

**UNITED STATES
 SECURITIES AND EXCHANGE COMMISSION**
 Washington, D.C. 20549

**FORM S-1
 REGISTRATION STATEMENT**

*Under
 The Securities Act of 1933*

ALECTOR, INC.

(Exact name of Registrant as specified in its charter)

Delaware
 (State or other jurisdiction of
 incorporation or organization)

2836
 (Primary Standard Industrial
 Classification Code Number)

82-2933343
 (I.R.S. Employer
 Identification Number)

131 Oyster Point Blvd. Suite 600
 South San Francisco, California 94080
 415-231-5660

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Arnon Rosenthal, Ph.D.
 Chief Executive Officer
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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box.

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

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 7(a)(2)(B) of the Securities Act.

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered(1)	Proposed Maximum Offering Price Per Share(2)	Proposed Maximum Aggregate Offering Price(1)(2)	Amount of Registration Fee
Common stock, \$0.0001 par value per share		\$	\$	\$

(1) Includes offering price of any additional shares of our common stock that the underwriters have the option to purchase.

(2) Estimated solely for the purpose of computing the amount of the registration fee. In accordance with Rule 457(c) under the Securities Act of 1933, as amended, the maximum price per share and maximum aggregate offering price are based on the average of the \$ (high) and \$ (low) sale price of the registrant's common stock as reported on The Nasdaq Global Select Market on , 2019, which date is within five business days prior to filing this Registration Statement.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED
, 2019

Shares



COMMON STOCK

This is a public offering of shares of common stock by Alector, Inc.

Our common stock is listed on the NASDAQ Global Select Market under the symbol "ALEC." On , 2019, the last reported sale price of our common stock on the NASDAQ Global Select Market was \$ per share.

We are an "emerging growth company" as defined under the federal securities laws and, as such, have elected to comply with certain reduced reporting requirements for this prospectus and may elect to do so in future filings.

Investing in our common stock involves risks. See the section titled "[Risk Factors](#)" beginning on page 11 to read about factors you should consider before buying shares of our common stock.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities, or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public offering price	\$	\$
Underwriting discounts and commissions ⁽¹⁾	\$	\$
Proceeds, before expenses, to us	\$	\$

(1) See the section titled "Underwriting" for a description of the compensation payable to the underwriters.

We have granted the underwriters an option to purchase up to additional shares of our common stock at the public offering price less underwriting discounts and commissions. The underwriters can exercise this option at any time within 30 days after the date of this prospectus.

The underwriters expect to deliver the shares of common stock to purchasers on or about , 2019.

Morgan Stanley

Goldman Sachs & Co. LLC

Prospectus dated , 2019.

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We incorporate by reference important information into this prospectus. You may obtain the information incorporated by reference without charge by following the instructions under the section of this prospectus entitled “Where You Can Find More Information.” You should carefully read this prospectus as well as additional information described under the section of this prospectus entitled “Incorporation of Certain Information by Reference,” before deciding to invest in our common stock.

We and the underwriters have not authorized anyone to provide you any information other than that contained or incorporated by reference in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. The information contained or incorporated by reference in this prospectus is accurate only as of the date of this prospectus or the date of the applicable document incorporated by reference, regardless of the time of the delivery of this prospectus or any sale of shares of our common stock. Our business, financial condition, results of operations, and prospects may have changed since that date.

For investors outside of the United States: we have not and the underwriters have not done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside of the United States.

PROSPECTUS SUMMARY

This summary highlights information contained in greater detail elsewhere in this prospectus and in the documents incorporated by reference. This summary is not complete and does not contain all of the information you should consider in making your investment decision.

You should carefully consider, among other things, our consolidated financial statements and related notes incorporated by reference into this prospectus from our Annual Report on Form 10-K for the year ended December 31, 2018, or our 2018 Annual Report, our Quarterly Report on Form 10-Q for the three and nine months ended September 30, 2019, or our 2019 Quarterly Report, and the sections titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included in our 2018 Annual Report and 2019 Quarterly Report and incorporated by reference into this prospectus. In this prospectus, unless context requires otherwise, references to “we,” “us,” “our,” “Alector,” or “the Company” refer to Alector, Inc.

ALECTOR, INC.

Overview

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

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, in the last six years, we have identified over forty immune system targets, progressed over ten programs into preclinical research, and advanced three product candidates, AL001, AL002, and AL003, into clinical development.

AL001, our first program in the clinic, modulates progranulin (PGRN), a regulator of immune activity in the brain with genetic links to multiple neurodegenerative disorders, including frontotemporal dementia (FTD), Alzheimer’s disease, and Parkinson’s disease. AL001 is initially designed to treat FTD, a severe, rapidly progressing neurodegenerative disorder that affects approximately 170,000 individuals in the United States and the European Union alone, with potentially higher prevalence in Asia and Latin America.

Our AL001 program is aimed at treating a genetic subset of patients with FTD who have a known genetic mutation that causes a deficiency in PGRN, which is called FTD-GRN. AL001 has successfully achieved proof-of-mechanism in the Phase 1b portion of the study in FTD-GRN subjects by restoring PGRN levels in plasma and cerebrospinal fluid back to the normal range. In the third quarter of 2019, we advanced AL001 into a Phase 2 study with proof-of-concept data in FTD-GRN patients expected in the first half of 2020, which also includes an additional genetic subset of FTD patients (FTD-C9orf72). In addition, in consultation with the U.S. Food and Drug Administration (FDA), we plan to advance AL001 into a Phase 3 study in FTD-GRN patients in 2020.

We are developing AL101, our second product candidate in our PGRN program, for patients 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. AL101 received orphan drug designation from the FDA for treatment of FTD in July 2019 and we expect to initiate a Phase 1 study of AL101 in the fourth quarter of 2019. We expect proof-of-mechanism data in 2020.

We own worldwide rights to both AL001 and AL101.

Our next development programs, AL002 and AL003, focus on modulating check-point receptors on the brain's immune cells, with AL002 targeting Triggering Receptor Expressed on Myeloid cells 2 (TREM2) and AL003 targeting sialic acid binding Ig-like lectin 3 (SIGLEC 3), respectively. The AL002 and AL003 programs are aimed at treating Alzheimer's disease patients.

In the third quarter of 2019, we completed the Phase 1a portion of the study in healthy subjects with AL002 and a dose dependent change in the target engagement biomarker in cerebrospinal fluid was observed upon treatment. In the second quarter of 2019, based on safety and tolerability observed in the Phase 1a study, we initiated the Phase 1b portion of the study with AL002 in Alzheimer's disease patients. We expect proof-of-mechanism data from Alzheimer's disease patients in the first half of 2020.

In the first quarter of 2019, we initiated a Phase 1a study in healthy subjects with AL003, a product candidate targeting Alzheimer's disease. Thirty-eight (38) healthy subjects were dosed over eight dose cohorts in the AL003 Phase 1a dose escalation trial. A dose dependent change in target engagement in the blood was observed upon treatment. One subject treated with the second highest dose experienced aseptic hip monoarthritis and a second subject treated with the highest dose experienced an adverse drug reaction characterized by rash, fever, and thrombocytopenia, which were both deemed treatment-related serious adverse events. The subjects were treated with corticosteroids and recovered. Based on the safety and tolerability observed in the Phase 1a study, we identified a dose and initiated screening for the Phase 1b portion of the study with AL003 in Alzheimer's disease patients in the fourth quarter of 2019.

We have partnered with AbbVie Biotechnology, Ltd. (AbbVie), a leader in neuroscience drug development, for the global development and potential commercialization of AL002 and AL003. We are responsible for execution of the Phase 1 and Phase 2 studies. Following AbbVie's potential 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. As part of this partnership, we received \$205.0 million in upfront payments, of which \$5.0 million and \$200.0 million was received by us in October 2017 and January 2018, respectively, \$20.0 million from the sale of shares of our preferred stock in October 2017 and are eligible for up to an additional \$985.6 million in option exercise and milestone payments and a global profit share with AbbVie upon commercialization.

Our Discovery Platform leverages large scale human genetic datasets, advanced tools in bioinformatics and imaging, and insights into neurodegeneration and immunology to identify immune system targets that play a critical role in the development of multiple neurodegenerative diseases. Our Discovery Platform focuses on:

- **Target Selection.** We identify mutations in genes that control the brain's immune system, which we believe are the root cause of neurodegeneration, employ a suite of genetic tools to elucidate the immune dysfunction caused by these mutations, and then engineer immune modulating antibodies to counteract the harmful consequences of these genetic mutations.
- **Biomarker Selection.** We are able to identify and employ molecular biomarkers, assays, and precise imaging techniques to confirm target engagement and measure the effect of our product candidates, allowing us to potentially obtain clinical data earlier than would otherwise be expected using traditional clinical measures.
- **Patient Selection.** We utilize genetic screening and other biomarkers to better align a patient's specific diagnosis with the targeted intervention in our clinical studies.

Our immuno-neurology approach and our Discovery Platform are designed to broadly address multiple neurodegenerative disorders. The breadth of our opportunity is reinforced by our ability to engineer therapeutics

capable of modulating a broad array of immune targets, validated by human genetics, across multiple mechanisms of action, including product candidates that activate, block, inhibit, or down-regulate a given target as therapeutically needed.

The following table highlights our preclinical and clinical programs.

Program	Research	Preclinical	Phase 1	Phase 2	Phase 3	Commercial Rights	Upcoming Milestones
PROGRAFANULIN AL001 ✓ Biomarker	Frontotemporal Dementia - GRN					ALECTOR	PoC: 1H 2020
	Frontotemporal Dementia - C9orf72						
AL101 ✓ Biomarker	Neurology					ALECTOR	FIH: 2H 2019 PoM: 2020
TRIM 2 AL002 ✓ Biomarker	Alzheimer's Disease					ALECTOR abbvie	PoM HVs ✓ PoM AD: 2020
SGLT-3 AL003 ✓ Biomarker	Alzheimer's Disease					ALECTOR abbvie	PoM: 2020

PoM = Proof-of-Mechanism PoC = Proof-of-Concept FIH = First-in-Human

The following table highlights ten of our identified programs in our research and development pipeline.

Program	Research	Preclinical	Phase 1	Phase 2	Phase 3	Commercial Rights
Immunoneurology 7 Candidates Biomarkers in development	ADP012					ALECTOR
	ADP014					
	ADP016					
	ADP017					
	ADP023					
	ADP026					
	ADP122					
Immunocology 3 Candidates Biomarkers in development	ADP008					ALECTOR
	ADP009					
	ADP022					

The above table reflects that we currently have ten research programs identified in our research and development pipeline focused on targeting Alzheimer’s disease, Parkinson’s disease, amyotrophic lateral sclerosis (ALS), progressive multiple sclerosis and oncology. Currently, we estimate that these programs are one to three years or more away from entering preclinical studies assuming that these programs meet our requirements for advancement into the preclinical stage. For each of our programs in our research and development pipeline we are working to identify biomarkers to be utilized in preclinical studies for each program.

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. For example, 22 of the top 25 risk genes identified by evaluating large-scale data on tens of thousands of Alzheimer’s disease patients regulate immune function in the

brain. 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 Team

Our team is led by seasoned executives with a proven track record of drug discovery and development in neuroscience, as well as substantial operational and business expertise. Our Co-Founder and Chief Executive Officer, Arnon Rosenthal, Ph.D., has spent over 35 years developing therapeutics in neuroscience and led teams responsible for the development of the non-addictive pain drug tanezumab and the migraine drug AJOVY, and multiple other programs in clinical development. He also held several leadership roles over a 16-year career at Genentech, where he led the team that discovered the target for the cancer drug Erivedge. Our Chief Medical Officer, Robert Paul, M.D., Ph.D., served as the Therapeutic Area Lead for Neuroscience at Genentech, where among other projects, he oversaw the clinical development of several product candidates, including the amyloid-beta antibody crenezumab in Alzheimer's disease, GDC-0134 in ALS, and GDC-0276 and GDC-0310 in pain. Our Chief Development Officer, Robert King, Ph.D., previously served as the Senior Vice President of development and supply chain at SciClone Pharmaceuticals. Our Chief Business Officer, Sabah Oney, Ph.D., previously served as the Head of Global Sales and Business Development at Ariosa Diagnostics until and through its acquisition by Roche.

Our Strategy

Our goal is to develop therapies that empower the immune system to cure neurodegeneration. 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;
- applying our proprietary development capabilities to rapidly advance our product candidates through clinical proof-of-concept studies and beyond;
- maximizing the therapeutic potential of our existing targets and product candidates; and
- continuing to focus on discovering new targets and product candidates, validated by human genetics, to prosecute the full power of our insights and platform.

Risks Associated with Our Business

Our business is subject to numerous risks and uncertainties that you should consider before investing in our company. These risks are described more fully in the section titled “Risk Factors” in this prospectus. These risks include, but are not limited to, the following:

- We are in the early stages of clinical drug development and have a limited operating history and no products approved for commercial sale.
- 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.
- Our share price has been and may continue to be highly volatile, and you could lose all or part of your investment.
- 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.
- Due to the significant resources required for the development of our products, and depending on our ability to access capital, we must prioritize development of certain product candidates.
- Research and development of biopharmaceutical products is inherently risky. Our business is heavily dependent on the successful development 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.
- 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.
- 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 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 the commercialization of our product candidates.

Initial Public Offering (IPO) Transaction

In February 2019, we issued and sold 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. We received aggregate net proceeds from the offering, net of underwriting discounts and commissions and offering expenses, of \$168.2 million.

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 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 into this prospectus and should not be considered to be part of this prospectus.

We use Alector, the Alector logo, and other marks as trademarks in the United States and other countries. This prospectus 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 prospectus, 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.

Implications of Being an Emerging Growth Company

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended (JOBS Act). We will remain an emerging growth company until the earliest to occur of: the last day of the fiscal year in which we have more than \$1.07 billion in annual revenue; the date we qualify as a "large accelerated filer," with at least \$700 million of equity securities held by non-affiliates; the issuance, in any three-year period, by us of more than \$1.0 billion in non-convertible debt securities; and December 31, 2024, which is the last day of the fiscal year ending after the fifth anniversary of our initial public offering. As a result of this status, we have taken advantage of reduced reporting requirements in this prospectus and may elect to take advantage of other reduced reporting requirements in our future filings with the Securities and Exchange Commission. In particular, in this prospectus, we have not included or incorporated by reference all of the executive compensation related information that would be required if we were not an emerging growth company. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards, delaying the adoption of these accounting standards until they would apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and we have adopted and will continue to adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies that are not emerging growth companies.

THE OFFERING

Common stock offered by us	shares
Common stock to be outstanding immediately after this offering	shares (or additional shares in full) shares if the underwriters exercise their option to purchase
Underwriters' option to purchase additional shares of common stock from us	shares
Use of proceeds	<p>We estimate that the net proceeds to us from the sale of the shares of our common stock in this offering will be approximately \$ million, or approximately \$ million if the underwriters exercise their option to purchase additional shares in full, based upon an offering price of \$ per share, which is the last reported sale price of our common stock on the NASDAQ Global Select Market on , 2019 and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.</p> <p>We intend to use the net proceeds from this offering, together with our existing resources, as follows: (1) to fund Phase 2 and Phase 3 clinical trials for AL001 in FTD-GRN and expand into FTD-C9orf72 and other potential indications; (2) to fund Phase 1 and Phase 2 clinical trials for AL002 and AL003; (3) to advance AL101 in and through Phase 1 clinical trials; (4) to continue to advance our preclinical development pipeline into Phase 1 clinical trials; (5) to further develop our Discovery Platform; and (6) to fund working capital and other general corporate activities. See the section titled "Use of Proceeds" for more information.</p>
Risk factors	See the section of this prospectus titled "Risk Factors" beginning on page 11 and other information included or incorporated by reference in this prospectus for a discussion of factors you should carefully consider before deciding to invest in shares of our common stock.
NASDAQ trading symbol	"ALEC"

The number of shares of our common stock to be outstanding after this offering is based on the 68,922,249 shares of our common stock outstanding as of September 30, 2019, and excludes the following:

- 4,822,524 shares of common stock issuable upon exercise of options to purchase shares of our common stock outstanding as of September 30, 2019 under our 2017 Stock Option and Grant Plan (2017 Plan), at a weighted-average exercise price of \$8.97 per share;
- 1,095,600 shares of common stock issuable upon exercise of options to purchase shares of our common stock outstanding as of September 30, 2019 under our 2019 Equity Incentive Plan (2019 Plan), at a weighted-average exercise price of \$19.15 per share;

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- 2,604,971 shares of common stock issuable upon exercise of options to purchase shares of our common stock that we granted after September 30, 2019 under our 2019 Plan, at a weighted-average exercise price of \$17.12 per share;
- 6,911,739 shares of common stock reserved for future issuance under our 2019 Plan as of September 30, 2019, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan; and
- 1,478,492 shares of common stock reserved for issuance under our 2019 Employee Stock Purchase Plan as of September 30, 2019, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan.

Unless otherwise indicated, this prospectus reflects and assumes the following:

- no exercise of outstanding options after September 30, 2019; and
- no exercise by the underwriters of their option to purchase additional shares of common stock from us in this offering.

SUMMARY CONSOLIDATED FINANCIAL DATA

The following tables summarize our consolidated financial data for the periods and as of the dates indicated. We derived the consolidated statement of operations data for the years ended December 31, 2018, 2017, and 2016 from our audited consolidated financial statements included in our 2018 Annual Report, which is incorporated by reference in this prospectus. We derived the consolidated statement of operations data for the nine months ended September 30, 2019 and 2018, and the consolidated balance sheet data as of September 30, 2019, from our unaudited interim condensed consolidated financial statements included in our 2019 Quarterly Report, which is incorporated by reference in this prospectus. The unaudited interim condensed consolidated financial statements have been prepared on the same basis as our annual audited consolidated financial statements and, in the opinion of management, reflect all adjustments, which include only normal, recurring adjustments that are necessary to present fairly the unaudited interim condensed consolidated financial statements. Our historical results are not necessarily indicative of the results that may be expected in the future, and our interim results are not necessarily indicative of the results to be expected for the full year or any other period. You should read the following summary consolidated financial data in conjunction with our consolidated financial statements and the related notes and the information in the sections titled “Selected Consolidated Financial Data” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included in our 2018 Annual Report and 2019 Quarterly Report and incorporated by reference into this prospectus.

