2019	2018
Cash flows from operating activities:			
Net loss	\$ (190,228)	\$ (105,385)	\$ (52,248)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	5,870	3,775	1,019
Stock-based compensation	30,522	16,281	6,925
Amortization of premiums and accretion of discounts on marketable securities	584	(4,701)	(2,745)
Amortization of right-of-use assets	1,395	1,799	—
Impairment loss on right-of-use assets	238	1,158	—
Loss from disposal of property and equipment, net	107	39	151
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(3,839)	(1,596)	(2,245)
Other assets	(2,498)	(42)	106
Accounts payable	2,409	152	(809)
Accrued liabilities and accrued clinical supply costs	12,232	9,210	4,743
Deferred revenue	(21,098)	(21,219)	172,492
Lease liabilities	(2,407)	868	—
Other long-term liabilities	(21)	353	75
Net cash provided by (used in) operating activities	(166,734)	(99,308)	127,464
Cash flows from investing activities:			
Purchase of property and equipment	(5,032)	(15,265)	(1,884)
Purchase of marketable securities	(506,809)	(529,609)	(472,235)
Maturities of marketable securities	406,790	496,000	250,000
Net cash used in investing activities	(105,051)	(48,874)	(224,119)
Cash flows from financing activities:			
Proceeds from issuance of common stock upon initial public offering, net of issuance costs	—	170,128	(1,904)
Proceeds from issuance of common stock upon follow-on public offering, net of issuance cost	224,603	(92)	—
Proceeds from issuance of convertible preferred stock, net of issuance costs	—	—	133,050
Proceeds from the exercise of options to purchase common stock	6,331	1,519	—
Proceeds from issuance of stock from employee stock purchase plan	1,179	798	—
Net cash provided by financing activities	232,113	172,353	131,146
Net increase (decrease) in cash, cash equivalents, and restricted cash	(39,672)	24,171	34,491
Cash, cash equivalents, and restricted cash at beginning of period	91,113	66,942	32,451
Cash, cash equivalents, and restricted cash at end of period	\$ 51,441	\$ 91,113	\$ 66,942
Non-cash investing and financing activities:			
Property and equipment purchases included in accounts payable and accrued liabilities	\$ 428	\$ 3,471	\$ 293
Deferred offering costs in accrued liabilities	\$ —	\$ 465	\$ 792
Tenant improvements paid by landlord	\$ —	\$ 8,286	\$ 7,449

The accompanying notes are an integral part of these consolidated financial statements.

1. **The Company and Liquidity**

Alector, Inc. (Alector or the Company) is a Delaware corporation headquartered in South San Francisco, California. Alector is a clinical stage biopharmaceutical company pioneering immuno-neurology, a novel therapeutic approach for the treatment of neurodegeneration.

Initial Public and Follow-on Offerings

On February 7, 2019, the Company completed an initial public offering (IPO) through issuing and selling 9,739,541 shares of common stock at a public offering price of \$19.00 per share, including 489,541 shares sold pursuant to the underwriters' partial exercise of their option to purchase additional shares, resulting in aggregate net proceeds of \$168.2 million, after deducting underwriting discounts and commissions and offering costs. Upon the closing of the IPO, all of the outstanding shares of convertible preferred stock automatically converted into 45,374,836 shares of common stock. Subsequent to the closing of the IPO, there were no shares of convertible preferred stock outstanding.

On January 30, 2020, the Company completed a follow-on offering through issuing and selling 9,602,500 shares of common stock at a public offering price of \$25.00 per share, including 1,252,500 shares sold pursuant to the underwriters' full exercise of their option to purchase additional shares, resulting in aggregate net proceeds of \$224.5 million, after deducting underwriting discounts and commissions and estimated offering costs.

2. **Summary of Significant Accounting Policies**

Basis of Presentation

The consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States (GAAP) as defined by the Financial Accounting Standards Board (FASB). The consolidated financial statements include the accounts of Alector, Inc. and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenue and expense during the reporting period. The Company evaluates its estimates, including those related to revenue recognition, manufacturing accruals, clinical accruals, fair value of assets and liabilities, income taxes uncertainties, stock-based compensation, and related assumptions on an ongoing basis using historical experience and other factors and adjusts those estimates and assumptions when facts and circumstances dictate. Actual results could materially differ from those estimates.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash, cash equivalents, and short-term marketable securities. Cash and cash equivalents are deposited in checking and sweep accounts at a financial institution. Such deposits may, at times, exceed federally insured limits.

Cash, Cash Equivalents, and Restricted Cash

The Company considers all highly liquid investments with original maturities of three months or less at the date of purchase to be cash and cash equivalents. Cash equivalents, which consist of amounts invested in money market funds, are stated at fair value.

Restricted cash as of December 31, 2020 relates to a letter of credit established for a lease entered into in June 2018.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the consolidated balance sheets that sum to the total of the same amounts shown in the consolidated statements of cash flows:

	Year Ended December 31,		
	2020	2019	2018
	(In thousands)		
Cash and cash equivalents	\$ 49,969	\$ 89,641	\$ 65,470
Restricted cash	1,472	1,472	1,472
Total cash, cash equivalents, and restricted cash	<u>\$ 51,441</u>	<u>\$ 91,113</u>	<u>\$ 66,942</u>

Marketable Securities

All marketable securities have been classified as “available-for-sale” and are carried at fair value, based upon quoted market prices. The Company considers its available-for-sale portfolio as available for use in current operations. Accordingly, the Company may classify certain investments as short-term marketable securities, even though the stated maturity date may be one year or more beyond the current balance sheet date. For available-for-sale debt securities, unrealized gains, net of any related tax effects, are excluded from earnings and are included in other comprehensive income and reported as a separate component of stockholders’ equity (deficit) until realized. The Company assesses available-for-sale debt securities on a quarterly basis to see if any unrealized loss is due to credit-related factors. Factors considered in determining whether an impairment is credit-related include the extent to which the investment’s fair value is less than its cost basis, declines in published credit ratings, changes in interest rates, and any other adverse factors related to the security. If it is determined that a credit-related impairment exists, the Company will measure the credit loss based on a discounted cash flows model. Credit-related impairments on available-for-sale debt securities are recognized as an allowance for credit losses with a corresponding adjustment to other income, net in the Company’s consolidated statement of operations. The unrealized loss position that is not credit-related is recorded, net of any related tax effects, in other comprehensive income until realized. There were no credit-related losses recognized for the periods presented.

The cost of securities sold is based on the specific-identification method. The amortized cost of securities is adjusted for amortization of premiums and accretion of discounts to maturity. In accordance with our investment policy, management invests in money market funds, U.S. treasury securities, corporate bonds, commercial paper, and overnight repurchase agreements collateralized by U.S. treasury securities. The Company has not experienced any losses on its deposits of cash, cash equivalents, and marketable securities.

Fair Value of Financial Instruments

The Company’s believes the carrying value of financial instruments, including cash and cash equivalents, receivables, accounts payable, and accrued liabilities, approximate fair value due to their short-term nature.

The Company utilizes valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible. The Company determines the fair value of its financial instruments based on assumptions that market participants would use in pricing an asset or liability in the principal or most advantageous market. When considering market participant assumptions in fair value measurements, the following fair value hierarchy distinguishes between observable and unobservable inputs, which are categorized in one of the following levels:

Level 1 – Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2 – Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

Level 3 – Unobservable inputs that are significant to the measurement of the fair value of the assets or liabilities that are supported by little or no market data.