	Year Ended December 31,			Nine Months Ended September 30,	
	2018	2017	2016	2019	2018
	(In thousands, except share and per share data)				
	(Unaudited)				
Consolidated Statement of Operations Data:					
Revenue:					
Collaboration revenue	\$ 27,508	\$ 2,872	\$ —	\$ 15,218	\$ 18,363
Grant revenue	169	863	416	—	169
Total revenue	27,677	3,735	416	15,218	18,532
Operating expenses:					
Research and development	73,031	29,911	13,674	74,766	48,934
General and administrative	11,934	6,503	1,874	22,514	7,869
Total operating expenses	84,965	36,414	15,548	97,280	56,803
Loss from operations	(57,288)	(32,679)	(15,132)	(82,062)	(38,271)
Other income, net	5,040	199	22	7,204	3,396
Net loss	\$ (52,248)	\$ (32,480)	\$ (15,110)	\$ (74,858)	\$ (34,875)
Net loss per share, basic and diluted	\$ (4.62)	\$ (3.55)	\$ (2.11)	\$ (1.25)	\$ (3.13)
Shares used in computing net loss per share, basic and diluted	11,302,788	9,142,688	7,173,411	59,663,773	11,154,391

	As of September 30, 2019	
	Actual	As Adjusted(1)
	(In thousands) (Unaudited)	
Consolidated Balance Sheet Data:		
Cash, cash equivalents, and marketable securities	\$	381,446
Working capital		326,765
Total assets		449,730
Deferred revenue		159,402
Total liabilities		231,143
Accumulated deficit		(189,293)
Total stockholders' equity		218,587

(1) The as adjusted consolidated balance sheet data reflects our receipt of net proceeds from the sale of _____ shares of common stock in this offering at an assumed public offering price of \$ _____ per share, which was the last sale price of our common stock as reported by the NASDAQ Global Select Market on _____, 2019, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

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 contained or incorporated by reference in this prospectus, including our financial statements and the related notes and the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included in our 2018 Annual Report and 2019 Quarterly Report and incorporated by reference into this prospectus, before deciding whether to invest in our common stock. 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.

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 frontotemporal dementia (FTD), Alzheimer’s disease, and Parkinson’s disease. 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 have begun a Phase 2 clinical trial for one product candidate, AL001, and two product candidates, AL002 and AL003, are currently in Phase 1 clinical trials, but to date, we have not initiated or 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 early-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 \$52.2 million, \$32.5 million, and \$15.1 million for the years ended December 31, 2018, 2017, and 2016, respectively, and \$74.9 million and \$34.9 million for the nine months ended September 30, 2019 and 2018, respectively. As of September 30, 2019, we had an accumulated deficit of \$189.3 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 Biotechnology, Ltd. (AbbVie) is variable and limited in amount based on such arrangements. 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.

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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;
- obtaining regulatory approvals and marketing authorizations for product candidates for which we successfully complete clinical development and clinical trials;

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- 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 U.S. Food and Drug Administration (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 through our government grant 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 September 30, 2019, we had cash, cash equivalents, and marketable securities of \$381.4 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. 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. Our

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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. 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.

To date, we have identified over forty immune system targets. In the last six years, we have progressed over ten programs into preclinical research. By the end of 2019, we expect to 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 the early 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 the product candidates currently in our programs. To date, we have invested substantially all of 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, and AL101, 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. Each of our product candidates is 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.

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We have never completed a clinical development program. We currently have one product candidate, AL001, in a Phase 2 clinical trial and two product candidates, AL002 and AL003, in Phase 1 clinical trials. None of our product candidates have advanced into late-stage development or a pivotal clinical trial and it may be years before any such trial is initiated, if at all. 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 Discover Platform, our commercial opportunity may be limited.

One of our strategies is to identify and pursue clinical development of additional product candidates. Our Discovery Platform has helped us identify over forty immune system targets. In the last six years, we have progressed over ten programs into early preclinical development. By the end of 2019, we expect to have four product candidates in clinical trials. Identifying, developing, obtaining regulatory approval, and commercializing additional product candidates for the treatment of neurodegenerative diseases will require substantial additional funding beyond the net proceeds of this offering 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 study with proof-of-concept data in FTD-GRN patients expected in the first half of 2020, which also includes an additional genetic subset of FTD patients (FTD-C9orf72). If we are unable to successfully identify, develop, obtain regulatory approval for, and commercialize AL001 for other indications, our commercial opportunity for AL001 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, 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, identify and develop product candidates that cross the blood brain barrier in sufficient quantity and potency to enable efficacious dosing in the brain and engage the intended target, identify and develop biomarkers that are signs of a disease or condition, to select the right patient population, and to demonstrate target engagement, pathway engagement, and 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 investigational new drug application (IND) or a clinical trial application (CTA) will result in the FDA or European Medicines Agency (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;

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- 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 Institutional Review Board (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 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

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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.

Histopathological analysis of a 26-week toxicology study of AL002 in non-human primates identified minimal to marked granulomatous inflammation in the ciliary body and/or choroid of the eye. There were no other AL002- related gross or histopathological findings in this toxicology study in the retina or any other tissues or organs. We have observed no drug-related, serious adverse events in the AL002 Phase 1 trial with over 50 subjects. In response to FDA feedback, we have implemented additional ophthalmological assessments in our AL002 clinical trial.

Thirty-eight (38) healthy subjects were dosed over eight dose cohorts in the AL003 Phase 1a dose escalation trial. One subject treated with the second highest dose experienced aseptic hip monoarthritis and a second subject treated with the highest dose experienced an adverse drug reaction characterized by rash, fever, and thrombocytopenia, which were both deemed treatment-related serious adverse events. The subjects were treated with corticosteroids and recovered. Based on the safety and tolerability observed in the Phase 1a study, we identified a dose and initiated screening for the Phase 1b portion of the study with AL003 in Alzheimer's disease patients in the fourth quarter of 2019.

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;

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- 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.

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.

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, 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

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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;

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- 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

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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 Biologics License Application (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.

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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, a U.S. federal government shutdown or budget sequestration, such as ones that occurred during 2013, 2018, and 2019, may 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.

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 new drug application (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.

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

We may 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

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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

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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.

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

Third-party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could impact our ability to sell our products profitably. In particular, in 2010, the Patient Protection and Affordable Care Act, or Affordable Care Act (ACA) was enacted, which, among other things, subjected biologic products to potential competition by lower-cost biosimilars, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjected manufacturers to new annual fees and taxes for certain branded prescription drugs, and provided incentives to programs that increase the federal government's comparative effectiveness research. The U.S. administration could repeal or change some or all of the ACA, and complying with any new legislation or reversing changes implemented under the ACA 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, 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.

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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. This could lower the price that we receive for any approved product. Any denial in coverage or reduction in reimbursement from Medicare or other government-funded programs may result in a similar denial or reduction in payments from private payors, which may prevent us from being able to generate sufficient revenue, attain profitability, or commercialize our product candidates, if approved.

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.
- 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.

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- 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 the such 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.

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Recently the Securities and Exchange Commission (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. For example, we have entered into the Co-Development and Option Agreement with AbbVie (the AbbVie Agreement) for the global development and potential commercialization of AL002 and AL003. We also collaborate with Adimab and others to further our development of product candidates and to enhance our research efforts directed to better understanding neurodegenerative diseases. For additional information on our relationships with AbbVie and Adimab, LLC (Adimab), see the sections titled “Business—Strategic Alliance with AbbVie” and “Business—Collaboration Agreements with Adimab.” 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;

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- 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.

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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 our product candidates is at an early stage, our intellectual property portfolio with respect to certain aspects 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

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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 United States Patent and Trademark Office (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 2013 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 the neurotrophic factor PGRN degrading receptor Sortilin (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

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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. We are in the early stage of this arbitration proceeding and are unable to assess or provide any assurances regarding its possible outcome. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

We may not be successful in obtaining, through acquisitions 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. Many of these companies 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 as with our arbitration claims against Dr. Asa Abeliovich, our former consulting Chief Scientific Officer/Chief Innovation Officer. 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. Although we believe that we do not infringe a valid claim of any third party's patents or other intellectual property, 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

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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 restricted stock and stock option grants that vest over time. The value to employees of these equity grants that vest over time may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. 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 September 30, 2019, we had 109 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

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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 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 earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, 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 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, 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;

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- 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, 2018, we had federal and state net operating loss (NOL) carryforwards of approximately \$17.5 million and \$17.1 million, respectively, which will begin to expire in 2037, if not utilized. In addition, due to tax reform, we also have federal NOL carryforwards of \$42.9 million generated after December 31, 2017, which do not expire. Under Sections 382 and 383 of the United States Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an "ownership change" (generally defined as a greater than 50-percentage-point cumulative change (by value) in the equity ownership of certain stockholders over a rolling three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change taxable income or taxes may be limited. As a result of our initial public offering in February 2019, and other transactions that have occurred since our incorporation, we may have experienced, and in connection with this offering may experience, 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, including a limitation on the use of NOLs generated in tax years beginning after December 31, 2017 to 80% of current year taxable income. The Tax Act also eliminates the carryback and permits the indefinite carryforward of NOLs arising in tax years ending after December 31, 2017, whereas NOLs arising in tax years ending prior to that date continue to have a two-year carryback and twenty-year carryforward.

Risks Related to This Offering and Ownership of Our Common Stock

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, including investors purchasing shares in this offering.

The trading price of our common stock has been and may continue to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. We priced our initial public offering at \$19.00 per share on February 6, 2019 and, our common stock reached a high of \$ _____ per share during _____ and a low of \$ _____ per share during _____. On _____, 2019, the last reported sale price of our common stock was \$ _____ per share. 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;
- 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;

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- 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. These fluctuations may be even more pronounced in the trading market for our stock shortly following this offering. 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.

You will incur immediate and substantial dilution as a result of this offering.

If you purchase common stock in this offering, you will incur immediate and substantial dilution of \$ _____ per share, representing the difference between the assumed offering price of \$ _____ per share, which is the last reported sale price of our common stock on the NASDAQ Global Select Market on _____, 2019 and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, and the as adjusted net tangible book value per share of our common stock as of September 30, 2019, because the price that you pay will be substantially greater than our net tangible book value per share of the common stock that you acquire. As of September 30, 2019, there were 5,918,124 shares subject to outstanding options with a weighted-average exercise price of \$10.84 per share. To the extent that these outstanding options are ultimately exercised or the underwriters exercise their option to purchase additional shares, you will incur further dilution. See the section titled “Dilution” for a further description of the dilution you will experience immediately after this offering.

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 expect to 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. 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 58.1% of our outstanding common stock as of November 1, 2019. 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 are an “emerging growth company,” and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012 (JOBS Act). For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002 (SOX), not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. As a result, the information we provide stockholders will be different than the information that is available with respect to other public companies. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock, and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards, and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

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, and particularly after we are no longer an emerging growth 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 SOX, 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.

Pursuant to SOX Section 404, we will be required to furnish a report by our management on our internal control over financial reporting beginning with our second filing of an Annual Report on Form 10-K with the SEC after we become a public company. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with SOX Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by SOX Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

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 SOX Section 404, which require annual management assessments of the effectiveness of our internal control over financial reporting. However, our auditors will not be required to formally attest to the effectiveness of our internal control over financial reporting pursuant to SOX Section 404 until we are no longer an emerging growth company if we continue to take advantage of the exemptions available to us through the JOBS Act.

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.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States. Any failure to maintain effective internal controls could have an adverse effect on our business, financial position, and results of operations.

We will have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

We cannot specify with certainty the particular uses of the net proceeds we will receive from this offering. Our management will have broad discretion in the application of the net proceeds, including for any of the purposes described in the section titled "Use of Proceeds." Our management may spend a portion or all of the net proceeds from this offering in ways that our stockholders may not desire or that may not yield a favorable return. The failure by our management to apply these funds effectively could harm our business, financial condition, results of operations and prospects. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

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;

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- 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, unless we consent to the selection of an alternative forum, the Court of Chancery of the State 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 of our directors, officers, or other employees to 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.

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, employees, control persons, underwriters, or agents, which may discourage lawsuits against us and our directors, employees, control persons, underwriters, or agents. Additionally, a court could determine that the exclusive forum 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. If a court were to find these provisions of our amended and restated bylaws inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business, financial condition, or results of operations.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference in this prospectus contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical facts contained or incorporated by reference in this prospectus, 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 prospectus and the documents incorporated by reference in this prospectus include, but are not limited to, statements about:

- 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;
- 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;

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- our financial performance;
- the sufficiency of our existing cash and cash equivalents to fund our future operating expenses and capital expenditure requirements;
- our expectations regarding the period during which we will qualify as an emerging growth company under the JOBS Act; and
- our anticipated use of our existing resources and the proceeds from this offering.

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 prospectus and are subject to a number of risks, uncertainties, and assumptions described in the section titled “Risk Factors” and elsewhere in this prospectus and the documents incorporated by reference in this prospectus. 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 prospectus, 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 prospectus, 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.

MARKET, INDUSTRY, AND OTHER DATA

This prospectus contains estimates, projections, and other information concerning our industry, our business, and the markets for our product candidates, including data regarding the estimated size of such markets and the incidence of certain medical conditions. We obtained the industry, market, and similar dataset forth in this prospectus from our internal estimates and research and from academic and industry research, publications, surveys, and studies conducted by third parties, including governmental agencies. In some cases, we do not expressly refer to the sources from which this information is derived. In that regard, when we refer to one or more sources of this type of information in any paragraph, you should assume that other information of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires. Information that is based on estimates, forecasts, projections, market research, or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. While we believe that the data we use from third parties are reliable, we have not separately verified these data. Further, while we believe our internal research is reliable, such research has not been verified by any third party. You are cautioned not to give undue weight to any such information, projections, and estimates.

In some cases, we do not expressly refer to the sources from which data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

The sources of industry and market data contained or incorporated by reference in this prospectus are listed below: `

1. The Alzheimer's Association. "2018 Alzheimer's Disease Facts and Figures."
2. The Alzheimer's Association. "Costs of Alzheimer's to Medicare and Medicaid."
3. Boeve, B., Baker, M., Dickson, D., Parisi, J., Giannini, C., et al. "Frontotemporal dementia and parkinsonism associated with the IVS1+1G->A mutation in progranulin: a clinicopathologic study." *Brain: a Journal of Neurology*. Volume 129, Issue 11, November 2006.
4. Hansen, D., Hanson, J., Sheng, M. "Microglia in Alzheimer's disease." *Journal of Cell Biology*. Volume 217, Number 2, February 2018.
5. 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.
6. The Parkinson's Disease Foundation. "Statistics."
7. Sha, S., Miller, Z., Min, S., Zhou, Y., Brown, J., et al. "An 8-week, open-label, dose-finding study of nimodipine for the treatment of progranulin insufficiency from GRN gene mutations." *Alzheimer's & Dementia: Translational Research & Clinical Interventions*. Volume 3, Issue 4, November 2017.
8. World Health Organization. "Neurological Disorders: Public Health Challenges." *World Health Organization Press*. 2007.
9. Arthur, K., Calvo, A., Price, T. et al. Projected increase in amyotrophic lateral sclerosis from 2015 to 2040. *Nat Commun* 7, 12408 (2016).

USE OF PROCEEDS

The net proceeds to us from the sale of the shares of our common stock in this offering will be approximately \$ _____ million, or approximately \$ _____ million if the underwriters exercise their option to purchase additional shares in full, based on an assumed offering price of \$ _____ per share, which is the last reported sale price of our common stock on the NASDAQ Global Select Market on _____, 2019, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The principal purposes of this offering are to obtain additional capital to support our operations. We currently anticipate that we will use the net proceeds from this offering, together with our existing resources, as follows:

- approximately \$ _____ million to fund Phase 2 and Phase 3 clinical trials for AL001 in FTD-GRN patients and expand into FTD-C9orf72 and other potential indications;
- approximately \$ _____ million to fund Phase 1 and Phase 2 clinical trials for AL002 and AL003;
- approximately \$ _____ million to advance AL101 in and through Phase 1 clinical trials;
- approximately \$ _____ million to continue to advance our preclinical development pipeline into Phase 1 clinical trials;
- approximately \$ _____ million to further develop our Discovery Platform; and
- the remainder to fund working capital and other general corporate activities.

We believe opportunities may exist from time to time to expand our current business through license or acquisitions of, or investments in, complementary businesses, products or technologies. While we currently have no agreements or commitments to complete any such transaction at this time, we may use a portion of the net proceeds for these purposes.

Our operating expenses have increased and we expect them to continue to increase in 2020 and beyond as we advance our development pipeline and accelerate our efforts to conduct clinical trials. Accordingly, we will need additional funds to complete our currently planned and future clinical trials and development programs. Based on our current operating plans and assumptions, we believe our existing cash, cash equivalents, and marketable securities, together with the expected net proceeds from this offering, will enable us to meet our financial needs at least into the second half of 2022. The net proceeds from this offering, together with our cash, cash equivalents, and marketable securities, will not be sufficient for us to fund any of our product candidates through regulatory approval, our preclinical development pipeline through Phase 1 clinical trials, or any product candidates resulting from our Discovery Platform into preclinical studies and clinical trials.

Our management will have broad discretion over the use of the net proceeds from this offering. The amounts and timing of our expenditures will depend upon numerous factors including the results of our research and development efforts, the timing and success of preclinical studies and any ongoing clinical trials or clinical trials we may commence in the future, the timing of regulatory submissions, the amount of cash obtained through our existing collaborations and future collaborations, if any, and any unforeseen cash needs.

Pending their uses, we plan to invest the net proceeds of this offering in short-term, interest-bearing, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

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.

CAPITALIZATION

The following table sets forth our cash, cash equivalents, and marketable securities and capitalization as of September 30, 2019, as follows:

- on an actual basis; and
- on an as adjusted basis to further reflect our issuance and sale of _____ shares of common stock in this offering at the assumed offering price of \$ _____ per share, which is the last reported sale price of our common stock on the NASDAQ Global Select Market on _____, 2019 after deducting the estimated underwriting discounts and commissions and estimated expenses payable by us.

You should read this table in conjunction with our consolidated financial statements and the related notes and the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” that are incorporated by reference in this prospectus.

	As of September 30, 2019	
	Actual	As Adjusted
	(In thousands, except share and per share data) (Unaudited)	
Cash, cash equivalents, and marketable securities	\$ 381,446	\$ _____
Stockholders’ equity:		
Preferred stock, par value \$0.0001 per share; 20,000,000 shares authorized and no shares issued and outstanding, actual and as adjusted	—	—
Common stock, par value \$0.0001 per share; 200,000,000 shares authorized and 68,922,249 shares issued and outstanding, actual; 200,000,000 shares authorized and _____ shares issued and outstanding, as adjusted	7	7
Additional paid-in capital	407,647	407,647
Accumulated other comprehensive income	226	226
Accumulated deficit	(189,293)	(189,293)
Total stockholders’ equity	218,587	218,587
Total capitalization	\$ 218,587	\$ _____

The number of shares of our common stock to be outstanding after this offering is based on the 68,922,249 shares of our common stock outstanding as of September 30, 2019, and excludes the following:

- 4,822,524 shares of common stock issuable upon exercise of options to purchase shares of our common stock outstanding as of September 30, 2019 under our 2017 Stock Option and Grant Plan (2017 Plan), at a weighted-average exercise price of \$8.97 per share;
- 1,095,600 shares of common stock issuable upon exercise of options to purchase shares of our common stock outstanding as of September 30, 2019 under our 2019 Equity Incentive Plan (2019 Plan), at a weighted-average exercise price of \$19.15 per share;
- 2,604,971 shares of common stock issuable upon exercise of options to purchase shares of our common stock that we granted after September 30, 2019 under our 2019 Plan, at a weighted-average exercise price of \$17.12 per share;

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- 6,911,739 shares of common stock reserved for future issuance under our 2019 Plan as of September 30, 2019, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan; and
- 1,478,492 shares of common stock reserved for issuance under our 2019 Employee Stock Purchase Plan (ESPP) as of September 30, 2019, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the public offering price per share of our common stock and the as adjusted net tangible book value per share of our common stock immediately after this offering.

Net tangible book value per share is determined by dividing our total tangible assets less our total liabilities by the number of shares of our common stock outstanding. Our net tangible book value as of September 30, 2019 was \$218.6 million, or \$3.17 per share, based on the total number of shares of our common stock outstanding as of September 30, 2019.

After giving further effect to our sale of _____ shares of common stock in this offering at an assumed public offering price of \$ _____ per share, which is the last reported sale price of our common stock on the NASDAQ Global Select Market on _____, 2019, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2019 would have been approximately \$ _____ million, or approximately \$ _____ per share. This represents an immediate increase in as adjusted net tangible book value per share of \$ _____ to our existing stockholders and an immediate dilution in as adjusted net tangible book value per share of approximately \$ _____ to new investors purchasing common stock in this offering. Dilution per share to new investors purchasing common stock in this offering is determined by subtracting as adjusted net tangible book value per share after this offering from the public offering price per share paid by new investors.

The following table illustrates this dilution on a per share basis:

Assumed public offering price per share	\$
Net tangible book value per share as of September 30, 2019	\$3.17
Increase in as adjusted net tangible book value per share attributable to new investors purchasing shares in this offering	_____
As adjusted net tangible book value per share after this offering	_____
Dilution per share to new investors purchasing shares in this offering	\$ _____

Each \$1.00 increase (decrease) in the assumed public offering price of \$ _____ per share, which is the last reported sale price of our common stock on the NASDAQ Global Select Market on _____, 2019, would increase (decrease) the as adjusted net tangible book value per share after this offering or dilution per share to new investors by approximately _____, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters exercise their option to purchase _____ additional shares of common stock in this offering in full at the assumed public offering price of \$ _____ per share, which is the last reported sale price of our common stock on the NASDAQ Global Select Market on _____, 2019, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, the as adjusted net tangible book value per share after this offering would be \$ _____ per share, and the dilution in as adjusted net tangible book value per share to new investors purchasing common stock in this offering would be \$ _____ per share.

The following table summarizes, on an as adjusted basis, as of September 30, 2019, the number of shares of common stock purchased from us on an as converted to common stock basis, the total consideration paid, or to be paid and the weighted-average price per share paid, or to be paid, by existing stockholders and by new investors in this offering at the assumed public offering price of \$ _____ per share, which is the last reported sale price of

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our common stock on the NASDAQ Global Select Market on _____, 2019, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

	Shares Purchased		Total Consideration		Weighted-Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders before this offering	68,922,249	%	\$379,531,689	%	\$ 5.51
Investors participating in this offering					
Total		100%	\$	100%	

The dilution information discussed above is illustrative only and will change based on the actual offering price, the number of shares we sell and other terms of this offering that will be determined at pricing. The table above assumes no exercise of the underwriters' option to purchase _____ additional shares in this offering. If the underwriters' option to purchase additional shares is exercised in full, the number of shares of our common stock held by existing stockholders would be reduced to _____ % of the total number of shares of our common stock outstanding after this offering, and the number of shares of common stock held by new investors participating in the offering would be increased to _____ % of the total number of shares outstanding after this offering.

The number of shares of our common stock to be outstanding after this offering is based on the 68,922,249 shares of our common stock outstanding as of September 30, 2019, and excludes the following:

- 4,822,524 shares of common stock issuable upon exercise of options to purchase shares of our common stock outstanding as of September 30, 2019 under our 2017 Plan, at a weighted-average exercise price of \$8.97 per share;
- 1,095,600 shares of common stock issuable upon exercise of options to purchase shares of our common stock outstanding as of September 30, 2019 under our 2019 Plan, at a weighted-average exercise price of \$19.15 per share;
- 2,604,971 shares of common stock issuable upon exercise of options to purchase shares of our common stock that we granted after September 30, 2019 under our 2019 Plan, at a weighted-average exercise price of \$17.12 per share;
- 6,911,739 shares of common stock reserved for future issuance under our 2019 Plan as of September 30, 2019, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan; and
- 1,478,492 shares of common stock reserved for issuance under our ESPP as of September 30, 2019, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan.

To the extent that any outstanding options are exercised or new options are issued under the equity benefit plans, or we issue additional shares of common stock or other securities convertible into or exercisable or exchangeable for shares of our capital stock in the future, there will be further dilution to investors participating in this offering.

A LETTER FROM ARNON

Prospective Alector co-owner,

At Alector, we do not view diseases of aging as immutable facts. We are on a mission to slow down their progression and prevent their occurrence. We envision a world where each individual retains his or her full brain function and cognitive faculties throughout life—a world where dementia and neurodegeneration are illnesses of the past just as smallpox, diphtheria, rubella, and polio have become.

Since the early 20th century, the root cause of neurodegeneration has been considered to be misfolded proteins such as amyloid-beta plaques and TAU tangles in Alzheimer's disease, alpha-synuclein in Parkinson's disease and TDP-43 in FTD and amyotrophic lateral sclerosis (ALS). Other pathologies that typify neurodegeneration, including the dysfunction and destruction of neuronal connections, the accelerated death of nerve cells, and the dysfunction of the brain support cells, were thought to be consequences of these misfolded proteins.

Since our founding six years ago, we have challenged this widely held belief. We made the case that multiple pathologies that typify neurodegeneration become autonomous of the misfolded proteins and of each other at early disease stages, and that for therapeutic purposes, these pathologies should be viewed as independent causes of the disorder. With this understanding, we searched for an underlying biological process that these pathologies share. Discoveries on the genetic underpinning of neurodegeneration and on the functions of the brain immune system led us to conclude that these parallel pathologies are primarily caused by a dysfunctional brain immune system.

The specific scientific advances that enabled our conclusion were: (1) the identification of harmful genetic mutations that increase the risk of developing Alzheimer's disease; (2) the revelation that the majority of these mutations are in proteins that regulate the brain immune system; and (3) the findings that the immune cells in the brain are responsible for a myriad of functions, which include compacting and disposing of misfolded proteins, the regulation of neuronal connections, and the survival and function of the brain's support cells and neurons.

Since most neurodegenerative diseases are diseases of aging, we postulated that the brain immune cells lose their competence with time and are no longer able to support normal brain function or to repair avoidable brain pathologies. In futile attempts to act, the senescing immune cells may further exacerbate the disease by secreting toxic immune mediators and by indiscriminate scavenging.

With this understanding, we devoted the last six years to the development of novel therapeutics that harness the brain's immune system to treat neurodegeneration. We have advanced four of our product candidates into clinical trials and plan to test the impact of these product candidates initially in patients suffering from Alzheimer's disease and FTD.

I have invested much of my 35 years in the biotech industry into building teams that develop innovative therapeutics in neuroscience. During my 16 years with Genentech, I built a team that discovered multiple neuronal survival factors and receptors in order to prevent degenerative nerve cell death. As the Founder, President, and Chief Science Officer of Rinat Neuroscience, my team and I discovered clinical antibodies designed to target misfolded proteins. As a Co-Founder and the former Chief Executive Officer of Annexon Biosciences, my team and I developed clinical antibodies that prevent destruction of neuronal connections. I am a named inventor on over 350 issued patents and patent applications and am an author on over 100 peer reviewed publications. My teams and I discovered the target for the approved cancer drug, Erivedge, and were responsible for the development of the non-addictive antibody pain drug candidate, tanezumab, and the approved migraine antibody drug, AJOVY. Our work at Alector is based upon our understanding of the basic biology of degenerative brain disorders and how to translate this understanding into effective therapeutics.

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The World Health Organization estimates that up to 1 billion people are affected by neurological disorders. There are currently over 50 million people with neurodegeneration worldwide, with over 10 million new cases each year. The Alzheimer's Association projected that the cumulative total cost of Medicare and Medicaid for individuals living with Alzheimer's disease will total \$750 billion by 2050 in the United States alone, an increase of over 300% from projected 2018 spending levels.

Degenerative brain disorders are among the last medical frontiers that have yet to be conquered. If we are successful in our mission to treat neurodegeneration, Alector will have a profound social and economic impact on humanity. We invite you to join us and become a partner in this meaningful venture.

Best Regards,
Arnon Rosenthal, Ph.D.
Co-Founder and Chief Executive Officer

BUSINESS

Overview

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

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, in the last six years, we have identified over forty immune system targets, progressed over ten programs into preclinical research, and advanced three product candidates, AL001, AL002, and AL003, into clinical development.

AL001, our first program in the clinic, modulates progranulin (PGRN), a regulator of immune activity in the brain with genetic links to multiple neurodegenerative disorders, including frontotemporal dementia (FTD), Alzheimer's disease, and Parkinson's disease. AL001 is initially designed to treat FTD, a severe, rapidly progressing neurodegenerative disorder that affects approximately 170,000 individuals in the United States and the European Union alone, with potentially higher prevalence in Asia and Latin America.

Our AL001 program is aimed at treating a genetic subset of patients with FTD who have a known genetic mutation that causes a deficiency in PGRN, which is called FTD-GRN. AL001 has successfully achieved proof-of-mechanism in the Phase 1b portion of the study in FTD-GRN subjects by restoring PGRN levels in plasma and cerebrospinal fluid back to the normal range. In the third quarter of 2019, we advanced AL001 into a Phase 2 study with proof-of-concept data in FTD-GRN patients expected in the first half of 2020, which also includes an additional genetic subset of FTD patients (FTD-C9orf72). In addition, in consultation with the FDA, we plan to advance AL001 into a Phase 3 study in FTD-GRN patients in 2020.

We are developing AL101, our second product candidate in our PGRN program, for patients 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. AL101 received orphan drug designation from the FDA for treatment of FTD in July 2019 and we expect to initiate a Phase 1 study of AL101 in the fourth quarter of 2019. We expect proof-of-mechanism data in 2020.

We own worldwide rights to both AL001 and AL101.

Our next development programs. AL002 and AL003, focus on modulating check-point receptors on the brain's immune cells, with AL002 targeting Triggering Receptor Expressed on Myeloid cells 2 (TREM2) and AL003 targeting sialic acid binding Ig-like lectin 3 (SIGLEC 3), respectively. The AL002 and AL003 programs are aimed at treating Alzheimer's disease patients.

In the third quarter of 2019, we completed the Phase 1a portion of the study in healthy subjects with AL002 and a dose dependent change in the target engagement biomarker in cerebrospinal fluid was observed upon treatment. In the second quarter of 2019, based on safety and tolerability observed in the Phase 1a study, we initiated the Phase 1b portion of the study with AL002 in Alzheimer's disease patients. We expect proof-of-mechanism data from Alzheimer's disease patients in the first half of 2020.

In the first quarter of 2019, we initiated a Phase 1a study in healthy subjects with AL003, a product candidate targeting Alzheimer's disease. Thirty-eight (38) healthy subjects were dosed over eight dose cohorts in the AL003 Phase 1a dose escalation trial. A dose dependent change in target engagement in the blood was observed upon treatment. One subject treated with the second highest dose experienced aseptic hip monoarthritis

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and a second subject treated with the highest dose experienced an adverse drug reaction characterized by rash, fever, and thrombocytopenia, which were both deemed treatment-related serious adverse events. The subjects were treated with corticosteroids and recovered. Based on the safety and tolerability observed in the Phase 1a study, we identified a dose and initiated screening for the Phase 1b portion of the study with AL003 in Alzheimer’s disease patients in the fourth quarter of 2019.

We have partnered with AbbVie, a leader in neuroscience drug development, for the global development and potential commercialization of AL002 and AL003. We are responsible for execution of the Phase 1 and Phase 2 studies. Following AbbVie’s potential 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. As part of this partnership, we received \$205.0 million in upfront payments, of which \$5.0 million and \$200.0 million was received by us in October 2017 and January 2018, respectively, \$20.0 million from the sale of shares of our preferred stock in October 2017 and are eligible for up to an additional \$985.6 million in option exercise and milestone payments and a global profit share with AbbVie upon commercialization.

Our Discovery Platform leverages large scale human genetic datasets, advanced tools in bioinformatics and imaging, and insights into neurodegeneration and immunology to identify immune system targets that play a critical role in the development of multiple neurodegenerative diseases. Our Discovery Platform focuses on:

- **Target Selection.** We identify mutations in genes that control the brain’s immune system, which we believe are the root cause of neurodegeneration, employ a suite of genetic tools to elucidate the immune dysfunction caused by these mutations, and then engineer immune modulating antibodies to counteract the harmful consequences of these genetic mutations.
- **Biomarker Selection.** We are able to identify and employ molecular biomarkers, assays, and precise imaging techniques to confirm target engagement and measure the effect of our product candidates, allowing us to potentially obtain clinical data earlier than would otherwise be expected using traditional clinical measures.
- **Patient Selection.** We utilize genetic screening and other biomarkers to better align a patient’s specific diagnosis with the targeted intervention in our clinical studies.

Our immuno-neurology approach and our Discovery Platform are designed to broadly address multiple neurodegenerative disorders. The breadth of our opportunity is reinforced by our ability to engineer therapeutics capable of modulating a broad array of immune targets, validated by human genetics, across multiple mechanisms of action, including product candidates that activate, block, inhibit, or down-regulate a given target as therapeutically needed.

Figure 1. The following table highlights our preclinical and clinical programs.

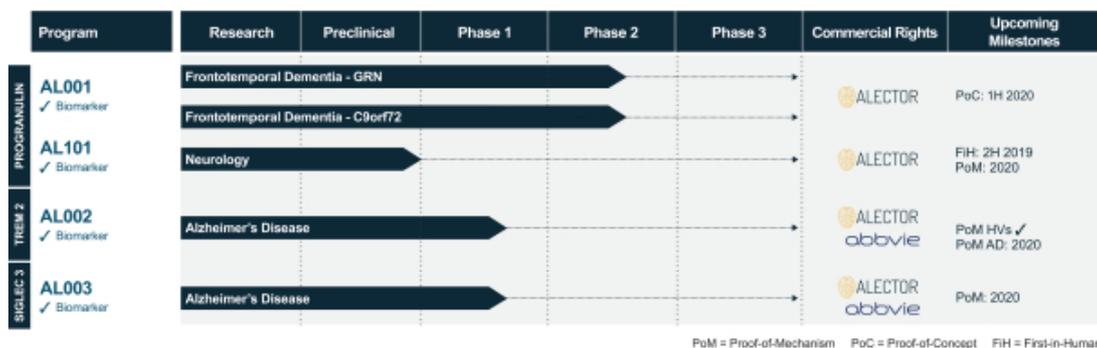


Figure 2. The following table highlights ten of our identified programs in our research and development pipeline.

Program	Research	Preclinical	Phase 1	Phase 2	Phase 3	Commercial Rights
Immunoneurology 7 Candidates Biomarkers in development	ADP012					
	ADP014					
	ADP016					
	ADP017					
	ADP023					
	ADP026					
	ADP122					
Immunoncology 3 Candidates Biomarkers in development	ADP008					
	ADP009					
	ADP022					

The above table reflects that we currently have ten research programs identified in our research and development pipeline focused on targeting Alzheimer’s disease, Parkinson’s disease, ALS, progressive multiple sclerosis, and oncology. Currently, we estimate that these programs are one to three years or more away from entering preclinical studies assuming that these programs meet our requirements for advancement into the preclinical stage. For each of our programs in our research and development pipeline we are working to identify biomarkers to be utilized in preclinical studies for each program.

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. For example, 22 of the top 25 risk genes identified by evaluating large-scale data on tens of thousands of Alzheimer’s disease patients regulate immune function in the brain. 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.

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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 Team

Our team is led by seasoned executives with a proven track record of drug discovery and development in neuroscience, as well as substantial operational and business expertise. Our Co-Founder and Chief Executive Officer, Arnon Rosenthal, Ph.D., has spent over 35 years developing therapeutics in neuroscience and led teams responsible for the development of the non-addictive pain drug tanezumab and the migraine drug AJOVY, and multiple other programs in clinical development. He also held several leadership roles over a 16-year career at Genentech, where he led the team that discovered the target for the cancer drug Erivedge. Our Chief Medical Officer, Robert Paul, M.D., Ph.D., served as the Therapeutic Area Lead for Neuroscience at Genentech, where among other projects, he oversaw the clinical development of various product candidates, including the amyloid-beta antibody crenezumab in Alzheimer's disease, GDC-0134 in ALS, and GDC-0276 and GDC-0310 in pain. Our Chief Development Officer, Robert King, Ph.D., previously served as the Senior Vice President of development and supply chain at SciClone Pharmaceuticals. Our Chief Business Officer, Sabah Oney, Ph.D., previously served as the Head of Global Sales and Business Development at Ariosa, Inc. until and through its acquisition by Roche.

As we grow our company, we will continue to bolster our team by attracting people and partners committed to transforming the neurodegenerative treatment landscape.

Our Strategy

Our goal is to develop therapies that empower the immune system to cure neurodegeneration. 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. 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 3).