Property and Equipment

Property and equipment are stated at cost, net of accumulated depreciation and amortization. Depreciation and amortization is computed using the straight-line method over the estimated useful lives of the respective assets, generally three to five years. Leasehold improvements are amortized over the lesser of their useful lives or the remaining life of the lease. When assets are retired or otherwise disposed of, the cost and related accumulated depreciation and amortization are removed from the consolidated balance sheet and the resulting gain or loss is reflected in the consolidated statements of operations in the period realized. Maintenance and repairs are charged to the consolidated statements of operations as incurred.

Leases

The Company adopted Accounting Standards Update No. 2016-02, *Leases* on January 1, 2019. There was no material effect on the statement of operations upon adoption.

The Company determines whether an arrangement is or contains a lease at the inception of the lease. Leases are recognized on the balance sheet as right-of-use assets and lease liabilities. Lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected lease term. The Company utilizes the appropriate incremental borrowing rate, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. Certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or incentives received and any prepaid or accrued rent. Rent expense for the operating lease is recognized on a straight-line basis over the lease term and is included in operating expenses on the statements of operations and comprehensive loss. Variable lease payments include lease operating expenses.

The Company excludes balance sheet recognition of operating leases having a term of 12 months or less (short-term leases) and does not separate lease components and non-lease components for its long-term leases.

Impairment of Long-Lived Assets

The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparing the carrying amount to the future net undiscounted cash flows which the assets are expected to generate. If the total of the undiscounted future cash flows is less than the carrying amount of the assets, an impairment loss is recognized for the amount by which the carrying amount of the assets exceeds its fair value. For the year ended December 31, 2020, the Company recognized a \$0.2 million impairment loss on its right-of-use asset related to decision to no longer utilize certain property through the end of the lease term. For the year ended December 31, 2019, the Company recognized a \$1.2 million impairment loss on its right of use assets related to the portion of its headquarters being subleased.

Revenue Recognition

The Company recognizes revenue when control of promised goods or services are transferred to customers in an amount that reflects the consideration that is expected to be received for those goods or services. In determining the appropriate amount of revenue to be recognized as the Company fulfills its obligations under arrangements, the Company performs the following steps: (i) identify the contract(s) with a customer, (ii) identify the performance obligations in the contract, (iii) determine the transaction price, (iv) allocate the transaction price to the performance obligations in the contract, and (v) recognize revenue when (or as) the entity satisfies the performance obligation.

Collaboration Revenue

The Company signed an agreement in October 2017 with AbbVie Biotechnology, Ltd. (AbbVie) to co-develop antibodies to two program targets in preclinical development (AbbVie Agreement). Under the terms of the AbbVie Agreement, AbbVie made \$205.0 million in upfront payments, of which \$5.0 million and \$200.0 million was received by the Company in October 2017 and January 2018, respectively. The Company will perform research and development services for the antibodies to the two programs through the end of Phase 2 clinical trials which the Company expects to conduct through 2023. AbbVie will then have the exclusive right to exercise an option to enter into a license and collaboration agreement with the Company for

one or both of the programs for \$250.0 million each. If AbbVie exercises its option for the programs, AbbVie will take over the development of the product candidates for such program and costs will be split between the parties. The Company will also share in profits and losses upon commercialization of any products from such program. However, following AbbVie's exercise of its option for a program, the Company may opt out of sharing in development costs and profits or losses for that program and instead receive tiered royalties. Additionally, under the terms of the AbbVie Agreement, the Company will be eligible to earn up to an additional \$242.8 million in milestone payments per program related to the initiation of certain clinical studies and regulatory approval for up to three indications per program. The Company assessed its collaboration agreement with AbbVie in the context of the delivery of the research and development services.

The Company has determined that there are two research and development performance obligations as part of the agreement with AbbVie, one research and development performance obligation for each of the two research and development programs. The non-refundable upfront cash payments of \$5.0 million and \$200.0 million received in October 2017 and January 2018, respectively, were included in the transaction price. None of the remaining development and regulatory milestone and program opt-in payment amounts have been included in the transaction price, as all these amounts were fully constrained as of December 31, 2020 and 2019. As part of the Company's evaluation of the constraint, the Company considered numerous factors, including that receipt of the milestone amounts is outside the control of the Company and contingent upon success in future clinical trials. Any consideration related to royalties on net product sales will be recognized when the related sales occur and therefore have also been excluded from the transaction price. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

The Company recognizes collaboration revenue by measuring the progress toward complete satisfaction of the performance obligation using an input measure. In order to recognize revenue over the research and development period, the Company measures actual costs incurred to date compared to the overall total expected costs to satisfy the performance obligation. Revenues are recognized as the program costs are incurred. The Company will re-evaluate the estimate of expected costs to satisfy the performance obligation each reporting period and make adjustments for any significant changes. Clinical trials are expensive and can take many years to complete, and the outcome is inherently uncertain. Changes in the Company's forecasted costs are likely to occur over time based upon changes in clinical trial procedures set forth in protocols, changes in estimates of manufacturing costs, or feedback from regulators on the design or operation of clinical trials. The Company has had changes to the overall expected costs to satisfy the performance obligations from period to period. For the year ended December 31, 2020, the Company had a 7% increase in the forecast of total expected costs due to changes to the clinical trial plans. For the year ended December 31, 2020, the increase in the overall expected costs to satisfy the performance obligation resulted in an approximately \$6.7 million reduction in revenue compared to if the expected costs had remained the same, as a result of the cumulative catch up for the change in estimate. Collaboration revenue under the Company's collaboration agreement with AbbVie during 2020, 2019, and 2018 was \$21.1 million, \$21.2 million, and \$27.5 million, respectively. Collaboration revenue recognized during the year ended December 31, 2020, was included in deferred revenue at the beginning of the period. The balance of deferred revenue was \$132.3 million as of December 31, 2020. The deferred revenue is expected to be recognized over the research and development period of the programs through the completion of Phase 2 clinical trials.

The Company entered into an agreement in March 2020 with Innovent Biologics (Innovent) to license, develop, and commercialize AL008 in China (Innovent Agreement). AL008 is the Company's novel antibody targeting the CD47-SIRP-alpha pathway, a potent survival pathway co-opted by tumors to evade the innate immune system. Under the terms of the Innovent Agreement, Innovent may pay the Company up to \$11.5 million in development milestones, \$112.5 million in sales milestones, and future royalties for any sales. The Company retains the rights to develop and commercialize AL008 outside of China. The Company has determined there is one performance obligation for the delivery of the license and will recognize revenue when it is probable that there will not be significant reversal of cumulative revenue. Development and sales milestones under the Innovent Agreement have not been included in the transaction price, as all these amounts were fully constrained as of December 31, 2020. As of December 31, 2020, no revenue has been recognized or payments received under the Innovent Agreement.

Research and Development Costs

Research and development costs are expensed as incurred and consist primarily of new product development. Research and development costs include salaries and benefits, consultants' fees, process development costs, stock-based compensation, and laboratory supplies, as well as fees paid to third parties that conduct certain research and development activities on the Company's behalf. In addition, research and development costs include the reimbursable costs incurred for the grant agreements, which includes payroll costs for time incurred on projects, laboratory supplies, and third-party research and development activities.