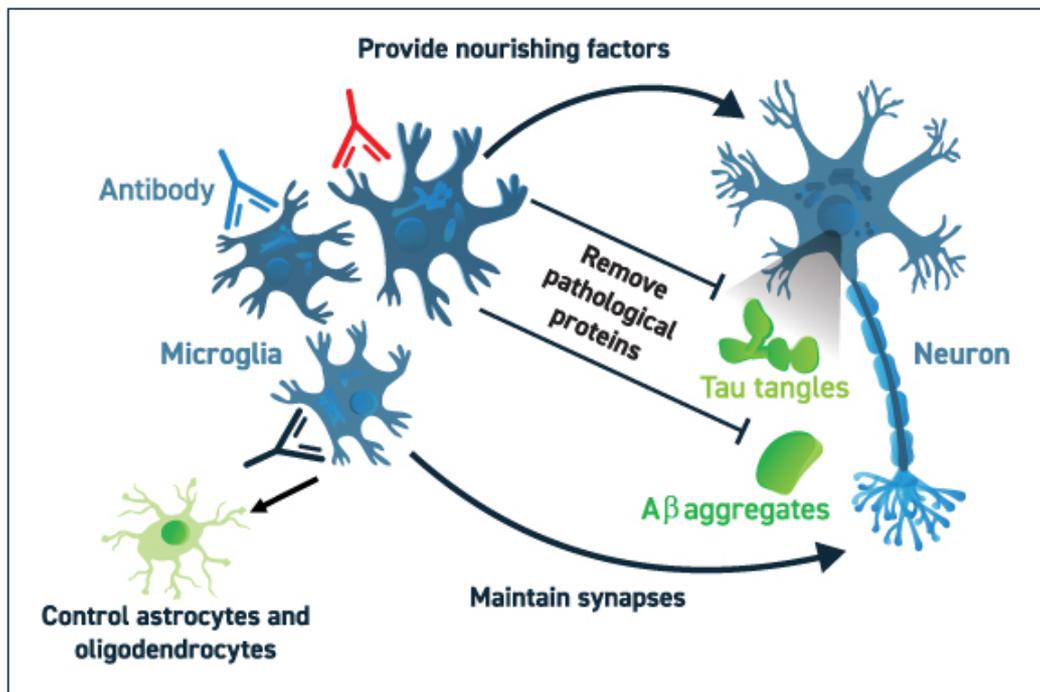


Figure 3. Our antibody product candidates target microglia to harness their many potential beneficial roles in treating neurodegenerative diseases.

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, especially in the last five years, has supported the importance of the interactions between the brain and the innate immune system. For example, 22 of the top 25 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 4).

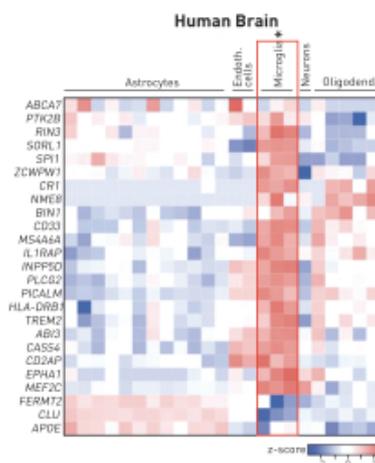


Figure 4. Expression of genes linked to Alzheimer’s disease is highly enriched in microglia.¹ * Red box added to highlight microglia.

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.

Recent 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.

Recent 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.

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

<u>Functional Microglia</u>	<u>Dysfunctional Microglia</u>
<ul style="list-style-type: none">• Clear/counteract and form a barrier around pathological proteins such as amyloid-beta	<ul style="list-style-type: none">• 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
<ul style="list-style-type: none">• Provide metabolic and functional support to nerve cells	<ul style="list-style-type: none">• Reduced ability to provide nourishing factors to neurons leading to neuronal cell death
<ul style="list-style-type: none">• Regulate healthy synaptic connections	<ul style="list-style-type: none">• Indiscriminate destruction of synapses leading to reduced number of synapses and dysfunctional neuronal connections
<ul style="list-style-type: none">• 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	<ul style="list-style-type: none">• Inducement and conversion of beneficial astrocytes to toxic astrocytes leading to neuronal cell death
<ul style="list-style-type: none">• Control the survival and function of oligodendrocytes that provide protective myelin sheaths around nerve fibers	<ul style="list-style-type: none">• 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.

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- **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.

In the last six years, we have identified over forty immune system targets through genetic analysis and efficiently advanced more than ten programs to preclinical research. Our AL001 program, initially aimed at treating a genetic subset of patients with FTD carrying a PGRN loss of function mutation (FTD-GRN), has successfully achieved proof-of-mechanism in the central nervous systems of healthy volunteers and FTD patients. By the end of 2019, we expect to have four product candidates in clinical trials.

Our Pipeline Programs

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 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 5), 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.

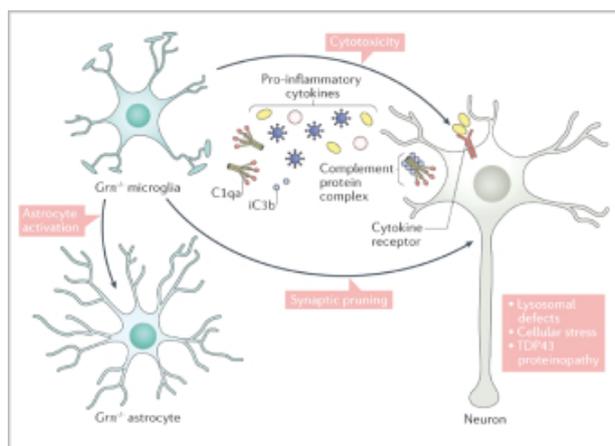


Figure 5. PGRN deficiency disrupts homeostasis between microglia and neurons, and promotes neurodegeneration during aging.¹

¹ 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.

SORT1 Controls PGRN Levels in the Body

Human and mouse genetic studies have identified the neurotrophic factor PGRN degrading receptor 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. 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.

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.

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 50,000 to 60,000 individuals in the United States and roughly 110,000 individuals in the European Union. There are multiple heritable forms of FTD, such as FTD-GRN, which represent 5% to 10% of all patients with FTD, and approximately 22% of heritable FTD cases. 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

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50% or greater decrease in the level of PGRN and lead to development of FTD with a greater than 90% probability. Researchers have identified over 70 inherited loss of function mutations in PGRN that lead to FTD to date.

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 6). We have tested our PGRN program antibodies in various animal models, including mice, rats, and non-human primates as well as in healthy volunteers and FTD-GRN patients and have achieved significantly elevated, long-lasting levels of PGRN in the brain after intravenous administration.

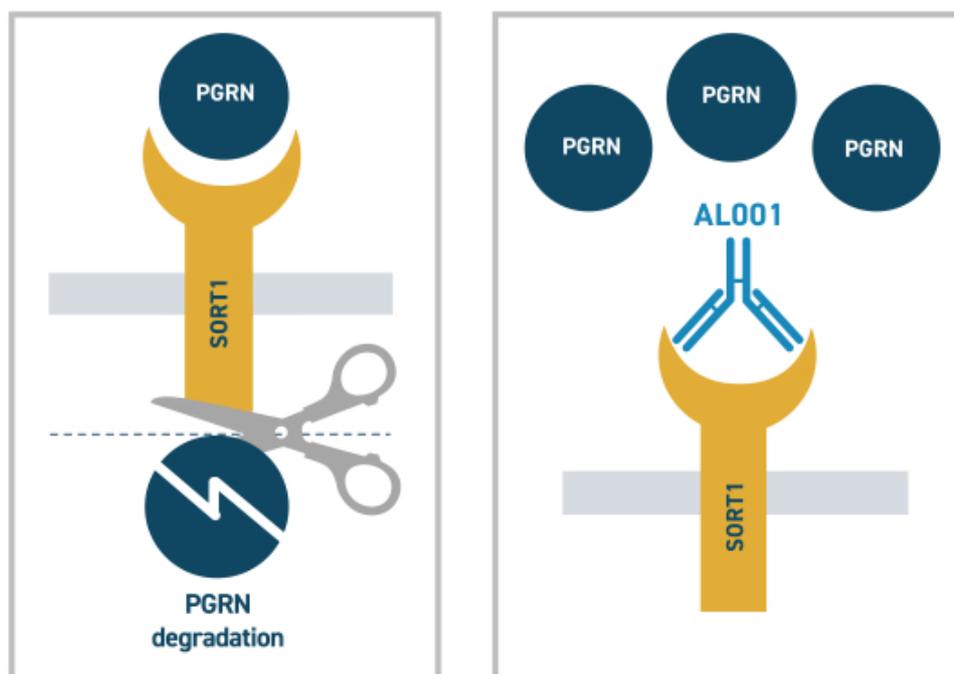


Figure 6. Mechanism of action for our PGRN programs. AL001 binds to SORT1 and prevents degradation of PGRN, increasing its circulating half-life significantly. A similar mechanism of action is also applicable for AL101.

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. AL101 received orphan drug designation from the FDA for the treatment of FTD in July 2019.

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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 following proof-of-concept in FTD patients.

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 2018, there are 5.7 million people in the United States suffering from Alzheimer's disease 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.

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 2018 for patients with Alzheimer's disease and other types of dementia in the United States was estimated to be \$232 billion, over half of which is borne by the Medicare system.

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. An estimated 930,000 people in the United States will be living with Parkinson's disease by the year 2020. This number is predicted to rise to 1.2 million by 2030.

Our PGRN Preclinical Data

We have conducted safety and efficacy studies of AL001 in non-human primates, also referred to as NHPs, and completed preclinical chronic good laboratory practice (GLP) toxicology testing through 26 weeks with no test article related adverse findings. In non-human primates, AL001 recognizes and binds to SORT1 with potency similar to that seen in the binding between AL001 and human SORT1. In these non-human primate experiments, AL001 delivered by intravenous injection to the blood stream blocked SORT1 and increased levels of PGRN in both plasma and the CSF (Figure 7). These experiments indicated that there were therapeutic levels of AL001 in

the brain following delivery to the bloodstream systemically. These effects were observed after a single dose of AL001 as well as during and after multiple dosing.

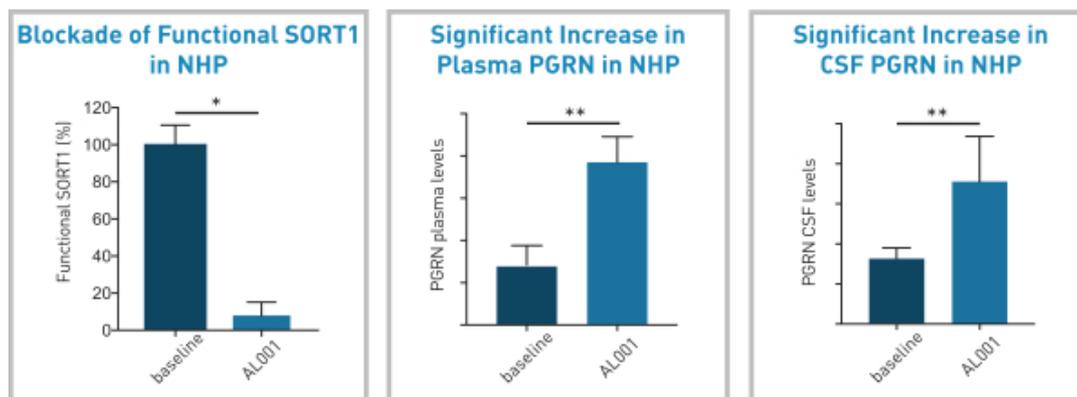


Figure 7. AL001 blocks SORT1 and increases the levels of PGRN in plasma and the cerebrospinal fluid in NHP following injection to the bloodstream, indicating that peripherally injected AL001 elicits the desired biological response in the brain (n=4) (* indicates $p<0.05$ and ** indicates $p<0.01$ by T-test).

AL101 is able to cross-react and bind to murine, rat, non-human primate as well as human SORT1. AL101 binds SORT1 with similar potency in multiple animal models. Following injection, AL101 was shown to block SORT1 and increase the levels of PGRN in the plasma and cerebrospinal fluid of mice (Figure 8), rats, and non-human primates, demonstrating again that administration of AL101 is effective in increasing PGRN levels in the brain in multiple animal models.

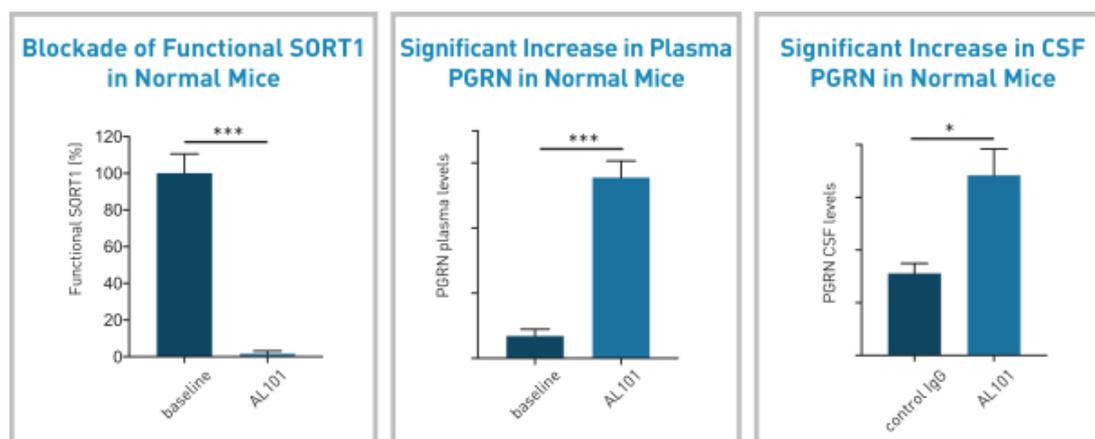


Figure 8. AL101 blocks SORT1 and increases the levels of PGRN in the plasma and cerebrospinal fluid in normal mice following intraperitoneal injection, indicating that peripherally injected AL101 elicits the desired biological response in the brain (* indicates $p<0.05$ and * indicates $p<0.001$ by T-test).**

In addition, we have conducted preclinical tests with AL101 in a mouse model created by introducing a mutation in one of the two copies for the mouse version of PGRN (FTD-GRN mice). AL101 blocked SORT1 and increased levels of PGRN in both the plasma and CSF of the FTD-GRN mice (Figure 9). These changes support

the hypothesis that targeting SORT1 by administration of anti-SORT1 antibodies would lead to an increase of PGRN in the brains of FTD-GRN patients.

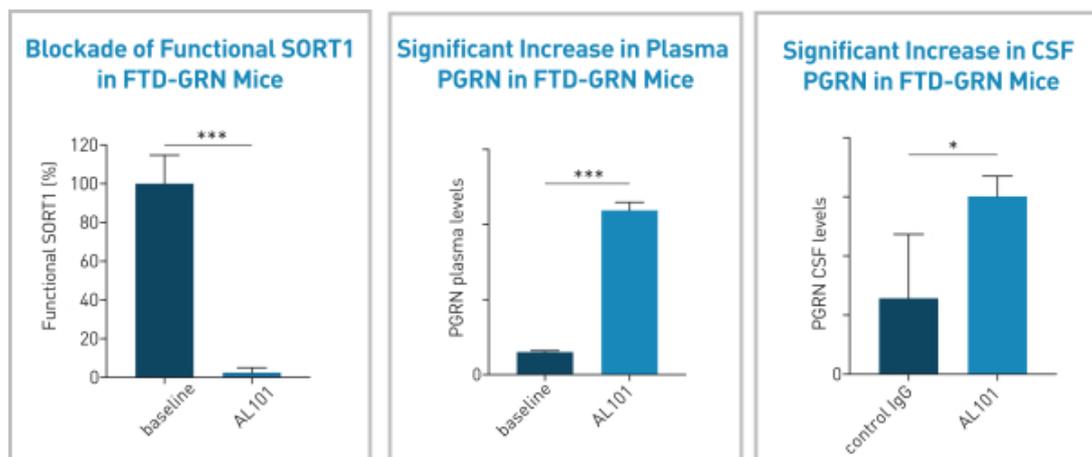


Figure 9. AL101 blocks SORT1 and increases the levels of PGRN in the plasma and CSF in FTD-GRN mice following intraperitoneal injection, indicating that peripherally injected AL101 elicits the desired biological response in the brain (* indicates $p < 0.05$ and * indicates $p < 0.001$ by T-test).**

The FTD-GRN mice also exhibit behavioral changes such as an increase in submissiveness and social aversion. This can be assessed in a social aversion test in which mice are introduced at opposite ends of a tube. Normal mice will approach each other in the tube until one of them retreats on average 50% of the time. When an FTD-GRN mouse is placed into the tube together with a normal mouse, it is about three times more likely to retreat first.

We tested our hypothesis that increasing levels of PGRN, through inhibition of SORT1, would slow disease progression and lead to a beneficial therapeutic effect in the FTD-GRN mouse model. In this experiment, administration of the FTD-GRN mice with AL101 for four weeks increased PGRN levels in the brains of FTD-GRN mice and significantly reduced the social deficit symptoms of FTD and restored healthy behavior in this social aversion test. Moreover, no adverse effects were observed in either FTD-GRN mouse model or normal mice after the treatment with AL101.

Our PGRN Product Candidates Development Plan

We are developing two PGRN product candidates, AL001 and AL101. 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. Our second PGRN product candidate, AL101 has demonstrated target engagement, increases in the disease associated pharmacodynamic marker PGRN in the brains of mice, rats and non-human primates, as well as reduction of social deficit symptoms of FTD in a social aversion test using FTD-GRN mice following intravenous injection. We expect to initiate a Phase 1, first-in-human study with AL101 in the fourth quarter of 2019.

AL001 successfully demonstrated proof-of-mechanism in a dose-escalating Phase 1a study in healthy volunteers and in the Phase 1b portion of the study 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.

AL001 was dosed in a randomized, double-blind, placebo-controlled, dose-escalating Phase 1a study in the United States with healthy volunteers being randomized and receiving a single dose of AL001 or placebo. Each of the dose levels consisted of a cohort of eight healthy volunteers, with six receiving AL001 and two receiving

placebo, representing a six to two randomization ratio of AL001 to placebo. 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.

The subjects were dosed in five cohorts in escalating dose levels of AL001. There were no drug-related serious adverse events or dose limiting adverse events reported in the study, achieving the primary endpoint. Moreover, 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. Results in this dose-escalating Phase 1a study in healthy subjects successfully demonstrate proof-of-mechanism for AL001 in both plasma and CSF.

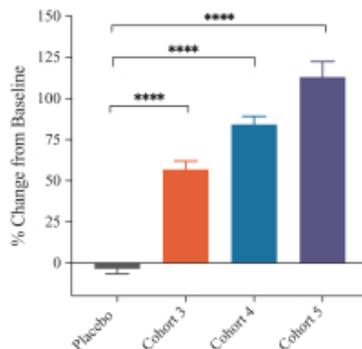


Figure 10. AL001 increases the level of PGRN in CSF in healthy volunteers in measured cohorts at the pre-specified follow-up time point (the thirteenth day following injection) compared to pooled placebo in CSF (** indicates $p < 0.0001$ by T-test).**

In the Phase 1b portion of the study, a total of 14 FTD-GRN mutation carriers, six asymptomatic FTD-GRN (aFTD-GRN) patients and eight symptomatic FTD-GRN (FTD-GRN) patients, were dosed with AL001 over a one-month period. There were no drug-related serious adverse events or dose limiting adverse events reported in the study, achieving the primary endpoint. In addition, an approximately two-fold increase in CSF PGRN levels from baseline was observed in all 14 FTD-GRN mutation carriers dosed with AL001, successfully demonstrating proof-of-mechanism for AL001 in this patient population.

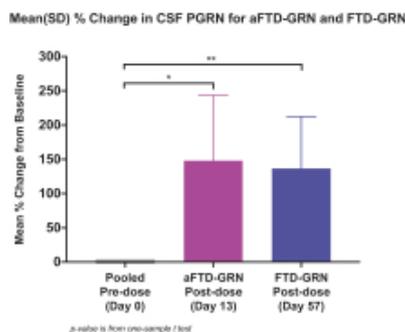


Figure 11. AL001 elevates the level of PGRN in CSF compared to baseline in aFTD-GRN (purple bar) and FTD-GRN (blue bar) mutation carriers after receiving one month of dosing with AL001 (* indicates $p < 0.05$ by T-test and ** indicates $p < 0.01$ by T-test).

As shown in the chart below, after receiving their infusion of AL001, all 14 FTD-GRN mutation carriers' CSF-PGRN levels increased up to the normal range observed in healthy volunteers. In the FTD-GRN patients, their CSF-PGRN levels remained elevated for one-month following their final infusion of AL001 (Day 57).

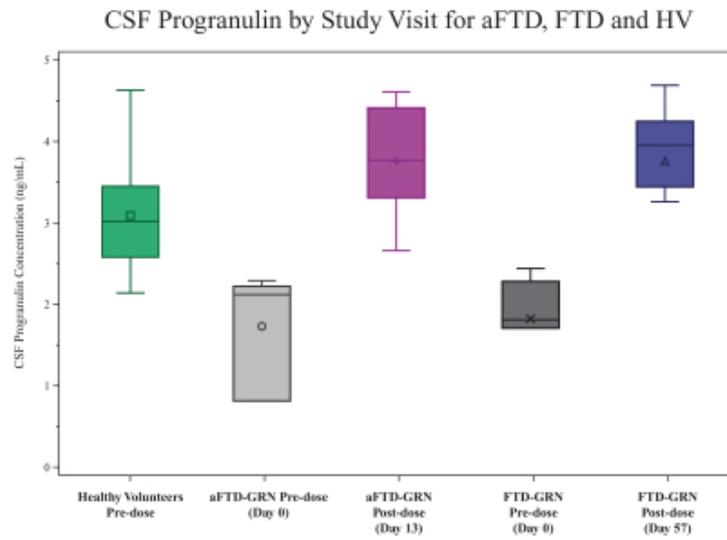


Figure 12. AL001 increases the level of PGRN in cerebral spinal fluid (CSF) from baseline level of aFTD-GRN and FTD-GRN mutation carriers, who initially have fifty-percent or less (grey bars) compared to healthy volunteers (green bar), up to the normal range of PGRN (purple and blue bars).

In the third quarter of 2019, we advanced AL001 into a Phase 2 study. We plan to have Phase 2 trial proof-of-concept data in FTD-GRN patients in the first half of 2020 and expect to include multiple CSF biomarkers, including neurofilament light chain (NFL), multiple types of brain imaging, including volumetric MRI, and multiple cognitive and behavioral tests.

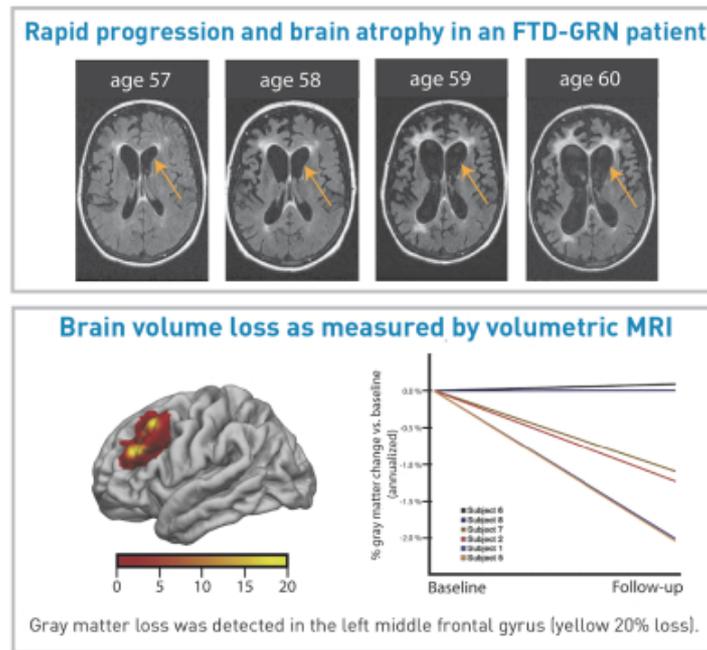


Figure 13. Decreasing clinical risk with volumetric brain imaging. The change in brain volume loss was driven by symptomatic mutation carriers.^{2,3}

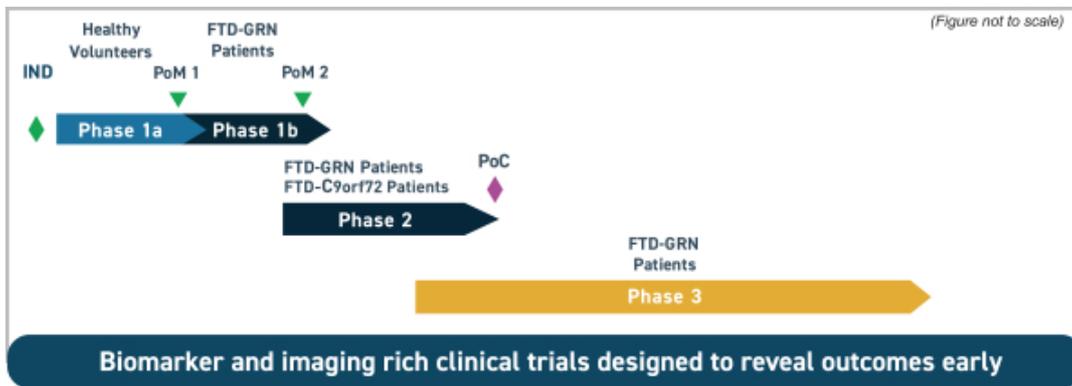


Figure 14. Clinical plan for AL001 in FTD-GRN. (Figure not to scale.)

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

- ² Boeve, B., Baker, M., Dickson, D., Parisi, J., Giannini, C., et al. "Frontotemporal dementia and parkinsonism associated with the IVS1+1G->A mutation in progranulin: a clinicopathologic study." *Brain: a Journal of Neurology*. Volume 129, Issue 11, November 2006.
- ³ Sha, S., Miller, Z., Min, S., Zhou, Y., Brown, J., et al. "An 8-week, open-label, dose-finding study of nimodipine for the treatment of progranulin insufficiency from GRN gene mutations." *Alzheimer's & Dementia: Translational Research & Clinical Interventions*. Volume 3, Issue 4, November 2017.

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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. Following proof-of-concept data in FTD-GRN, we intend to expand to additional FTD subpopulations.

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 15). For our other programs, we anticipate following a similar development approach to expand into additional patient populations as appropriate.

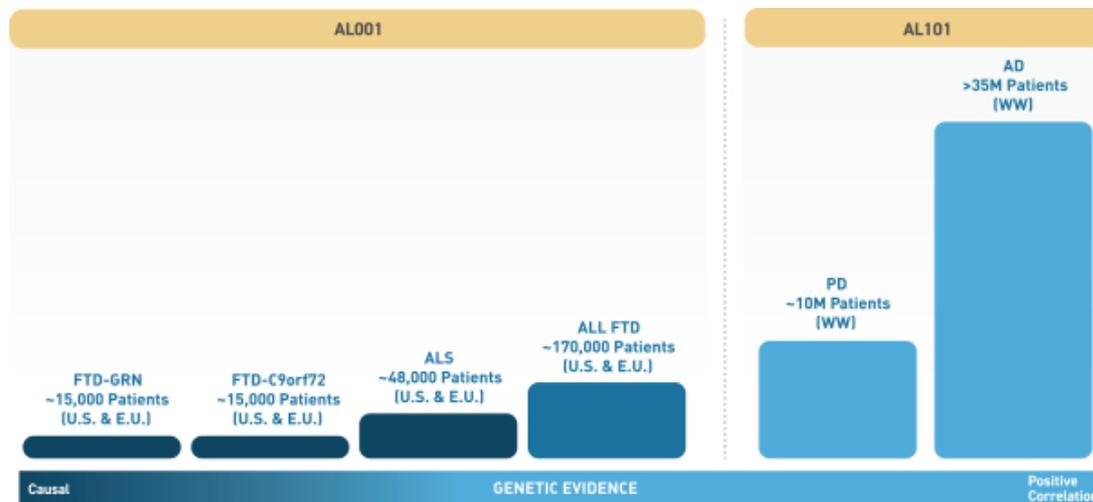


Figure 15. Our PGRN programs have broad therapeutic potential, including FTD and other more prevalent neurodegenerative diseases such as Parkinson's disease and Alzheimer's disease. (Figure not to scale.)

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 16). 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.

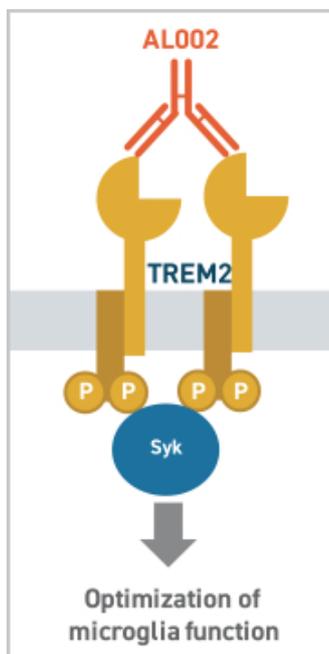


Figure 16. Mechanism of action of our TREM2 activating product candidate AL002.

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). 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, induce microglial proliferation, increase microglial survival, increase the number of microglia surrounding amyloid-beta plaques, and increase the compaction, insulation, and phagocytosis of these pathological proteins (Figure 17). Moreover, AL002s following intraperitoneal injection increases migration of microglia to sites of neurodegenerative damage, and restores cognitive ability in animal models (Figure 18).

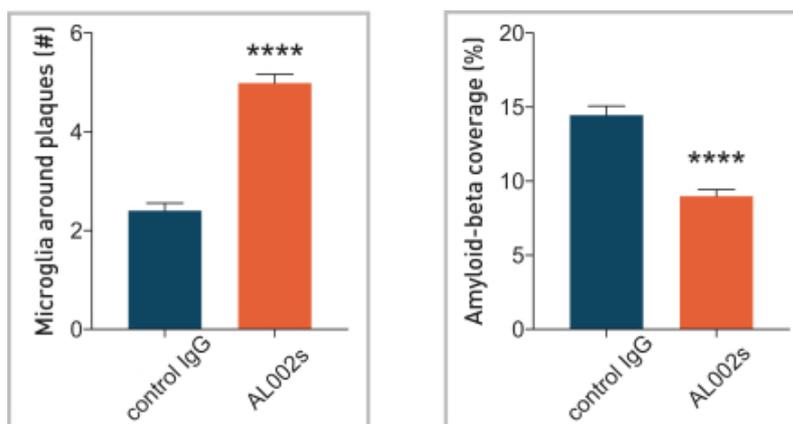


Figure 17. AL002s statistically significantly increases the number of microglia around amyloid-beta plaques (left) and reduces the area occupied by amyloid-beta plaques (right) in a mouse model of Alzheimer’s disease (**** indicates $p < 0.0001$ by T-test).

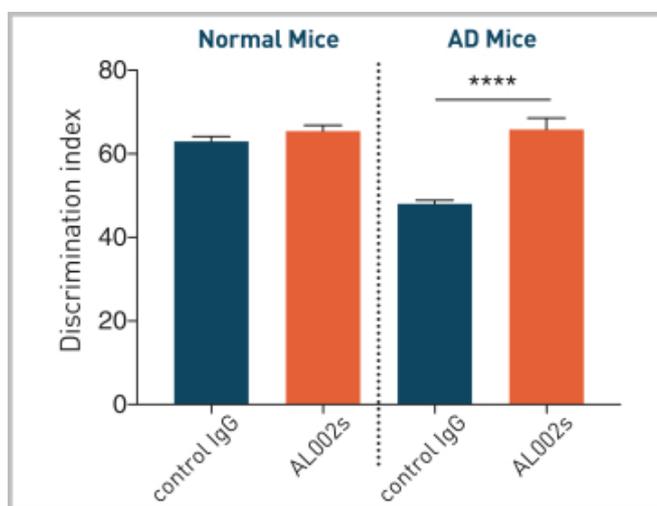


Figure 18. AL002s statistically significantly improves cognitive deficit in a mouse model of Alzheimer’s disease (**** indicates $p < 0.0001$ by T-test).

AL002 Development Strategy

In the third quarter of 2019, we completed a Phase 1a study of AL002 in healthy subjects and a dose dependent change in target engagement biomarker in cerebrospinal fluid was observed upon treatment. In the second quarter of 2019, based on safety and tolerability observed in the Phase 1a study, we initiated the Phase 1b portion of the study with AL002 in Alzheimer’s disease patients.

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Histopathological analysis of a 26-week toxicology study of AL002 in non-human primates identified minimal to marked granulomatous inflammation in the ciliary body and/or choroid of the eye. There were no other AL002-related gross or histopathological findings in this toxicology study in the retina or any other tissues or organs. We have observed no drug-related, serious adverse events in the AL002 Phase 1 trial with over 50 subjects. In response to FDA feedback, we have implemented additional ophthalmological assessments in our AL002 clinical trial. We expect proof of mechanism data from Alzheimer's disease patients in the first half of 2020.

Following the Phase 1 study, we intend to initiate a double-blind placebo-controlled Phase 2 proof-of-concept trial in Alzheimer's disease patients in early stages of the disease (Figure 19). In addition to measuring molecular and genetic biomarkers, we will also employ imaging techniques focused on pathological proteins and neuronal health for an early read-out on various molecular and genetic biomarkers, imaging assessments and clinical measures to establish proof-of-concept enabling pivotal Phase 3 studies.

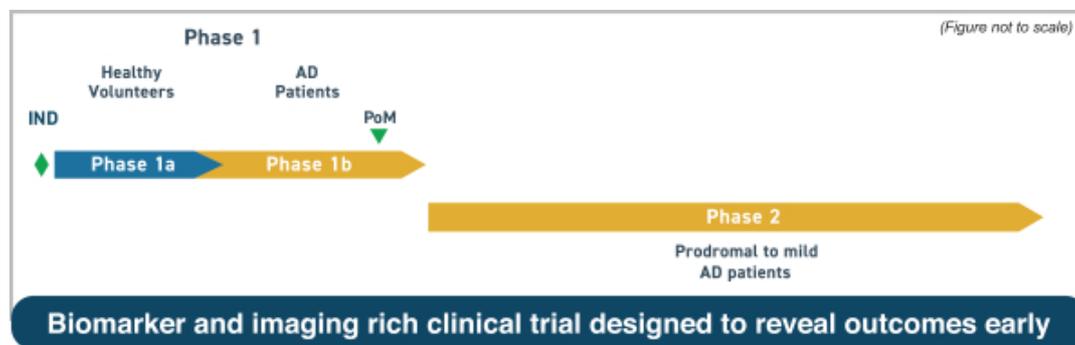


Figure 19. Clinical plan for AL002 in Alzheimer's disease. (Figure not to scale.)

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 20) 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.

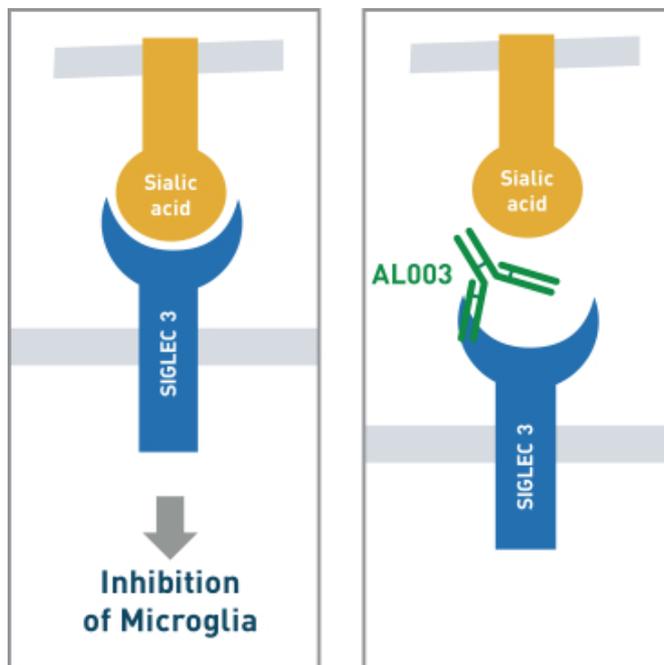


Figure 20. Mechanism of action of our SIGLEC 3 blocking product candidate AL003.

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 able to cross the blood brain barrier and exert its desired activity (Figure 21).