A substantial portion of the Company's ongoing research and development activities are conducted by third-party service providers. The Company records accrued expenses for estimated preclinical study and clinical trial expenses. Estimates are based on the services performed pursuant to contracts with research institutions, contract research organizations in connection with clinical studies, investigative sites in connection with clinical studies, vendors in connection with preclinical development activities, and contract manufacturing organizations in connection with the production of materials for clinical trials. Further, the Company accrues expenses related to clinical trials based on the level of patient enrollment and activity according to the related agreement. The Company monitors patient enrollment levels and related activity to the extent reasonably possible and make judgments and estimates in determining the accrued balance in each reporting period. If the Company underestimates or overestimates the level of services performed or the costs of these services, actual expenses could differ from estimates. To date, the Company has not experienced significant changes in its estimates of preclinical studies and clinical trial accruals.

Stock-based Compensation

Stock-based compensation for employee awards is measured on the grant date based on the fair value of the award and recognized on a straight-line basis over the requisite service period. The fair value of options to purchase common stock are measured using the Black-Scholes option-pricing model. The Company accounts for forfeitures as they occur.

Comprehensive Loss

Comprehensive loss includes net loss and certain changes in stockholders' equity that are the result of transactions and economic events other than those with stockholders. The Company's only element of other comprehensive loss was net unrealized gain (loss) on marketable securities.

Income Taxes

The Company accounts for income taxes under the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial statement and tax bases of assets and liabilities and are measured using enacted tax rates and laws that will be in effect when the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income in the period that includes the enactment date.

The deferred tax assets are recognized to the extent the Company believes that these assets are more likely than not to be realized. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized. Due to the Company's historical operating performance and the recorded cumulative net losses in prior periods, the net deferred tax assets have been fully offset by a valuation allowance.

The Company records uncertain tax positions using a two-step process. First, the Company determines whether it is more likely than not that the tax positions will be sustained on the basis of the technical merits of the position. Second, for those tax positions that meet the more-likely-than-not recognition threshold, the Company recognizes the largest amount of tax benefit that is more than 50% likely to be realized upon ultimate settlement with the related tax authority.

The Company recognizes interest and penalties related to unrecognized tax benefits on the interest expense line and other expense line, respectively, in the accompanying statements of operations. To date, there have been no interest or penalties charged in relation to the unrecognized tax benefits.

Employee 401(k) Plan

The Company has a qualified contributory savings plan under Section 401(k) of the Internal Revenue Code (the “Code”) covering substantially all U.S. employees of Alector. The 401(k) plan is designed to provide tax-deferred retirement benefits in accordance with the provisions of Section 401(k) of the Code. Eligible employees may defer up to 100% of their eligible compensation up to the annual maximum as determined by the Internal Revenue Service. The Company’s contributions to the plan are discretionary. For the year ended December 31, 2020, the Company made matching contributions of \$0.7 million. The Company did not make any matching contributions for the years ended December 31, 2019 or 2018.

Segments

The Company operates in one segment. The Company’s chief operating decision maker, its Chief Executive Officer, manages the Company’s operations on a consolidated basis for purposes of allocating resources.

Recent Accounting Pronouncements

Effective January 1, 2020, the Company adopted Accounting Standards Update (ASU) No. 2016-13, *Financial Instruments—Credit Losses (Topic 326)*. This ASU implements an impairment model, known as the current expected credit loss model that is based on expected losses rather than incurred losses. For available-for-sale debt securities, entities are required to recognize an allowance for credit losses rather than an other-than-temporary impairment that reduces the cost basis of the investment. Further, an entity will recognize any changes in estimated credit losses immediately in earnings. There was no material impact to the Company’s consolidated financial statements from the adoption of ASU No. 2016-13.

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740) Simplifying the Accounting for Income Taxes*. This ASU modifies ASC 740 to simplify several aspects of accounting for income taxes, including eliminating certain exceptions to the guidance in ASC 740 related to the approach for intraperiod tax allocation, and the methodology for calculating income taxes in an interim period. The Company has early adopted this ASU as of January 1, 2020. There was no material impact to the Company’s consolidated financial statements. There was no material impact to the Company’s consolidated financial statements from the adoption of ASU No. 2019-12.

3. Fair Value Measurements

The following tables summarize the Company’s financial assets measured at fair value on a recurring basis by level within the fair value hierarchy:

	Fair Value Hierarchy	December 31, 2020				Fair Market Value
		Amortized Cost	Unrealized Gains	Unrealized Losses		
(In thousands)						
Money market funds	Level 1	\$ 37,951	\$ —	\$ —	\$ 37,951	
U.S. government treasury securities	Level 1	357,725	620	(6)	358,339	
Corporate bonds	Level 2	5,000	—	—	5,000	
Total cash equivalents and marketable securities		<u>\$ 400,676</u>	<u>\$ 620</u>	<u>\$ (6)</u>	<u>\$ 401,290</u>	

	Fair Value Hierarchy	December 31, 2019				Fair Market Value
		Amortized Cost	Unrealized Gains	Unrealized Losses		
(In thousands)						
Money market funds	Level 1	\$ 61,104	\$ —	\$ —	\$ 61,104	
U.S. government treasury securities	Level 1	227,446	149	(8)	227,587	
Commercial paper	Level 2	43,735	—	—	43,735	
Corporate bonds	Level 2	10,103	3	(2)	10,104	
Total cash equivalents and marketable securities		<u>\$ 342,388</u>	<u>\$ 152</u>	<u>\$ (10)</u>	<u>\$ 342,530</u>	

The Company's Level 2 securities are valued using third-party pricing sources. The pricing services utilize industry standard valuation models for which all significant inputs are observable. There were no transfers between levels of the fair value hierarchy during the year ended December 31, 2020. The Company classifies marketable securities available to fund current operations as current assets. As of December 31, 2020, the remaining contractual maturities of \$336.9 million investments were less than one year and \$64.4 million investments were after one year through two years. The Company does not intend to sell the investments that are in an unrealized loss position before recovery of their amortized cost basis, which may be maturity.

4. Balance Sheet Components

Property and Equipment, Net

Property and equipment, net consists of the following:

	December 31,	
	2020	2019
(In thousands)		
Leasehold improvements	\$ 25,542	\$ 25,222
Lab equipment	11,610	10,458
Furniture and fixtures	2,222	2,031
Computer equipment	1,764	1,554
Property and equipment, gross	41,138	39,265
Less accumulated depreciation and amortization	(10,957)	(5,413)
Total property and equipment, net	<u>\$ 30,181</u>	<u>\$ 33,852</u>

Accrued Liabilities

Accrued liabilities consist of the following:

	December 31,	
	2020	2019
(In thousands)		
Accrued research and development costs	\$ 13,375	\$ 6,400
Accrued employee compensation	7,288	5,730
Accrued professional services	1,094	2,040
Accrued property and equipment	428	3,471
Other	353	615
Total accrued liabilities	<u>\$ 22,538</u>	<u>\$ 18,256</u>

5. Commitments and Contingencies

On June 18, 2019, the Company initiated a confidential arbitration proceeding against Dr. Asa Abeliovich, the Company's former consulting co-founder, related to alleged breaches of his consulting agreement and the improper use of Alector's confidential information that he learned during the course of rendering services to the Company as consulting Chief Scientific Officer/Chief Innovation Officer. An independent arbitrator issued

a confidential decision in favor of Alector, finding Dr. Abeliovich liable for breach of his confidentiality agreement and for spoliation based on his destruction of documents relevant to the proceeding. The arbitrator awarded damages for breach of the agreement and sanctions for the spoliation, as well as violation of orders during the proceeding, and the amount of such monetary damages will be determined in a pending further proceeding.