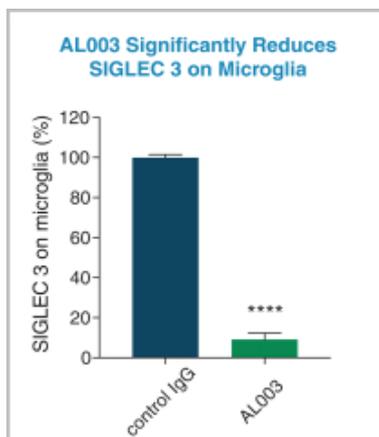


Figure 21. AL003 blocks SIGLEC 3 on microglia in mouse brain following injection to the blood stream (** indicates $p < 0.0001$ by T-test).**

AL003 Development Strategy

Our AL003 product candidate follows a similar clinical development plan to AL002 with some modifications. In the first quarter of 2019, we initiated a Phase 1a study in healthy subjects with AL003, a product candidate targeting Alzheimer’s disease. Thirty-eight (38) healthy subjects were dosed over eight dose cohorts in the AL003 Phase 1a dose escalation trial. A dose dependent change in target engagement in the blood was observed upon treatment. One subject treated with the second highest dose experienced aseptic hip monoarthritis and a second subject treated with the highest dose experienced an adverse drug reaction characterized by rash, fever, and thrombocytopenia, which were both deemed treatment-related serious adverse events. The subjects were treated with corticosteroids and recovered.

Based on the safety and tolerability observed in the Phase 1a study, we identified a dose and initiated screening for the Phase 1b portion of the study with AL003 in Alzheimer’s disease patients in the fourth quarter of 2019.

Following positive results in this trial, we intend to launch a double-blind placebo-controlled Phase 2 proof-of-concept trial in Alzheimer’s disease patients (Figure 22). During this planned Phase 2 trial, in addition to measuring molecular and genetic biomarkers, we intend to employ imaging techniques focused on pathological proteins and neuronal health for an early read out on various molecular and genetic biomarkers, imaging assessments and clinical measures to establish proof-of-concept enabling pivotal Phase 3 studies.

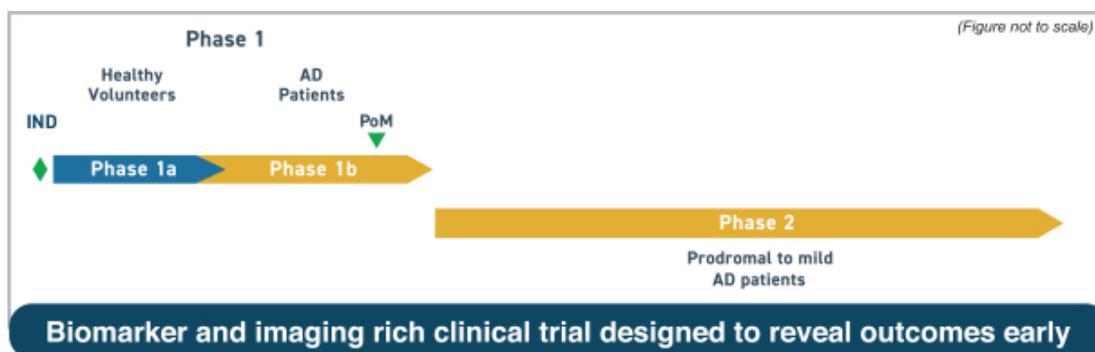


Figure 22. Clinical plan for AL003 in Alzheimer’s disease. (Figure not to scale.)

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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.”

Expansion of Our Discovery Platform to Other Indications

Immuno-oncology

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 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 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.

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 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 Series E preferred 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 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 — 2014 Adimab Collaboration Agreement (2014 Adimab Agreement)

In 2014, we entered into the 2014 Adimab Collaboration Agreement. Under the 2014 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 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.

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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

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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 30 families, which include three issued patents and over 185 pending patent applications, directed to over 15 different targets and/or technologies, that are solely owned or exclusively licensed 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 regimens. 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 four 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. Two patent families are expected to expire in 2036, the third family is expected to expire in 2039, and the fourth 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, in 2040, in all cases excluding any patent term adjustments and any patent term extensions.

TREM2 Program

We own three patent families directed to the TREM2 program covering the compositions and uses of our TREM2 program product candidates. The patent families are expected to expire in 2035, 2036, and 2038, respectively, in all cases excluding any patent term adjustments and any patent term extensions.

SIGLEC 3 Program

We own four 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, and the fourth patent family in 2039, in all cases excluding any patent term adjustments and any patent term extensions.

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

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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. For example, on June 18, 2019, we initiated confidential arbitration proceedings 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. We are in the early stage of this arbitration proceeding and are unable to assess or provide any assurances regarding its possible outcome.

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 and Parkinson's disease, 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 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 IND, which must become effective before human clinical trials may begin;
- Approval by an independent 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 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.

Preclinical Studies and IND

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

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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 subjects 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.

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.

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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 FY 2020 fee schedule for prescription drug user fees, which became effective on October 1, 2019, and will remain in effect through September 30, 2020, 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 (\$325,424 in 2020) 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

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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 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 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

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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 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.

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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 Neuroscience Clinical Research Unit
Marco Colonna, M.D.	Washington University School of Medicine in St. Louis
Stephen Hauser, M.D.	Chair of the Department of Neurology at UCSF
Michael Heneka, M.D.	Chair of the Department of Neurology at University of Bonn
Lewis Lanier, Ph.D.	Chair of the Department of Microbiology and Immunology at UCSF
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 Feinberg School of Medicine

Employees

As of September 30, 2019, we had 109 full-time employees, over 70% 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.

Facilities

Our corporate headquarters are currently located in South San Francisco, California, where we lease approximately 105,000 square feet of office, research and development, engineering, and laboratory space pursuant to a lease agreement that expires in April 2029, with an option to extend the term of the lease for an additional 10 years. The new lease agreement also provides us a right of first offer to expand into available office space in the building. We lease 8,763 square feet of additional office and laboratory space in Milpitas, 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.

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 initiated an arbitration against a third party as set forth below. Regardless of outcome, litigation can have an adverse impact on us because of defense 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. We are in the early stage of this arbitration proceeding and are unable to assess or provide any assurances regarding its possible outcome.

MANAGEMENT

Executive Officers and Directors

The following table sets forth the names, ages, and positions of our executive officers and directors as of September 30, 2019:

<u>Name</u>	<u>Age</u>	<u>Position</u>
Executive Officers:		
Arnon Rosenthal, Ph.D.	64	Co-Founder, Chief Executive Officer, and Director
Robert Paul, M.D., Ph.D.	52	Chief Medical Officer
Robert King, Ph.D.	56	Chief Development Officer
Sabah Oney, Ph.D.	37	Chief Business Officer
Calvin Yu	43	Vice President, Finance
Non-Employee Directors:		
Tillman Gerngross, Ph.D.	55	Co-Founder and Chairperson
Louis J. Lavigne, Jr.* ⁽¹⁾⁽²⁾	71	Director
Terry McGuire ⁽¹⁾⁽³⁾	63	Director
Richard Scheller, Ph.D. ⁽²⁾⁽³⁾	65	Director
David Wehner ⁽¹⁾	50	Director
Kristine Yaffe, M.D. ⁽³⁾	57	Director

* Lead independent director

(1) Member of the audit committee.

(2) Member of the compensation committee.

(3) Member of the corporate governance and nominating committee.

Executive Officers

Arnon Rosenthal, Ph.D., Co-Founder, Chief Executive Officer, and Director. Dr. Rosenthal co-founded Alector in 2013 and has served as a member of our board of directors, as Chief Executive Officer, and as our President since 2013. Dr. Rosenthal co-founded Annexon Biosciences, Inc. and served as its acting Chief Executive Officer from August 2011 to December 2014 and served as a member of the board of directors, including as Chairman from August 2011 February 2017. Dr. Rosenthal co-founded Rinat Neuroscience Corporation (acquired by Pfizer Inc. in August 2006), and served as President, Chief Scientific Officer and as a member of the board of directors from August 2001 to August 2006. From January 1985 to August 2001, Dr. Rosenthal served in various roles at Genentech, Inc., where he ultimately served as Staff Scientist and was appointed as a permanent member of Genentech's Research Review Committee where his team discovered the target for the cancer drug Erivedge. Dr. Rosenthal conducted his post-doctoral fellowship at Genentech, Inc. He holds a Ph.D. in biology from the Hebrew University of Jerusalem.

We believe Dr. Rosenthal is qualified to serve on our board of directors because of the perspective and experience he provides as one of our founders and as our Chief Executive Officer, his experience as a founder and director of other life sciences companies, his educational background, as well as his broad experience within the pharmaceutical industry, particularly in the area of neuroscience and drug discovery and development.

Robert Paul, M.D., Ph.D., Chief Medical Officer. Dr. Paul has served as our Chief Medical Officer since October 2016. Dr. Paul joined Alector from Genentech, Inc., where he held various roles of increasing responsibility between 2009 and 2016, including as Assistant Group Medical Director and TA Head Neuroscience Early Clinical Development gRED from October 2015 to October 2016, as Senior Medical Director from October 2013 to September 2015, as Medical Director from September 2011 to October 2013, and as Associate Medical Director from January 2009 to September 2011. From May 2002 to December 2008,

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Dr. Paul served as a Neurologist at the University of Munich. Dr. Paul is a board certified neurologist in Germany. He received a M.D. and a Ph.D. from Ludwig-Maximilians Universität München.

Robert King, Ph.D., Chief Development Officer. Dr. King has served as our Chief Development Officer since January 2017. Dr. King joined Alector from SciClone Pharmaceuticals, Inc. (acquired by a consortium led by GL Capital Partners, LLC), a biotechnology company, where he served as Senior Vice President of Product Development and Supply Chain from June 2011 to January 2017. Prior to SciClone Pharmaceuticals, Dr. King served as VP of Product Development and Manufacturing at Bayhill Therapeutics, Inc., a biotechnology company from 2006 to 2011. Dr. King served as VP Product Development and Manufacturing at Rinat Neuroscience Corp. (acquired by Pfizer), a biotechnology company, from 2003 to 2006. Dr. King served in positions of increasing responsibility at COR Therapeutics, Inc. (acquired by Millennium Pharmaceuticals, Inc. in 2002) from 1993 to 2003. From 1991 to 1993, Dr. King served as a Scientist in the Purification and Pharmaceutical Sciences groups at California Biotechnology/Scios. From 1988 to 1991, Dr. King was a Scientist at Molecular Devices Corporation. Dr. King received a Ph.D. in Chemical Engineering from the University of California, Berkeley, and a B.S. in Chemical Engineering from the University of Washington.

Sabah Oney, Ph.D., Chief Business Officer. Dr. Oney joined Alector in October 2016. He has served as our Chief Business Officer since January 2018 and previously as our Vice President of Business Development and Operations since October 2016. From January 2016 until October 2016, Dr. Oney served as a consultant to a number of biotechnology companies. Dr. Oney previously served as Head of Global Sales and Business Development at Ariosa Diagnostics, Inc. (now a member of Roche Holding AG), a biotechnology company, from October 2015 to January 2016, and as Director of Business Development from September 2012 to October 2015. Dr. Oney received a Ph.D. in Genetics and Genomics from Duke University, an M.B.A. from Stanford University Graduate School of Business, and a B.S. in Genetics from the University of Kansas.

Calvin Yu, Vice President, Finance. Mr. Yu has led our Finance team since June 2017. Mr. Yu joined Alector from Stemcentrx, Inc. (acquired by AbbVie), a biotechnology company, where he served as Corporate Controller from February 2016 to June 2017. Prior to Stemcentrx, Mr. Yu held several senior level finance roles at publicly traded biotechnology companies, including Senior Director of Finance and SEC Reporting at Adverum Biotechnologies, Inc. from September 2014 to February 2016, and Controller at Five Prime Therapeutics, Inc. from March 2010 to September 2014. Mr. Yu received his B.S. in Accounting from San Francisco State University, College of Business.

Non-Employee Directors

Tillman Gerngross, Ph.D., Co-Founder and Chairperson. Dr. Gerngross co-founded Alector in 2013 and has served as a member of our board of directors and as Chairperson since 2013. Dr. Gerngross is a founder, director, and executive officer of numerous biotechnology companies. He is a founder and currently serving as Chief Executive Officer and as a director of Adimab, LLC. He is also a founder and Chairman of the board of directors of Avitide, Inc. and a founder and the Chairman of the board of directors of Arsanis, Inc. Dr. Gerngross is currently a Venture Partner at SV Life Sciences Advisors, LLC, which he joined in 2006. Dr. Gerngross co-founded GlycoFi, Inc. and served as its Chief Scientific Officer from 2000 to 2006 until it was acquired by Merck & Company, Inc. Dr. Gerngross currently teaches in the departments of Biology and Chemistry, as well as at the School of Engineering at Dartmouth College, where he has taught since 1998. Dr. Gerngross attended the Technical University of Vienna, Austria, where he received a B.S. and M.S. in Chemical Engineering and a Ph.D. in Molecular Biology.

We believe Dr. Gerngross is qualified to serve on our board of directors because of the perspective and experience he provides as one of our founders, his expertise and experience in antibody drug discovery and development, his experience as a founder and director of other life sciences companies, his educational background, and his experience working in the venture capital industry.

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Louis J. Lavigne, Jr. Mr. Lavigne has served as a member of our board of directors and as our Lead Independent Director since October 2018. Mr. Lavigne has been a Managing Director of Lavrite, LLC, a management consulting firm specializing in the areas of corporate finance, accounting, growth strategy, and management, since 2005. Mr. Lavigne served in various executive capacities with Genentech, Inc. for over 20 years, including, Chief Financial Officer from 1988 to 2005, Executive Vice President from 1997 to 2005, Senior Vice President from 1994 to 1997, Vice President from 1986 to 1994, and Controller from 1983 to 1986. He has served as a director, chair of the audit committee, and member of the compensation committee of DocuSign Inc., an eSignature transaction management company, since July 2013; as a member of the board of directors of Zynga Inc., a social game company, since 2015, including as audit committee chairman and compensation committee member since 2015 and as Lead Director since 2017; and as chairman of the board of directors and chairperson of the compensation committee of Accuray Incorporated, a radiation oncology company, since September 2009. Within the last five years, Mr. Lavigne also served on the board of directors, the audit committee, and the science and technology committee of Allergan, Inc., a global health care company, from 2005 until its acquisition by Actavis plc in 2015; as a director and chair of the audit committee of NovoCure Limited, an oncology company, from 2013 until October 2018; as a director, chair of the compensation committee and member of the audit committee of Assertio Therapeutics, Inc., a pharmaceutical company, since July 2013 until his resignation in May 2019; as a director and chair of the audit committee of SafeNet, Inc., a private information security company, from 2010 until its acquisition by Gemalto NV in 2015; and as a director and chair of the audit committee of BMC Software, Inc., an enterprise systems software vendor, from 2004 to 2007 and from 2008 to 2013, when it was acquired by a private investor group. Mr. Lavigne serves as a board member and is the former chairman of the UCSF Benioff Children's Hospitals and the UCSF Benioff Children's Hospitals Foundation where he is also a member of the audit and finance committees. Mr. Lavigne holds a B.S. in Business Administration from Babson College and an M.B.A. from Temple University.

We believe Mr. Lavigne is qualified to serve on our board of directors because of his extensive experience in business operations and management, strategy, finance, accounting, and public company governance as a chief financial officer of a large, complex publicly-traded company and his extensive board leadership positions with a number of public company boards and audit committees.

Terry McGuire. Mr. McGuire has served as a member of our board of directors since 2013. Additionally, Mr. McGuire is a Founding Partner of Polaris Partners, a venture capital firm investing in technology and healthcare companies across all stages of development, where he has worked since 1996. Mr. McGuire serves on the board of directors of Cycleron, Inc., a publicly traded biotechnology company, since January 2019 and Pulmatrix, Inc., a publicly traded biopharmaceutical company, where he has served since May 2016. Mr. McGuire served on the board of directors of Trevena, Inc., a publicly traded biopharmaceutical company, from January 2008 to July 2014; on the board of Ironwood Pharmaceuticals, Inc., a publicly traded drug manufacturer, from 1998 to 2019 and on the board of directors of Arsanis, Inc., a publicly traded biopharmaceutical company, from 2011 to 2019. Mr. McGuire is emeritus Chairman of the National Venture Capital Association, Chairman of the Global Ventures Capital Congress and chairs the board of the Thayer School of Engineering at Dartmouth College. He also sits on the boards of Massachusetts Institute of Technology's The David H. Koch Institute for Integrative Cancer Research, The Arthur Rock Center for Entrepreneurship at Harvard Business School and The Healthcare Initiative Advisory Board. Mr. McGuire holds an M.B.A. from Harvard Business School, and a M.S. in engineering from the Thayer School at Dartmouth College, and a B.S. in physics and economics from Hobart College.

We believe Mr. McGuire is qualified to serve on our board of directors because of his expertise and experience in the biotechnology industry through his role as a Founding Partner of Polaris Partners and his cumulative career in venture capital over a period spanning over 35 years, in which he has been involved in the evaluation, investment and oversight of numerous biotechnology companies, as well as his experience as a director of several biotechnology companies, including other public companies.

Richard Scheller, Ph.D. Dr. Scheller has served as a member of our board of directors since October 2018. Dr. Scheller has served as the Chairman of Research and Development at BridgeBio Pharma LLC since January

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2019 and as a member of its board of directors since January 2018. Dr. Scheller previously served as Chief Scientific Officer at 23andMe, a personal genetics company, from April 2015 to April 2019. Previously, Dr. Scheller was the Executive Vice President of Research and Early Development and a member of the Executive Committee at Genentech, Inc. from February 2001 to December 2014. From January 2009 to December 2014, Dr. Scheller was also a member of the Enlarged Executive Committee at Hoffmann-La Roche Ltd. Since February 2015, Dr. Scheller has served as a member of the board of directors for ORIC Pharmaceuticals, Inc. Since March 2015, Dr. Scheller has served as a member of the board of directors for Xenon Pharmaceuticals Inc. Since January 2018, Dr. Scheller has served as a member of the board of directors of BridgeBio Inc. Dr. Scheller's research on elucidating the molecular machinery and regulatory mechanism that underlie the release of neurotransmitters earned him the 2013 Albert Lasker Basic Medical Research Award. He is a member of the National Academy of Sciences and a member of the National Academy of Medicine. Dr. Scheller holds a Ph.D. in Chemistry from the California Institute of Technology and B.Sc. in Biochemistry from the University of Wisconsin-Madison. He completed his post-doctorate in Molecular Neurobiology at Columbia University.

We believe Dr. Scheller is qualified to serve on our board of directors because of his scientific background and his senior management experience in the pharmaceutical industry.