6. Leases

In June 2018, the Company signed a lease agreement to lease approximately 105,000 square feet in office and laboratory space in South San Francisco which serves as the Company's headquarters (the "Headquarters"). The lease expires in 2029 with an option to renew for a period of ten years. The landlord paid for \$15.7 million of tenant improvements. In connection with the lease, the Company entered into a letter of credit arrangement in the amount of \$1.5 million as collateral for the lease, which is classified as restricted cash on the consolidated balance sheets. In October 2020, the Company signed a lease agreement to lease approximately 18,700 square feet of office and laboratory space in Newark, California. The lease term ends on February 6, 2028 with an option to extend for an additional five years. The landlord is obligated to pay for up to \$0.4 million of tenant improvements. The measurement of the lease liabilities for the leases excludes the options to extend the term of the lease as such extensions are not reasonably certain to occur. Variable lease costs for all of the Company's leases consist of operating expenses for the spaces.

In May 2019, the Company entered into an agreement to sublease approximately 25,000 square feet of the Headquarters (the "Sublease"), which was amended to approximately 23,600 square feet in December 2020. The Sublease expires in November 2021. The sublessor has the option to extend the Sublease for one additional year subject to the consent of the Company. The sublessee is required to pay its proportionate share of operating expenses for the space.

In June 2019, in connection with the Sublease, the Company evaluated the related right-of-use asset for impairment. The lease costs plus amortization expense of the leasehold improvements in the subleased space exceeded the sublease income over the remaining sublease term. As such, the Company recorded an impairment charge of \$1.2 million in general and administrative expenses to write-down the right-of-use asset such that no loss is expected to be recognized over the sublease period.

The components of lease expense were as follows:

	December 31,	
	2020	2019
	(In thousands)	
Operating lease cost	\$ 5,589	\$ 5,875
Variable lease cost	2,255	1,328
Short-term lease cost	—	68
Sublease income and reimbursement of variable lease cost	(2,288)	(1,263)
Total	\$ 5,556	\$ 6,008

Rent expense under legacy guidance for the year ended December 31, 2018 was \$1.1 million.

As of December 31, 2020, the weighted-average remaining lease term for operating leases was 8.2 years and the weighted-average discount rate was 8.5%. Cash paid for amounts included in the measurement of lease liabilities for the year ended December 31, 2020 and 2019 was \$6.9 million and \$3.2 million, respectively, was included in net cash used in operating activities in our consolidated statements of cash flows.

The following are the lease payments owed under the Company's operating leases as of December 31, 2020:

	<u>(In thousands)</u>
2021	\$ 7,872
2022	8,171
2023	8,436
2024	8,732
2025	9,037
Thereafter	30,130
Total undiscounted lease payments	\$ 72,378
Less: Present value adjustment	(21,122)
Total lease liability	<u>\$ 51,256</u>

7. Stock-based Compensation

The Company recognized stock-based compensation as follows:

	<u>Year Ended December 31,</u>		
	<u>2020</u>	<u>2019</u>	<u>2018</u>
	<u>(In thousands)</u>		
Research and development	\$ 14,980	\$ 8,031	\$ 4,195
General and administrative	15,542	8,250	2,730
Total stock-based compensation	<u>\$ 30,522</u>	<u>\$ 16,281</u>	<u>\$ 6,925</u>

Determination of Fair Value

The estimated grant-date fair value of all the Company's options to purchase common stock was calculated using the Black-Scholes option pricing model, based on the following assumptions:

	<u>Year Ended December 31,</u>		
	<u>2020</u>	<u>2019</u>	<u>2018</u>
Expected term (in years)	5.3-6.1	5.3 – 6.1	5.1 – 6.1
Expected volatility	74%-78%	76% – 82%	73% – 81%
Risk-free interest rate	0.3% - 1.8%	1.4% – 2.6%	2.5% – 3.1%
Dividend yield	0%	0%	0%

The fair value of each stock option was determined by the Company using the methods and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment and estimation by management.

Expected Term—The expected term represents the period that stock-based awards are expected to be outstanding. The expected term was derived by using the simplified method which uses the midpoint between the average vesting term and the contractual expiration period of the stock-based award.

Expected Volatility—The Company has limited information on the volatility of stock options as the shares were not actively traded on any public markets prior to February 7, 2019. The expected volatility was derived from the historical stock volatilities of comparable peer public companies within its industry. These companies are considered to be comparable to the Company's business over a period

equivalent to the expected term of the stock-based awards. In 2020, the Company began giving weight to its own historical volatility in the determination of expected volatility.

Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the date of grant for zero-coupon U.S. Treasury notes with maturities approximately equal to the expected term.

Expected Dividend Rate—The expected dividend is zero as the Company has not paid nor does it anticipate paying any dividends on its common stock underlying its stock options in the foreseeable future.

Restricted Common Stock

The restricted common stock generally vests over a four-year period with straight-line vesting with a 25% one-year cliff.

Activity for the restricted common stock is shown below:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Unvested restricted common stock as of December 31, 2018	1,917,848	\$ 6.95
Vested	(866,037)	6.95
Forfeited	(56,973)	6.95
Unvested restricted common stock as of December 31, 2019	994,838	6.95
Vested	(726,659)	6.95
Forfeited	(81,754)	6.95
Unvested restricted common stock as of December 31, 2020	<u>186,425</u>	6.95

As of December 31, 2020, total unrecognized stock-based compensation related to unvested restricted common stock issued to employees was \$0.9 million, which the Company expects to recognize over a remaining weighted-average period of 0.8 years.

2019 Equity Incentive Plan

On February 6, 2019, the Company adopted the 2019 Equity Incentive Plan (2019 Plan) under which the Board may issue incentive stock options, nonstatutory stock options, restricted stock, restricted stock units, stock appreciation rights, performance units, and performance shares to the Company's employees, directors, and consultants. The Company's 2017 Stock Option and Grant Plan (2017 Plan) was terminated; however, shares subject to awards granted under it will continue to be governed by the 2017 Plan. Shares reserved for issuance but not issued pursuant to, or not subject to, awards granted under the 2017 Plan were added to the available shares in the 2019 Plan. Shares subject to awards granted under the 2017 Plan that are repurchased by, or forfeited to, the Company will also be reserved for issuance under the 2019 Plan. The board of directors, or a committee appointed by the board of directors, has the authority to determine to whom options or shares will be granted, the number of shares, the term, and the exercise price. If an individual owns stock representing 10% or more of the outstanding shares, the exercise price of each share shall be at least 110% of the fair market value and the term of the award shall not exceed five years. All other options granted under the 2019 Plan must have an exercise price at least equal to the fair market value on the date of grant and have a term not to exceed ten years. The shares generally vest over a four-year period with straight-line vesting with a 25% one-year cliff. As of December 31, 2020, the Company had reserved 15,628,217 shares of common stock for issuance under the 2019 Plan, of which 2,973,219 shares were available for issuance.

Activity for the options to purchase common stock shown below:

	Number of Options	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value (In thousands)
Outstanding as of December 31, 2018	5,063,688	\$ 8.94		
Granted	3,738,071	17.74		
Exercised	(180,287)	8.43		
Forfeited	(178,648)	11.52		
Outstanding as of December 31, 2019	8,442,824	12.79		
Granted	5,597,148	15.35		
Exercised	(655,772)	9.65		
Forfeited	(729,202)	14.96		
Outstanding as of December 31, 2020	<u>12,654,998</u>	\$ 13.96	8.7	\$ 39,633
Exercisable as of December 31, 2020	<u>3,588,568</u>	\$ 12.74	8.1	\$ 13,393
Vested and expected to vest as of December 31, 2020	<u>12,654,998</u>	\$ 13.96	8.7	\$ 39,633

The aggregate intrinsic value is calculated as the difference between the exercise price of the underlying stock options and the fair value of the Company's common stock for stock options that were in-the-money. The aggregate intrinsic value of options exercised was \$11.1 million and \$1.8 million for the years ended December 31, 2020 and 2019. There were no options exercised in 2018. The weighted-average grant-date fair value per share of options granted was \$10.14, \$12.06, and \$6.27, for the years ended December 31, 2020, 2019, and 2018, respectively. As of December 31, 2020, total unrecognized stock-based compensation related to unvested stock options was \$82.9 million, which the Company expects to recognize over a remaining weighted-average period of 2.6 years.