David Wehner. Mr. Wehner has served as a member of our board of directors since October 2018. He has served as Chief Financial Officer of Facebook, Inc. since June 2014. Mr. Wehner joined Facebook, Inc. in November 2012 as Vice President, Corporate Finance and Business Planning. From August 2010 until November 2012, Mr. Wehner served as Chief Financial Officer at Zynga Inc., a provider of social game services. From February 2001 to July 2010, Mr. Wehner served in various positions at Allen & Company, an investment bank, including as a Managing Director from November 2006 to July 2010 and as a director from December 2005 to November 2006. Mr. Wehner holds an M.S. in applied physics from Stanford University and a B.S. in chemistry from Georgetown University.

We believe Mr. Wehner is qualified to serve on our board of directors based on his substantial executive, strategy, finance, and operational experience.

Kristine Yaffe, M.D. Dr. Yaffe has served as a member of our board directors since August 2019. Dr. Yaffe is currently a professor of psychiatry, neurology and epidemiology at the University of California, San Francisco (UCSF) and has served in that role since 2007. Dr. Yaffe has also served as the Roy and Marie Scola Endowed Chair since 2009 and Vice Chair in Psychiatry at UCSF since 2016. Dr. Yaffe has received numerous awards for her groundbreaking contributions to the field including the American Academy of Neurology Potamkin Prize for Research in Pick's, Alzheimer's, and Related Diseases. Dr. Yaffe holds a B.S. in biology-psychology from Yale University, an M.D. from the University of Pennsylvania School of Medicine and has completed residencies in neurology and psychiatry at the University of California, San Francisco.

We believe Dr. Yaffe is qualified to serve on our board of directors based on her experience as an internationally recognized expert in the field of cognitive aging, neurodegeneration and dementia.

Board Composition

Our board of directors currently consists of seven members. The number of directors will be fixed by our board of directors, subject to the terms of our amended and restated certificate of incorporation and amended and restated bylaws. Each of our current directors will continue to serve as a director until the election and qualification of his or her successor, or until his or her earlier death, resignation or removal.

Our amended and restated certificate of incorporation provides that our board of directors is divided into three classes with staggered three-year terms. Only one class of directors will be elected at each annual meeting

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of stockholders, with the other classes continuing for the remainder of their respective three-year terms. Our current directors are divided among the three classes as follows:

- the Class I directors consist of Dr. Rosenthal and Mr. Wehner, and their terms will expire at the annual meeting of stockholders to be held in 2022;
- the Class II directors consist of Mr. McGuire and Dr. Yaffe, and their terms will expire at the annual meeting of stockholders to be held in 2020; and
- the Class III directors consist of Drs. Gerngross and Scheller and Mr. Lavigne, and their terms will expire at the annual meeting of stockholders to be held in 2021.

At each annual meeting of stockholders, upon the expiration of the term of a class of directors, the successor to each such director in the class will be elected to serve from the time of election and qualification until the third annual meeting following his or her election and until his or her successor is duly elected and qualified, in accordance with our amended and restated certificate of incorporation. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of our directors.

This classification of our board of directors may have the effect of delaying or preventing changes in control of our company.

Director Independence

Our common stock is listed on the NASDAQ Global Select Market (NASDAQ). Under the rules of NASDAQ, independent directors must comprise a majority of a listed company's board of directors within one year of the completion of our initial public offering. In addition, the rules of NASDAQ require that, subject to specified exceptions, each member of a listed company's audit, compensation and corporate governance, and nominating committees be independent. Audit committee members and compensation committee members must also satisfy the independence criteria set forth in Rule 10A-3 and Rule 10C-1, respectively, under the Exchange Act. Under the rules of NASDAQ, a director will only qualify as an "independent director" if, in the opinion of that company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

To be considered to be independent for purposes of Rule 10A-3 and under the rules of NASDAQ, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors or any other board committee: (1) accept, directly or indirectly, any consulting, advisory or other compensatory fee from the listed company or any of its subsidiaries or (2) be an affiliated person of the listed company or any of its subsidiaries.

To be considered independent for purposes of Rule 10C-1 and under the rules of NASDAQ, the board of directors must affirmatively determine that each member of the compensation committee is independent, including a consideration of all factors specifically relevant to determining whether the director has a relationship to the company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (1) the source of compensation of such director, including any consulting, advisory, or other compensatory fee paid by the company to such director and (2) whether such director is affiliated with the company, a subsidiary of the company or an affiliate of a subsidiary of the company.

Our board of directors undertook a review of its composition, the composition of its committees, and the independence of our directors and considered whether any director has a material relationship with us that could compromise his or her ability to exercise independent judgment in carrying out his or her responsibilities. Based upon information requested from and provided by each director concerning his background, employment, and

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affiliations, including family relationships, our board of directors has determined that Drs. Scheller and Yaffe and Messrs. Lavigne, McGuire, and Wehner do not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is “independent” as that term is defined under the rules of NASDAQ.

In making these determinations, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director, and the transactions involving them described in the section titled “Certain Relationships and Related Party Transactions” incorporated by reference into this prospectus. There are no family relationships among any of our directors or executive officers.

Lead Independent Director

Our board of directors has appointed Louis J. Lavigne, Jr. to serve as our Lead Independent Director. As a general matter, our board of directors believes that appointing a Lead Independent Director, when either our Chief Executive Officer serves as Chairman or when our Chairman is not independent, creates an environment that encourages objective oversight of management’s performance and enhances the effectiveness of our board of directors as a whole. As Lead Independent Director, Mr. Lavigne will preside over periodic meetings of our independent directors, serve as a liaison between our Chairperson, Chief Executive Officer, and our independent directors and perform such additional duties as our board of directors may otherwise determine and delegate.

Role of the Board in Risk Oversight

Our board of directors has an active role, as a whole and also at the committee level, in overseeing the management of our risks. Our board of directors is responsible for general oversight of risks and regular review of information regarding our risks, including credit risks, liquidity risks, and operational risks. The compensation committee is responsible for overseeing the management of risks relating to our executive compensation plans and arrangements. The audit committee is responsible for overseeing the management of risks relating to accounting matters and financial reporting and potential conflicts of interest. The corporate governance and nominating committee is responsible for overseeing the management of risks associated with the independence of our board of directors. Although each committee is responsible for evaluating certain risks and overseeing the management of such risks, our entire board of directors is regularly informed through discussions from committee members about such risks. Our board of directors believes its administration of its risk oversight function has not negatively affected the board of directors’ leadership structure.

Board Committees

Our board of directors has an audit committee, a compensation committee, and a corporate governance and nominating committee, each of which has the composition and the responsibilities described below.

Audit Committee

The members of our audit committee are Messrs. Lavigne, McGuire and Wehner. Mr. Lavigne is the chairperson of our audit committee and both Mr. Lavigne and Mr. Wehner have been designated as audit committee financial experts, as that term is defined under the SEC rules implementing Section 407 of SOX, as each possesses financial sophistication, as defined under the rules of NASDAQ. Our audit committee oversees our corporate accounting and financial reporting process and assists our board of directors in monitoring our financial systems. Our audit committee will also:

- select and hire the independent registered public accounting firm to audit our financial statements;
- help to ensure the independence and performance of the independent registered public accounting firm;

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- approve audit and non-audit services and fees;
- review financial statements and discuss with management and the independent registered public accounting firm our annual audited and quarterly financial statements, the results of the independent audit and the quarterly reviews and the reports and certifications regarding internal controls over financial reporting and disclosure controls;
- prepare the audit committee report that the SEC requires to be included in our annual proxy statement;
- review reports and communications from the independent registered public accounting firm;
- review the adequacy and effectiveness of our internal controls and disclosure controls and procedure;
- review our policies on risk assessment and risk management;
- review and monitor conflicts of interest situations, and approve or prohibit any involvement in matters that may involve a conflict of interest or taking of a corporate opportunity;
- review related party transactions; and
- establish and oversee procedures for the receipt, retention, and treatment of accounting related complaints and the confidential submission by our employees of concerns regarding questionable accounting or auditing matters.

Our audit committee operates under a written charter, which satisfies the applicable rules of the SEC and the listing standards of NASDAQ.

Compensation Committee

The members of our compensation committee are Dr. Scheller and Mr. Lavigne. Dr. Scheller is the chairperson of our compensation committee. Our compensation committee oversees our compensation policies, plans, and benefits programs. The compensation committee will also:

- oversee our overall compensation philosophy and compensation policies, plans, and benefit programs;
- review and approve or recommend to the board of directors for approval compensation for our executive officers and directors;
- prepare the compensation committee report that the SEC will require to be included in our annual proxy statement; and
- administer our equity compensation plans.

Our compensation committee operates under a written charter, which satisfies the applicable rules of the SEC and the listing standards of NASDAQ.

Corporate Governance and Nominating Committee

The members of our corporate governance and nominating committee are Drs. Scheller and Yaffe and Mr. McGuire. Mr. McGuire is the chairperson of our corporate governance and nominating committee. Our corporate governance and nominating committee oversees and assists our board of directors in reviewing and recommending nominees for election as directors. Specifically, the corporate governance and nominating committee will:

- identify, evaluate, and make recommendations to our board of directors regarding nominees for election to our board of directors and its committees;
- consider and make recommendations to our board of directors regarding the composition of our board of directors and its committees;

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- review developments in corporate governance practices;
- evaluate the adequacy of our corporate governance practices and reporting; and
- evaluate the performance of our board of directors and of individual directors.

Our corporate governance and nominating committee operates under a written charter, which satisfies the applicable rules of the SEC and the listing standards of NASDAQ.

Scientific Advisory Board Compensation

We also reimburse each member of our scientific advisory board for all reasonable and necessary expenses in connection with the performance of his or her services. In addition, we grant each new member an option to purchase shares of our common stock and in the future, we may make additional grants or may make cash compensation payments to our scientific advisory board members for continued service on the scientific advisory board.

Director Compensation

Directors who are also our employees receive no additional compensation for their service as directors. Dr. Rosenthal was our only employee director during 2018. See the section titled “Executive Compensation” for additional information about Dr. Rosenthal’s compensation.

The following table presents the total compensation each of our non-employee directors received during the year ended December 31, 2018. Dr. Yaffe is not included in this table, as she joined our board of directors in August 2019. Other than as set forth in the table, we did not pay any compensation, make any equity awards or non-equity awards to or pay any other compensation to any of our non-employee directors in 2018.

	<u>Fees Earned or Paid in Cash (\$)</u>	<u>Option Awards (\$)(1)</u>	<u>All Other Compensation (\$)</u>	<u>Total (\$)</u>
Tillman Gerngross, Ph.D.(2)	—	—	25,000	25,000
Christine Brennan, Ph.D.(3)	—	—	—	—
Louis J. Lavigne, Jr.(4)	—	501,900	—	501,900
Carl Gordon, Ph.D., C.F.A.(5)	—	—	—	—
Terry McGuire	—	—	—	—
Richard Scheller, Ph.D.(6)	—	583,221	—	583,221
David Wehner(7)	—	500,630	—	500,630

- (1) The amounts disclosed represent the aggregate grant date fair value of the award as calculated in accordance with ASC 718. The assumptions used in calculating the grant date fair value of the award disclosed in this column are set forth in the notes to our audited financial statements incorporated by reference in this prospectus. These amounts do not correspond to the actual value that may be recognized by the directors upon vesting of the applicable awards.
- (2) We paid Dr. Gerngross \$25,000 in consulting fees in 2018. As of December 31, 2018, Dr. Gerngross held 70,208 restricted shares of our common stock. One-fourth of the total number of shares subject to the restricted stock grant vested on the one year anniversary of July 15, 2015, and an additional 1/48th of the total number of shares subject to the restricted stock grant vested, and continue to vest, on the same day of each month thereafter, subject to Dr. Gerngross’ continued status as a service provider through each such vesting date.
- (3) Dr. Brennan resigned from our board of directors in February 2019.
- (4) As of December 31, 2018, Mr. Lavigne held an option to purchase 70,000 shares of our common stock. One-fourth of the total number of shares subject to the option grant vest on the one year anniversary of October 25, 2018, and an additional 1/48th of the total number of shares subject to the option grant vest on

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- the same day of each month thereafter, subject to Mr. Lavigne's continued status as a service provider through each such vesting date.
- (5) Dr. Gordon resigned from our board of directors in June 2019.
- (6) As of December 31, 2018, Dr. Scheller held an option to purchase 70,000 shares of our common stock. One-fourth of the total number of shares subject to the option grant vest on the one year anniversary of October 22, 2018, and an additional 1/48th of the total number of shares subject to the option grant vest on the same day of each month thereafter, subject to Dr. Scheller's continued status as a service provider through each such vesting date. As of December 31, 2018, Dr. Scheller held an option to purchase 11,834 shares of our common stock. The shares subject to this option vest one forty-eighth per month beginning on the one month anniversary of October 22, 2018, subject to Dr. Scheller's continued status as a service provider on each such vesting date. As of December 31, 2018, Dr. Scheller held 19,981 restricted shares of our common stock. One-fourth of the total number of shares subject to the restricted stock grant vested on the one year anniversary of July 31, 2015, and an additional 1/48th of the total number of shares subject to the restricted stock grant vested, and continued to vest, on the same day of each month thereafter, subject to Dr. Scheller's continued status as a service provider through each such vesting date.
- (7) As of December 31, 2018, Mr. Wehner held an option to purchase 70,000 shares of our common stock. One-fourth of the total number of shares subject to the option grant vest on the one year anniversary of October 9, 2018, and an additional 1/48th of the total number of shares subject to the option grant vest on the same day of each month thereafter, subject to Mr. Wehner's continued status as a service provider through each such vesting date.

Non-Employee Director Compensation Policy

We have retained Radford, a national compensation consultant, to provide our board of directors with an analysis of market data compiled from certain comparable public companies and assistance in determining compensation of directors. Our board of directors has adopted our Outside Director Compensation Policy. Our Outside Director Compensation Policy provides that all non-employee directors will be entitled to receive the following cash compensation for their services:

- \$35,000 retainer per year for each non-employee director;
- \$20,000 retainer per year for service as non-executive chairman of the board of directors;
- \$20,000 retainer per year for service as lead non-employee director;
- \$15,000 retainer per year for the chairman of the audit committee or \$7,500 retainer per year for each other member of the audit committee;
- \$10,000 retainer per year for the chairman of the compensation committee or \$5,000 retainer per year for each other member of the compensation committee; and
- \$8,000 retainer per year for the chairman of the nominating and corporate governance committee or \$4,000 retainer per year for each other member of the nominating and corporate governance committee.

Each non-employee director who serves as the chair of a committee will receive only the additional annual fee as the chair of the committee and will not receive the additional annual fee as a member of the committee. All cash payments to non-employee directors are paid quarterly in arrears on a prorated basis.

In addition to the cash compensation structure described above, our Outside Director Compensation Policy provides the following equity incentive compensation program for non-employee directors. Each non-employee director who first joins us (other than a director who becomes a non-employee director as a result of terminating employment with us) automatically will be granted on the first trading date on or after his or her start date as a non-employee director a one-time, initial option covering 40,000 shares of our common stock. Further, on the date of each of our annual stockholder meetings, each non-employee director who is continuing as a director

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following our annual stockholder meeting automatically will be granted an annual option covering 20,000 shares of our common stock.

Each initial option will vest as to 1/4th of the underlying shares on the one-year anniversary of the date the director's service as a non-employee director started and as to 1/48th of the underlying shares each following month, subject to continued service through each relevant vesting date. Each annual option will vest as to 1/12th of the underlying shares each month after the award's grant date and will vest in full on the earlier of the 12-month anniversary of the date of grant or on the date of our annual stockholder meetings following the date the annual option is granted, subject to continued service through each relevant vesting date. In the event of a change in control of our company, all equity awards granted to a non-employee director (including those granted pursuant to our Outside Director Compensation Policy) will fully vest and become immediately exercisable, subject to continued service through such date. Each initial option and annual option will have a term of 10 years and will have an exercise price per share equal to 100% of the fair market value of a share of our common stock.

In any fiscal year, a non-employee director may be paid, issued, or granted cash compensation and equity awards with a total value of no greater than \$750,000 (increased to \$1,000,000 in the fiscal year of his or her initial service as an outside director) with the value of an equity award based on its grant date fair value for purposes of this limit (annual director limit). Equity awards or cash compensation granted to a non-employee director for his or her service as an employee or consultant (other than a non-employee director) will not count toward the annual director limit.

Our Outside Director Compensation Policy also provides for the reimbursement of our non-employee directors for reasonable, customary and documented travel expenses to attend meetings of our board of directors and committees of our board of directors.

Compensation for our non-employee directors is not limited to the equity awards and payments set forth in our Outside Director Compensation Policy. Our non-employee directors will remain eligible to receive equity awards and cash or other compensation outside of the Outside Director Compensation Policy, as may be provided from time to time at the discretion of our board of directors. For further information regarding the equity compensation of our non-employee directors, see the section of this prospectus titled "*Executive Compensation—Employee Benefit and Stock Plans—2019 Equity Incentive Plan.*"

Compensation Committee Interlocks and Inside Participation

None of the members of our compensation committee is or has been an officer or employee of our company. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors, or compensation committee (or other board committee performing equivalent functions or, in the absence of any such committee, the entire board of directors) of any entity that has one or more executive officers serving on our board of directors or compensation committee.

Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers, and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller or, persons performing similar functions. The code of business conduct and ethics is available on our website at www.alector.com. We intend to disclose future amendments to such code, or any waivers of its requirements, applicable to any principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions, or our directors on our website identified above. Information contained on the website is not incorporated by reference into this prospectus and should not be considered to be part of this prospectus.

EXECUTIVE COMPENSATION

Our named executive officers for the year ended December 31, 2018, which consist of our principal executive officer and the next two most highly compensated executive officers, are:

- Arnon Rosenthal, Ph.D., our Co-Founder and Chief Executive Officer;
- Robert Paul, M.D., Ph.D., our Chief Medical Officer; and
- Robert King, Ph.D., our Chief Development Officer.

Summary Compensation Table

The following table sets forth information regarding the compensation of our named executive officers for the year ended December 31, 2018.