2019 Employee Stock Purchase Plan

On February 6, 2019, the Company adopted the 2019 Employee Stock Option Plan (2019 ESPP). The 2019 ESPP will enable eligible employees of the Company to purchase shares of common stock at a discount. Each offering period will be approximately six months long beginning on the first trading day on or after December 1 and June 1 each year. ESPP participants purchase shares of common stock at a price per share equal to 85% of the lesser of (1) the fair market value per share of the common stock on the first trading day of the offering period or (2) the fair market value of the common stock on the purchase date. As of December 31, 2020, there was \$0.4 million in unrecognized compensation expense related to the 2019 ESPP to be recognized over five months.

8. Income Taxes

The Company incurred net operating losses for the years ended December 31, 2020, 2019, and 2018. The Company has not reflected a benefit of such net operating loss carryforwards in the accompanying financial statements. The Company has established a full valuation allowance against its net deferred tax assets due to the uncertainty surrounding realization of such assets.

A reconciliation of the federal statutory rate to the Company's effective tax rate is as follows for the years ended December 31, 2020, 2019, and 2018 (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Tax benefit at federal statutory rate	\$ (39,948)	\$ (22,081)	\$ (10,972)
State income taxes	(16,570)	(4,694)	—
Tax credits	(8,010)	(6,530)	(2,387)
Uncertain tax positions	2,003	2,044	708
Stock-based compensation	353	1,493	1,251
Nondeductible expense	51	124	58
Tax benefit recognized on utilization of attributes previous reserved	—	(13,582)	—
Deferred adjustment from amended tax return	—	(1,073)	—
Change in valuation allowance	62,280	44,748	11,346
Others	(159)	(449)	(4)
Income tax provision	<u>\$ —</u>	<u>\$ —</u>	<u>\$ —</u>

The tax effects of temporary differences that give rise to significant components of the Company's deferred tax assets consist of (in thousands):

	December 31,	
	2020	2019
Deferred tax assets:		
Net operating loss	\$ 54,382	\$ 2,223
Accrued bonus	1,201	370
Tax credits	13,000	7,319
Stock-based compensation	6,493	2,015
Deferred revenue	32,129	37,621
Lease liability	12,457	11,781
Others	463	209
Gross deferred tax assets	120,125	61,538
Less valuation allowance	(105,226)	(47,053)
Total deferred tax assets	<u>\$ 14,899</u>	<u>\$ 14,485</u>
Deferred tax liabilities:		
Depreciation and amortization	\$ (6,815)	\$ (7,495)
Right-of-use assets	(7,934)	(6,990)
Others	(150)	—
Gross deferred tax liabilities	(14,899)	(14,485)
Deferred tax assets, net	<u>\$ —</u>	<u>\$ —</u>

In assessing the realization of deferred tax assets, management considers whether it is more likely than not that some portion or all of the deferred assets will be realized. The ultimate realization of the deferred tax assets is dependent upon the generation of future taxable income during the periods in which those temporary differences become deductible. Evaluating the need for a valuation allowance for deferred tax assets often requires judgment and analysis of all the positive and negative evidence available, including cumulative losses in recent years and projected future taxable income, to determine whether all or some portion of the deferred tax assets will not be realized. As of December 31, 2020, the Company has utilized a full valuation allowance to offset the net deferred tax assets as the Company believes it is not more likely than not that the net deferred tax assets will be fully realizable. The valuation allowance for deferred tax assets increased by \$58.2 million during the year ended December 31, 2020.

As of December 31, 2020, the Company had federal and state net operating loss (NOL) carryforwards of approximately \$195.3 million and \$191.4 million, respectively. Federal NOL carryforwards have an indefinite life and deductions cannot exceed 80% of taxable income. State NOL carryforwards will begin to expire as early as 2030, if not utilized, or have an indefinite life. As of December 31, 2020, the Company also had

federal and California tax credit carryforward of approximately \$14.4 million and \$3.8 million, respectively. The federal tax credits will begin to expire in 2036 while the California tax credits have no expiration date.

Generally, utilization of the NOL carryforwards and credits may be subject to an annual limitation due to the ownership change limitations provided by Section 382, which provides for limitations on NOL carryforwards and certain built-in losses following ownership changes, and Section 383, which provides for special limitations on certain excess credits, etc., of the Code, and similar state provisions. Accordingly, the Company's ability to utilize NOL carryforwards may be limited as the result of such an "ownership change." The carryforwards could be subject to an annual limitation, resulting in a reduction in the gross deferred tax assets before considering the valuation allowance. Further, a portion of the carryforwards may expire before being applied to reduce future earnings. The Company is not aware of any changes in ownership that would result in material limitations under Section 382 at this time.

The following table summarizes the activity related to the Company's unrecognized tax benefits for the years ended December 31, 2020 and 2019 (in thousands):

Balance as of December 31, 2018	\$ 1,507
Decreases related to tax positions taken during the prior year	(80)
Increases related to tax positions taken during the current year	1,608
Balance as of December 31, 2019	3,035
Decreases related to tax positions taken during the prior year	(446)
Increases related to tax positions taken during the current year	2,003
Balance as of December 31, 2020	<u>\$ 4,592</u>

If the unrecognized tax benefits for uncertain tax positions as of December 31, 2020, is recognized, there will be no impact to the effective tax rate as the tax benefit would increase the net deferred tax assets, which is currently offset with a full valuation allowance. The Company's policy is to include interest and penalties related to unrecognized tax benefits, if any, within the provision for taxes in the consolidated statements of operations. The Company did not accrue any interest or penalties and does not have any tax positions for interest or penalties for the year ended December 31, 2020. The Company does not have any tax positions for which it is reasonably possible that the total amount of gross unrecognized tax benefits will significantly change within 12 months of December 31, 2020.

The Company recognizes the tax benefit of an uncertain tax position only if it is more likely than not that the position is sustainable upon examination by the taxing authority, based on the technical merits. During the year ended December 31, 2020, the Company recorded a tax reserve of \$2.0 million as a reduction of the tax credit carryover. The Company's income tax returns generally remain subject to examination by federal and most state tax authorities. The Company is currently not subject to any income tax audits by federal or state taxing authorities. The statute of limitations for tax liabilities for all years remains open.

9. Related Party Transactions

The Company has a collaboration agreement with Adimab, LLC (Adimab) under which the Company is developing antibodies discovered by Adimab in its AL001 and AL101 product candidates, and the Company is developing antibodies optimized by Adimab in its AL002 and AL003 product candidates (2014 Adimab Agreement). In August 2019, the Company signed a new collaboration agreement with Adimab for research and development of additional antibodies (2019 Adimab Agreement). The Chief Executive Officer of Adimab is a Co-founder and Chairperson of the board of directors of Alector. For the years ended December 31, 2020, 2019, and 2018, Alector incurred expenses of zero, \$2.8 million, and \$2.3 million for services provided by Adimab, respectively. The Company had no accrued liabilities due to Adimab as of December 31, 2020 and 2019. Under the 2014 Adimab Agreement, the Company will owe up to \$3.5 million in milestone payments per program to Adimab for its product candidates. The Company will also owe low- to mid- single-digit royalty payments for commercial sales of such product candidates. Under the 2019 Adimab Agreement, the

Company will owe certain milestone payments per program for its product candidates and low single-digit royalty payments for commercial sales of such product candidates.

On January 30, 2020, in connection with the Company's follow-on offering, a member of the Company's board of directors purchased 20,000 shares of the Company's common stock at the public offering price of \$25.00 per share.

10. Net Loss Per Share

The following outstanding potentially dilutive shares have been excluded from the calculation of diluted net loss per share for the periods presented due to their anti-dilutive effect:

	Year Ended December 31,		
	2020	2019	2018
Convertible preferred stock	—	—	45,374,836
Restricted stock subject to future vesting	186,425	994,838	1,917,848
Options to purchase common stock	12,654,998	8,442,824	5,063,688
Shares committed under ESPP	86,677	44,464	—
Total	<u>12,928,100</u>	<u>9,482,126</u>	<u>52,356,372</u>

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.**Conclusions Regarding the Effectiveness of Disclosure Controls and Procedures**

As of December 31, 2020, management, with the participation of our Principal Executive Officer and Principal Financial and Accounting Officer, performed an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including the Principal Executive Officer and the Principal Financial and Accounting Officer, to allow timely decisions regarding required disclosures. Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our Principal Executive Officer and Principal Financial and Accounting Officer concluded that, as of December 31, 2020, the design and operation of our disclosure controls and procedures were effective at a reasonable assurance level.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting during the quarter ended December 31, 2020, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of consolidated financial statements for external purposes in accordance with generally accepted accounting principles. Under the supervision of and with the participation of our principal executive officer and principal financial officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2020 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in "Internal Control—Integrated Framework" (2013). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2020.

The effectiveness of our internal control over financial reporting as of December 31, 2020 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report which is included herein.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Alector, Inc.

Opinion on Internal Control Over Financial Reporting

We have audited Alector, Inc.'s internal control over financial reporting as of December 31, 2020, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Alector, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2020, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2020 and 2019, the

related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2020, and the related notes and our report dated February 25, 2021 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's 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 generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

San Jose, California
February 25, 2021

Item 9B. Other Information.

None

Item 10. Directors, Executive Officers and Corporate Governance.

Information required by this item will be contained in our definitive proxy statement to be filed with the SEC on Schedule 14A in connection with the Proxy Statement to be filed within 120 days after December 31, 2020, and is incorporated herein by reference.

Item 11. Executive Compensation.

Information required by this item will be contained in the Proxy Statement to be filed within 120 days of December 31, 2020, and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

Information required by this item will be contained in the Proxy Statement to be filed within 120 days of December 31, 2020, and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

Information required by this item will be contained in the Proxy Statement to be filed within 120 days of December 31, 2020, and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

Information required by this item will be contained in the Proxy Statement to be filed within 120 days of December 31, 2020, and is incorporated herein by reference.

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as part of this report:

(1) Financial Statements

The consolidated financial statements of Alector, Inc. are filed as part of this report on Form 10-K under Item 8. Financial Statements and Supplementary Data.

(2) Financial Statement Schedules

All other schedules have been omitted because they are not required, not inapplicable, or the required information is included in the consolidated financial statements or notes thereto.

(3) Exhibits

The documents listed in the Exhibit Index are incorporated by reference or are filed with this report, in each case as indicated herein (numbered in accordance with Item 601 of Regulation S-K).

Item 16. Form 10-K Summary

None.

Exhibit Index

Number	Exhibit Title	Incorporated by Reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
3.1	Amended and Restated Certificate of Incorporation of the Registrant.	8-K	001-38792	3.1	2/11/2019	
3.2	Amended and Restated Bylaws of the Registrant.	8-K	001-38792	3.1	10/6/2020	
4.1	Amended and Restated Registration Rights Agreement among the Registrant and certain of its stockholders, dated April 26, 2018.	S-1	333-229152	4.1	1/7/2019	
4.2	Specimen common stock certificate of the Registrant.	S-1	333-229152	4.2	1/7/2019	
4.3	Description of securities of the Registrant.					X
10.1+	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.	S-1	333-229152	10.1	1/7/2019	
10.2+	2017 Stock Option and Grant Plan, as amended, and forms of agreement thereunder.	S-1	333-229152	10.2	1/7/2019	
10.3+	2019 Equity Incentive Plan and forms of agreements thereunder.	S-1	333-229152	10.3	1/7/2019	
10.4+	2019 Employee Stock Purchase Plan	S-1	333-229152	10.4	1/7/2019	
10.5+	Confirmatory Offer Letter between the Registrant and Arnon Rosenthal, Ph.D.	S-1/A	333-229152	10.5	1/29/2019	
10.6+	Confirmatory Offer Letter between the Registrant and Robert Paul, M.D., Ph.D.	S-1/A	333-229152	10.6	1/29/2019	
10.7+	Confirmatory Offer Letter between the Registrant and Robert King, Ph.D.	S-1/A	333-229152	10.7	1/29/2019	
10.8+	Confirmatory Offer Letter between the Registrant and Sabah Oney, Ph.D.	S-1/A	333-229152	10.8	1/29/2019	
10.9+	Confirmatory Offer Letter between the Registrant and Calvin Yu.	S-1/A	333-229152	10.9	1/29/2019	
10.10+	Executive Incentive Compensation Plan.	S-1	333-229152	10.10	1/7/2019	
10.11+	Outside Director Compensation Policy.	10-K	001-38792	10.11	3/24/2020	
10.12+	Form of Change in Control and Severance Agreement between the Registrant and certain of its executive officers.	S-1	333-229152	10.12	1/7/2019	
10.13	Lease between the Registrant and HCP Oyster Point III, LLC, dated June 27, 2018.	S-1	333-229152	10.14	1/7/2019	
10.14#	Third Amended and Restated Collaboration Agreement between the Registrant and Adimab, dated September 19, 2016, as amended.	S-1	333-229152	10.15	1/7/2019	
10.15#	Co-Development and Option Agreement between the Registrant and AbbVie Biotechnology, Ltd., dated October 16, 2017.	S-1	333-229152	10.16	1/7/2019	
10.16#	2019 Collaboration Agreement between the Registrant and Adimab, LLC, dated August 16, 2019.	10-Q	001-38792	10.17	11/12/2019	
10.17+	Offer Letter between the Registrant and Shehnaaz Suliman, M.D.	8-K	001-38792	99.1	12/11/2019	

21.1	List of subsidiaries of Registrant.					X
23.1	Consent of Independent Registered Public Accounting Firm.					X
24.1	Power of Attorney (included on the signature page to this Annual Report on Form 10-K).					X

31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
32.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
32.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
101.INS	XBRL Instance Document					X
101.SCH	XBRL Taxonomy Extension Schema Document					X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	Taxonomy Extension Definition Linkbase Document					X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document					X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document					X

+ Indicated management contract or compensatory plan.

Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment and this exhibit has been filed separately with the SEC.

* The certifications attached as Exhibits 32.1 and 32.2 that accompany this Annual Report on Form 10-K are not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of the Registrant under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

ALECTOR, INC.

Date: February 25, 2021

By: /s/ Arnon Rosenthal

Arnon Rosenthal, Ph.D.

Co-founder and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Arnon Rosenthal, Ph.D., Shehnaaz Suliman, M.D., and Calvin Yu as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and substitution, for him or her and in his or her name, place, and stead, in any and all capacities (including his capacity as a director and/or officer of Alector, Inc.) to sign any or all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and all other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as they, he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agents or any of them, or their, his, or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Arnon Rosenthal</u> Arnon Rosenthal, Ph.D.	Co-founder, Chief Executive Officer, and Director <i>(Principal Executive Officer)</i>	February 25, 2021
<u>/s/ Calvin Yu</u> Calvin Yu	Vice President, Finance <i>(Principal Financial and Accounting Officer)</i>	February 25, 2021
<u>/s/ Tillman Gerngross</u> Tillman Gerngross, Ph.D.	Chairperson of the Board	February 25, 2021
<u>/s/ Paula Hammond</u> Paula Hammond, Ph.D.	Director	February 25, 2021
<u>/s/ Louis J. Lavigne, Jr.</u> Louis J. Lavigne, Jr.	Director	February 25, 2021
<u>/s/ Terry McGuire</u> Terry McGuire	Director	February 25, 2021
<u>/s/ Richard Scheller</u> Richard Scheller, Ph.D.	Director	February 25, 2021
<u>/s/ David Wehner</u> David Wehner	Director	February 25, 2021

Signature

Title

Date

/s/ Kristine Yaffe

Director

February 25, 2021

Kristine Yaffe, M.D.

DESCRIPTION OF CAPITAL STOCK

The following description summarizes certain important terms of the capital stock of Alector, Inc. (the “company,” “we,” “us” and “our”), as well as certain provisions of our amended and restated certificate of incorporation and amended and restated bylaws. This summary does not purport to be complete and is qualified in its entirety by the provisions of our amended and restated certificate of incorporation and amended and restated bylaws, copies of which have been filed as exhibits to this Annual Report on Form 10-K, as well as by the applicable provisions of the Delaware General Corporation Law.

Authorized Capital Stock

Our authorized capital stock consists of 200,000,000 shares of common stock, par value \$0.0001 per share, and 20,000,000 shares of convertible preferred stock, par value \$0.0001 per share. All of our outstanding shares of common stock are fully paid and non-assessable.

Common Stock

Our common stock is listed on the Nasdaq Global Select Market (“Nasdaq”) under the symbol “ALEC.” The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent and registrar’s address is 6201 15th Avenue, Brooklyn, New York 11219.

Voting Rights

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our certificate of incorporation and bylaws do not provide for cumulative voting rights. Because of this, the holders of a plurality of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they should so choose. With respect to matters other than the election of directors, at any meeting of the stockholders at which a quorum is present or represented, the affirmative vote of a majority of the voting power of the shares present in person or represented by proxy at such meeting and entitled to vote on the subject matter shall be the act of the stockholders, except as otherwise required by law. The holders of a majority of the stock issued and outstanding and entitled to vote, present in person, or represented by proxy, shall constitute a quorum for the transaction of business at all meetings of the stockholders.

Dividends

Subject to preferences that may be applicable to any then-outstanding convertible preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

Liquidation

In the event of our liquidation, dissolution, or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then-outstanding shares of convertible preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion, subscription, or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences, and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our convertible preferred stock that we may designate in the future.

Preferred Stock

Our board of directors has the authority, without further action by the stockholders, to issue up to 20,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges, and restrictions thereof. These rights, preferences, and privileges could include dividend rights, conversion rights, voting rights, redemption rights, liquidation preferences, sinking fund terms, and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of common stock. The issuance of preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring, or preventing change in our control or other corporate action.

Registration Rights of Certain Stockholders

Under our registration rights agreement, as amended, certain holders of shares of common stock or their transferees have the right to require us to register the offer and sale of their shares, or to include their shares in any registration statement we file, in each case as described below.

Demand Registration Rights

Certain holders of shares of our common stock are entitled to certain demand registration rights. The holders of at least 25% of the shares (or a lesser percent for which the anticipated aggregate offering price would be at least \$15 million) having registration rights then outstanding can request that we file a registration statement to register the offer and sale of their shares. We are only obligated to effect up to two such registrations. Each such request for registration must cover securities the anticipated aggregate public offering price of which, before deducting underwriting discounts and commissions, is at least \$15 million. These demand registration rights are subject to specified conditions and limitations, including the right of the underwriters to limit the number of shares included in any such registration under certain circumstances. If we determine that it would be seriously detrimental to us and our stockholders to effect such a demand registration, we have the right to defer such registration, not more than once in any twelve month period, for a period of up to 60 days.

Form S-3 Registration Rights

Certain holders of shares of our common stock are entitled to certain Form S-3 registration rights. At any time when we are eligible to file a registration statement on Form S-3, the holders of the shares having these rights then outstanding can request that we register the offer and sale of their shares of our common stock on a registration statement on Form S-3 so long as the request covers securities the anticipated aggregate public offering price of which is at least \$3 million. These stockholders may make an unlimited number of requests for registration on a registration statement on Form S-3. However, we will not be required to effect a registration

on Form S-3 if we have effected two such registrations within the twelve month period preceding the date of the request. Additionally, if we determine that it would be seriously detrimental to us and our stockholders to effect such a demand registration, we have the right to defer such registration, not more than once in any twelve month period, for a period of up to 60 days.

Piggyback Registration Rights

Certain holders of shares of our common stock are entitled to certain “piggyback” registration rights. If we propose to register the offer and sale of shares of our common stock under the Securities Act, all holders of these shares then outstanding can request that we include their shares in such registration, subject to certain marketing and other limitations, including the right of the underwriters to limit the number of shares included in any such registration statement under certain circumstances. As a result, whenever we propose to file a registration statement under the Securities Act, other than with respect to (1) a registration related to any employee benefit plan or a corporate reorganization or other transaction covered by Rule 145 promulgated under the Securities Act, (2) a registration in which the only stock being registered is common stock issuable upon conversion of debt securities also being registered, or (3) a registration on any form that does not include substantially the same information as would be required to be included in a registration statement covering the sale of our common stock, the holders of these shares are entitled to notice of the registration and have the right, subject to certain limitations, to include their shares in the registration.

Expenses of Registration

We will pay all expenses relating to any demand registrations, Form S-3 registrations, and piggyback registrations, subject to specified exceptions.

Termination

The registration rights terminate upon the earliest of (1) the date that is five years after the closing of our initial public offering and (2) a deemed liquidation event (as defined in our amended and restated certificate of incorporation, in effect prior to the completion of our initial public offering).

Anti-Takeover Effects of Certain Provisions of Delaware Law, Our Amended and Restated Certificate of Incorporation and Our Amended and Restated Bylaws

Certain provisions of Delaware law and certain provisions that are included in our amended and restated certificate of incorporation and amended and restated bylaws summarized below may be deemed to have an anti-takeover effect and may delay, deter, or prevent a tender offer or takeover attempt that a stockholder might consider to be in its best interests, including attempts that might result in a premium being paid over the market price for the shares held by stockholders.

Preferred Stock

Our amended and restated certificate of incorporation contains provisions that permit our board of directors to issue, without any further vote or action by the stockholders, shares of preferred stock in one or more series and, with respect to each such series, to fix the number of shares constituting the series and the designation of the series, the voting rights (if any) of the shares of the series and the powers, preferences, or relative, participation, optional, and other special rights, if any, and any qualifications, limitations, or restrictions, of the shares of such series.

Classified Board of Directors

Our amended and restated certificate of incorporation provides that our board of directors is divided into three classes, designated Class I, Class II, and Class III. Each class is an equal number of directors, as nearly as possible, consisting of one-third of the total number of directors constituting the entire board of directors. The term of initial Class I directors shall terminate on the date of the 2022 annual meeting, the term of the initial Class II directors shall terminate on the date of the 2020 annual meeting, and the term of the initial Class III directors shall terminate on the date of the 2021 annual meeting. At each annual meeting of stockholders, successors to the class of directors whose term expires at that annual meeting will be elected for a three-year term.

Removal of Directors

Our amended and restated certificate of incorporation provides that stockholders may only remove a director for cause by a vote of no less than a majority of the shares present in person or by proxy at the meeting and entitled to vote.

Director Vacancies

Our amended and restated certificate of incorporation authorizes only our board of directors to fill vacant directorships.

No Cumulative Voting

Our amended and restated certificate of incorporation provides that stockholders do not have the right to cumulate votes in the election of directors.

Special Meetings of Stockholders

Our amended and restated certificate of incorporation and amended and restated bylaws provides that, except as otherwise required by law, special meetings of the stockholders may be called only by the Chairperson of our board of directors, the Chief Executive Officer, the President, or our board of directors acting pursuant to a resolution adopted by a majority of the board of directors.

Advance Notice Procedures for Director Nominations

Our bylaws provide that stockholders seeking to nominate candidates for election as directors at an annual or special meeting of stockholders must provide timely notice thereof in writing. To be timely, a stockholder's notice generally will have to be delivered to and received at our principal executive offices before notice of the meeting is issued by the secretary of the company, with such notice being served not less than 90 nor more than 120 days before the meeting. Although the amended and restated bylaws do not give the board of directors the power to approve or disapprove stockholder nominations of candidates to be elected at an annual meeting, the amended and restated bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the company.

Action by Written Consent

Our amended and restated certificate of incorporation and amended and restated bylaws provide that any action to be taken by the stockholders must be effected at a duly called annual or special meeting of stockholders and may not be effected by written consent.

Amending our Certificate of Incorporation and Bylaws

Our amended and restated certificate of incorporation may be amended or altered in any manner provided by the Delaware General Corporation Law (“DGCL”). Our amended and restated bylaws may be adopted, amended, altered, or repealed by stockholders only upon approval of at least majority of the voting power of all the then outstanding shares of the common stock, except for any amendment of certain provisions set forth in the bylaws, which would require the approval of a two-thirds majority of our then outstanding common stock. Additionally, our amended and restated certificate of incorporation provides that our bylaws may be amended, altered, or repealed by the board of directors.

Authorized but Unissued Shares

Our authorized but unissued shares of common stock and preferred stock are available for future issuances without stockholder approval, except as required by the listing standards of Nasdaq, and could be utilized for a variety of corporate purposes, including future offerings to raise additional capital, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could render more difficult or discourage an attempt to obtain control of the company by means of a proxy contest, tender offer, merger, or otherwise.

Exclusive Jurisdiction

Our amended and restated bylaws provide that, unless we consent to the selection of an alternative forum, the Court of Chancery of the State of Delaware, or if the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware, is the exclusive forum for (i) any derivative action or proceeding brought on behalf of us, (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer, or other employee to the us or our stockholders, (iii) any action arising pursuant to any provision of the DGCL or our certificate of incorporation or bylaws (as either may be amended from time to time), or (iv) any action asserting a claim governed by the internal affairs doctrine, except, in each case, (A) any claim as to which such court determines that there is an indispensable party not subject to the jurisdiction of such court (and the indispensable party does not consent to the personal jurisdiction of such court within 10 days following such determination), (B) which is vested in the exclusive jurisdiction of a court or forum other than such court, or (C) for which such court does not have subject matter jurisdiction. Although our amended and restated bylaws contain the exclusive of forum provisions described above, it is possible that a court could find that such provision is inapplicable for a particular claim or action or that such provision is unenforceable, and our stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

Business Combinations with Interested Stockholders

We are governed by Section 203 of the DGCL. Subject to certain exceptions, Section 203 of the DGCL prohibits a public Delaware corporation from engaging in a business combination (as defined in such section) with an “interested stockholder” (defined generally as any person who beneficially owns 15% or more of the outstanding voting stock of such corporation or any person affiliated with such person) for a period of three

years following the time that such stockholder became an interested stockholder, unless (i) prior to such time the board of directors of such corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder; (ii) upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of such corporation at the time the transaction commenced (excluding for purposes of determining the voting stock of such corporation outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (A) by persons who are directors and also officers of such corporation and (B) by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer); or (iii) at or subsequent to such time the business combination is approved by the board of directors of such corporation and authorized at a meeting of stockholders (and not by written consent) by the affirmative vote of at least 66 2/3% of the outstanding voting stock of such corporation not owned by the interested stockholder.

Our amended and restated certificate of incorporation and our amended and restated bylaws provide that we must indemnify our directors and officers to the fullest extent authorized by the DGCL. We are expressly authorized to, and do, carry directors' and officers' insurance providing coverage for our directors, officers and certain employees for some liabilities. We believe that these indemnification provisions and insurance are useful to attract and retain qualified directors and executive directors.

The limitation on liability and indemnification provisions in our certificate of incorporation and bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duty. These provisions may also have the effect of reducing the likelihood of derivative litigation against directors and officers, even though such an action, if successful, might otherwise benefit us and our stockholders. In addition, your investment may be adversely affected to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions.

SUBSIDIARIES OF REGISTRANT

Alector LLC

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

- (1) Registration Statement (Form S-3 No. 333-238230) of Alector, Inc., and
- (2) Registration Statement (Form S-8 No. 333-237369) pertaining to the 2019 Equity Incentive Plan and 2019 Employee Stock Purchase Plan of Alector, Inc.,

of our reports dated February 25, 2021, with respect to the consolidated financial statements of Alector, Inc. and the effectiveness of internal control over financial reporting of Alector, Inc. included in this Annual Report (Form 10-K) of Alector, Inc. for the year ended December 31, 2020.

/s/ Ernst & Young LLP

San Jose, California
February 25, 2021

A member firm of Ernst & Young Global Limited

A member firm of Ernst & Young Global Limited

**CERTIFICATION PURSUANT TO SECTION 302
OF THE SARBANES-OXLEY ACT OF 2002**

I, Arnon Rosenthal, certify that:

1. I have reviewed this Annual Report on Form 10-K of Alector, Inc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize, and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 25, 2021

/s/ Arnon Rosenthal

Arnon Rosenthal, Ph.D.
Chief Executive Officer
(Principal Executive Officer)

**CERTIFICATION PURSUANT TO SECTION 302
OF THE SARBANES-OXLEY ACT OF 2002**

I, Calvin Yu, certify that:

1. I have reviewed this Annual Report on Form 10-K of Alector, Inc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize, and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 25, 2021

/s/ Calvin Yu

Calvin Yu
Vice President, Finance
(Principal Financial and Accounting Officer)

**CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of Alector, Inc. (the "Company") for the period ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned officer of the Company certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: February 25, 2021

/s/ Arnon Rosenthal

Arnon Rosenthal, Ph.D.
Chief Executive Officer
(Principal Executive Officer)

**CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of Alector, Inc. (the "Company") for the period ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned officer of the Company certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: February 25, 2021

/s/ Calvin Yu

Calvin Yu

Vice President, Finance

(Principal Financial and Accounting Officer)