Name and Principal Position	Year	Salary (\$)	Bonus (\$)	Stock Awards (\$)(1)	Option Awards (\$)(1)	All Other Compensation (\$)	Total (\$)
Arnon Rosenthal, Ph.D	2018	\$396,764	\$237,540(2)	—	\$4,816,115	\$3,564(3)	\$5,453,983
<i>Co-Founder and Chief Executive Officer</i>	2017	\$370,001	\$140,600(4)	\$2,881,057	—	\$3,564(3)	\$3,395,222
Robert King, Ph.D	2018	\$352,297	\$147,800(2)	—	\$1,570,355	\$2,323(3)	\$2,072,775
<i>Chief Development Officer</i>	2017	\$316,898	\$103,700(4)	\$1,309,005	—	\$1,180(3)	\$1,730,783
Robert Paul, M.D., Ph.D	2018	\$326,367	\$180,670(2)(5)	—	\$2,707,815	\$1,243(3)	\$3,216,095
<i>Chief Medical Officer</i>							

- (1) The amounts disclosed represent the aggregate grant date fair value of the award as calculated in accordance with ASC 718. The assumptions used in calculating the grant date fair value of the award disclosed in this column are set forth in the notes to our audited financial statements incorporated by reference in this prospectus. These amounts do not correspond to the actual value that may be recognized by the named executive officers upon vesting of the applicable awards.
- (2) The amounts reported represent a bonus earned upon the achievement of company objectives for the fiscal year ended December 31, 2018, which is expected to be paid in March 2019.
- (3) The amounts reported include life insurance premiums paid by us on behalf of our named executive officers.
- (4) The amounts reported represent a bonus based upon the achievement of company objectives for the year ended December 31, 2017, which was paid in March 2018.
- (5) The amount included in the “Bonus” column includes a portion of a signing bonus earned and paid in 2018 to Dr. Paul in the aggregate amount of \$43,750.

Outstanding Equity Awards at Fiscal Year-End

The following table sets forth information concerning outstanding equity awards held by each of our named executive officers as of December 31, 2018:

Name	Grant Date	Option Awards				Stock Awards	
		Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price (\$)(1)	Option Expiration Date	Number of Shares of Stock That Have Not Vested (#)	Market Value of Shares of Stock That Have Not Vested (\$)(2)
Arnon Rosenthal, Ph.D.	04/10/2015(3)					12,370(4)	125,432
	07/17/2015(3)					30,716(5)	311,461
	08/09/2017(3)					195,905(6)	1,986,477
	08/09/2017(7)					121,655(8)	1,233,582
	07/02/2018(9)	52,083(10)	447,917(10)	\$ 8.16	07/02/2028		—
	11/06/2018(9)		275,000(11)	\$ 10.14	11/06/2028		—
Robert King, Ph.D.	01/26/2017(3)					279,853(12)	2,837,710
	07/02/2018(9)	15,625(13)	134,375(13)	\$ 8.16	07/02/2028		—
	11/06/2018(9)		100,000(14)	\$ 10.14	11/06/2028		—
Robert Paul, M.D., Ph.D.	11/04/2016(3)					131,123(15)	1,329,588
	08/09/2017(3)					31,761(16)	322,057
	07/02/2018(9)	36,458(17)	313,542(17)	\$ 8.16	07/02/2028		—
	11/06/2018(9)		100,000(18)	\$ 10.14	11/06/2028		—

- (1) This column represents the fair market value of a share of our common stock on the date of grant, as determined by our board of directors or its authorized committee.
- (2) Because our common stock was not traded on a public market on December 31, 2018, the market value has been calculated based on an estimated fair market value of \$10.14 per share as of December 31, 2018.
- (3) This restricted stock grant of our common stock was granted pursuant to our 2017 Plan and was converted from restricted units and profit interest units of Alector LLC pursuant to the Conversion (as defined and discussed in Note 1 of the notes to our consolidated financial statements included in the 2018 Annual Report incorporated by reference into this prospectus).
- (4) One-fourth of the total number of shares subject to the restricted stock grant vested on January 15, 2016, and an additional 1/16th of the total number of shares subject to the restricted stock grant vested, and continued to vest, quarterly thereafter, subject to Dr. Rosenthal's continued status as a service provider through each such vesting date.
- (5) One-fourth of the total number of shares subject to the restricted stock grant vested on July 17, 2016, and an additional 1/48th of the total number of shares subject to the restricted stock grant vested, and continued to vest, on the same day of each month thereafter, subject to Dr. Rosenthal's continued status as a service provider through each such vesting date.
- (6) The shares subject to the restricted stock grant vested, and continue to vest, 1/48th per month beginning on the one month anniversary of August 1, 2017, subject to Dr. Rosenthal's continued status as a service provider on each such vesting date.
- (7) This restricted stock grant of our common stock was granted outside of the 2017 Plan, but is subject to the terms of the 2017 Plan as if the grant was made under the 2017 Plan (except with respect to the forfeiture of unvested shares). The applicable grant listed above was converted from grants of restricted units of Alector LLC pursuant to the Conversion. For more information regarding the Conversion, see Note 1 of the notes to our consolidated financial statements.
- (8) The shares subject to the restricted stock grant vested, and continue to vest, 1/48th per month beginning on the one month anniversary of August 1, 2017, subject to Dr. Rosenthal's continued status as a service provider on each such vesting date.
- (9) This option to purchase shares of our common stock was granted pursuant to our 2017 Plan.

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- (10) The shares subject to this option vested, and continue to vest, 1/48th per month beginning on the one month anniversary of July 2, 2018, subject to Dr. Rosenthal's continued status as a service provider on each such vesting date.
- (11) One-fourth of the total number of shares subject to the option grant vest on the one year anniversary of November 1, 2018, and an additional 1/48th of the total number of shares subject to the option grant continue to vest, on the same day of each month thereafter, subject to Dr. Rosenthal's continued status as a service provider through each such vesting date.
- (12) One-fourth of the total number of shares subject to the restricted stock grant vested on January 26, 2018, and an additional 1/48th of the total number of shares subject to the restricted stock grant vested, and continued to vest, on the same day of each month thereafter, subject to Dr. King's continued status as a service provider through each such vesting date.
- (13) The shares subject to this option vested, and continue to vest, 1/48th per month beginning on the one month anniversary of July 2, 2018, subject to Dr. King's continued status as a service provider on each such vesting date.
- (14) One-fourth of the total number of shares subject to the option grant vest on the one year anniversary of November 1, 2018, and an additional 1/48th of the total number of shares subject to the option grant continue to vest, on the same day of each month thereafter, subject to Dr. King's continued status as a service provider through each such vesting date.
- (15) One-fourth of the total number of shares subject to the restricted stock grant vested on October 3, 2017, and an additional 1/48th of the total number of shares subject to the restricted stock grant vested, and continued to vest, on the same day of each month thereafter, subject to Dr. Paul's continued status as a service provider through each such vesting date.
- (16) The shares subject to the restricted stock grant vested, and continue to vest, 1/48th per month beginning on the one month anniversary of August 1, 2017, subject to Dr. Paul's continued status as a service provider through each such vesting date.
- (17) The shares subject to this option vested, and continue to vest, 1/48th per month beginning on the one month anniversary of July 2, 2018, subject to Dr. Paul's continued status as a service provider on each such vesting date.
- (18) One-fourth of the total number of shares subject to the option grant vest on the one year anniversary of November 1, 2018, and an additional 1/48th of the total number of shares subject to the option grant continue to vest, on the same day of each month thereafter, subject to Dr. Paul's continued status as a service provider through each such vesting date.

Employment Arrangements with Our Named Executive Officers

Dr. Arnon Rosenthal

We entered into a confirmatory employment letter with Arnon Rosenthal, our Co-Founder and Chief Executive Officer. The confirmatory employment letter has no specific term and provides that Dr. Rosenthal is an at-will employee. Dr. Rosenthal's current annual base salary is \$525,000 and he is eligible for an annual target cash incentive payment equal to 50% of his annual base salary.

Dr. Robert King

We entered into a confirmatory employment letter with Robert King, our Chief Development Officer. The confirmatory employment letter has no specific term and provides that Dr. King is an at-will employee. Dr. King's current annual base salary is \$362,500 and he is eligible for an annual target cash incentive payment equal to 40% of his annual base salary.

Dr. Robert Paul

We entered into a confirmatory employment letter with Robert Paul, our Chief Medical Officer. The confirmatory employment letter has specific term and provides that Dr. Paul is an at-will employee. Dr. Paul's

current annual base salary is \$392,100 and he is eligible for an annual target cash incentive payment equal to 40% of his annual base salary.

Executive Change in Control and Severance Agreements

We maintain a change in control and severance agreement for each of our named executive officers, which agreement would provide for certain severance and change in control benefits as described below. Each change in control and severance agreement will supersede any prior agreement or arrangement the named executive officer may have had with us that provides for severance and/or change in control payments or benefits.

If a named executive officer's employment is terminated outside the period beginning on the date of a change in control and ending 12 months following that change in control (the Change in Control Period) either (1) by the Company or any of its subsidiaries (the Company Group) without "cause" (excluding by reason of death or disability) or (2) by the named executive officer for "good reason" (as such terms are defined in the named executive officer's change in control and severance agreement), the named executive officer will receive the following benefits if he or she timely signs and does not revoke a release of claims in our favor:

- a lump-sum payment equal to 9 months (or 12 months in the case of Dr. Rosenthal) of the named executive officer's annual base salary as in effect immediately prior to such termination (or if such termination is due to a resignation for good reason based on a material reduction in base salary, then as in effect immediately prior to the reduction); and
- payment of premiums for coverage under the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended (COBRA), for the named executive officer and the named executive officer's eligible dependents, if any, for up to 9 months (or 12 months in the case of Dr. Rosenthal), or taxable monthly payments for the equivalent period in the event payment of the COBRA premiums would violate or be subject to an excise tax under applicable law.

If, within the Change in Control Period, the named executive officer's employment is terminated either (1) by the Company (or any of its subsidiaries) without cause (excluding by reason of death or disability) or (2) by the named executive officer for good reason, the named executive officer will receive the following benefits if the named executive officer timely signs and does not revoke a release of claims in our favor:

- a lump-sum payment equal to 12 months (or 18 months in the case of Dr. Rosenthal) of the named executive officer's annual base salary as in effect immediately prior to such termination (or if such termination is due to a resignation for good reason based on a material reduction in base salary, then as in effect immediately prior to the reduction) or if greater, at the level in effect immediately prior to the change in control);
- a lump-sum payment equal to 100% (or 150% in the case of Dr. Rosenthal) of the named executive officer's target annual bonus as in effect for the fiscal year in which such termination occurs;
- payment of premiums for coverage under COBRA for the named executive officer and the named executive officer's eligible dependents, if any, for up to 12 months (or 18 months in the case of Dr. Rosenthal), or taxable monthly payments for the equivalent period in the event payment of the COBRA premiums would violate or be subject to an excise tax under applicable law; and
- 100% accelerated vesting and exercisability of all outstanding equity awards and, in the case of an equity award with performance-based vesting, unless otherwise specified all performance goals and other vesting criteria generally will be deemed achieved at 100% of target levels.

If any of the amounts provided for under these change in control and severance agreements or otherwise payable to our named executive officers would constitute "parachute payments" within the meaning of Section 280G of the Internal Revenue Code and could be subject to the related excise tax, the named executive officer would be entitled to receive either full payment of benefits under his or her change in control or severance

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agreement or such lesser amount which would result in no portion of the benefits being subject to the excise tax, whichever results in the greater amount of after-tax benefits to the named executive officer. The change in control and severance agreements do not require us to provide any tax gross-up payments.

Under each named executive officer's change in control and severance agreement, the following definitions are used:

- "Cause" means:
 - the named executive officer's dishonest statements or acts with respect to any Company Group member, or any current or prospective customers, suppliers vendors or other third parties with which such entity does business;
 - the named executive officer's commission of (1) a felony or (2) any misdemeanor involving moral turpitude, deceit, dishonesty or fraud;
 - the named executive officer's failure to perform his assigned duties and responsibilities to the reasonable satisfaction of the applicable Company Group member, which failure continues, in the reasonable judgment of the Company Group member, after written notice given to him by the Company Group member;
 - the named executive officer's gross negligence, willful misconduct or insubordination with respect to any Company Group member; or
 - the named executive officer's material violation of any provision of any agreement(s) between him and any Company Group member relating to non-competition, non-solicitation, non-disclosure and/or assignment of inventions (such as the at-will employment, confidential information, invention assignment, and arbitration agreement with the named executive officer or any written Company Group policy or procedure to which the named executive officer is subject).
- "Good Reason" means that the named executive officer resigns from a Company Group member if one of the following events occurs without his consent:
 - a material reduction of his duties, authorities, or responsibilities relative to his duties, authorities, or responsibilities in effect immediately prior to the reduction, provided that (1) any change that results in Dr. Rosenthal not serving as the chief executive officer of, or reporting directly to the board of directors of, the parent corporation in a group of controlled corporations including the Company or its assets (Parent) following a change in control (other than as the result of his voluntary resignation not at the request of the successor or the Parent) will be deemed to constitute a material reduction in his duties, authorities, and responsibilities constituting "Good Reason" and (2) that continued employment of a named executive officer (other than Dr. Rosenthal) following a change in control with substantially the same duties, authorities, or responsibilities with respect to the Company Group's business and operations will not constitute "Good Reason";
 - a material diminution in his base salary except for across-the-board salary reductions similarly affecting all or substantially all similarly situated employees of the applicable Company Group member, or
 - a change of more than 50 miles in the geographic location at which he provides services to the applicable Company Group member.

For "Good Reason" to be established, the named executive officer must provide written notice to our Chief Executive Officer (or our board of directors in the case of Dr. Rosenthal) and the applicable Company Group member within 90 days immediately following such alleged events, the applicable Company Group member must fail to materially remedy such event within 30 days after receipt of such notice, and the named executive officer's resignation must be effective not later than 90 days from the occurrence of the alleged triggering event, and must not be effective until after the expiration of the notice and cure periods described above.

Executive Incentive Compensation Plan

Our board of directors has adopted our Executive Incentive Compensation Plan (the Incentive Compensation Plan). The Incentive Compensation Plan will be administered by a committee appointed by our board of directors. Unless and until our board of directors determines otherwise, our compensation committee will be the administrator of the Incentive Compensation Plan. The Incentive Compensation Plan allows our compensation committee to provide cash incentive awards to selected employees, including our named executive officers, determined by our compensation committee, based upon performance goals established by our compensation committee. Our compensation committee, in its sole discretion, will establish a target award for each participant under the Incentive Compensation Plan, which may be expressed as a percentage of the participant's average annual base salary for the applicable performance period, a fixed dollar amount, or such other amount or based on such other formula as our compensation committee determines to be appropriate.

Under the Incentive Compensation Plan, our compensation committee will determine the performance goals applicable to awards, which goals may include, without limitation: attainment of research and development milestones, bookings, business divestitures and acquisitions, cash flow, cash position, contract awards or backlog, customer renewals, customer retention rates from an acquired company, subsidiary, business unit or division, earnings (which may include earnings before interest and taxes, earnings before taxes, and net taxes), earnings per share, expenses, gross margin, growth in stockholder value relative to the moving average of the S&P 500 Index or another index, internal rate of return, market share, net income, net profit, net sales, new product development, new product invention or innovation, number of customers, operating cash flow, operating expenses, operating income, operating margin, overhead or other expense reduction, product defect measures, product release timelines, productivity, profit, retained earnings, return on assets, return on capital, return on equity, return on investment, return on sales, revenue, revenue growth, sales results, sales growth, stock price, time to market, total stockholder return, working capital, and individual objectives such as peer reviews or other subjective or objective criteria. As determined by our compensation committee, the performance goals may be based on GAAP or non-GAAP results and any actual results may be adjusted by our compensation committee for one-time items or unbudgeted or unexpected items and/or payments of actual awards under the Incentive Compensation Plan when determining whether the performance goals have been met. The goals may be on the basis of any factors our compensation committee determines relevant, and may be on an individual, divisional, business unit, segment or company-wide basis. Any criteria used may be measured on such basis as our compensation committee determines. The performance goals may differ from participant to participant and from award to award. Our compensation committee also may determine that a target award or a portion thereof will not have a performance goal associated with it but instead will be granted (if at all) in the compensation committee's sole discretion.

Our compensation committee may, in its sole discretion and at any time, increase, reduce or eliminate a participant's actual award, and/or increase, reduce or eliminate the amount allocated to the bonus pool. The actual award may be below, at or above a participant's target award, in our compensation committee's discretion. Our compensation committee may determine the amount of any increase, reduction or elimination on the basis of such factors as it deems relevant, and it will not be required to establish any allocation or weighting with respect to the factors it considers.

Actual awards will generally be paid in cash (or its equivalent) in a single lump sum only after they are earned and approved by our compensation committee. Our compensation committee has the right, in its sole discretion, to settle an actual award with a grant of an equity award under our then-current equity compensation plan, which equity award may have such terms and conditions, including vesting, as our compensation committee determines in its sole discretion. Unless otherwise determined by our compensation committee, to earn an actual award, a participant must be employed by us (or an affiliate of us, as applicable) through the date the actual award is paid. Payment of bonuses occurs as soon as administratively practicable after the end of the applicable performance period, but no later than the dates set forth in the Incentive Compensation Plan.

Our board of directors has the authority to amend or terminate the Incentive Compensation Plan provided such action does not alter or impair the existing rights of any participant with respect to any earned actual award without the participant's consent. The Incentive Compensation Plan will remain in effect until terminated in accordance with the terms of the Incentive Compensation Plan.

Employee Benefit and Stock Plans

2019 Equity Incentive Plan

Our 2019 Plan provides for the grant of incentive stock options, within the meaning of Section 422 of the Code, to our employees and any of our parent and subsidiary corporations' employees, and for the grant of nonstatutory stock options, restricted stock, restricted stock units, stock appreciation rights, performance units, and performance shares to our employees, directors, and consultants and our subsidiary corporations' employees and consultants. As of September 30, 2019, options to purchase 1,095,600 shares of our common stock remained outstanding under our 2019 Plan.

Authorized Shares. A total of 7,688,156 shares of our common stock were initially reserved for issuance pursuant to our 2019 Plan. In addition, the shares reserved for issuance under our 2019 Plan will also include (1) those shares reserved but unissued under our 2017 Plan as of the date of stockholder approval of the 2019 Plan and (2) shares of our common stock subject to or issued pursuant to awards granted under our 2017 Plan that, after the date our stockholders approved the 2019 Plan, expire or otherwise terminate without having been exercised in full or are forfeited to or repurchased by us (provided that the maximum number of shares that may be added to the 2019 Plan pursuant to (1) and (2) is 5,184,750 shares). The number of shares available for issuance under our 2019 Plan will also include an annual increase on the first day of each fiscal year beginning with our 2020 fiscal year, equal to the least of:

- 7,096,760 shares;
- 5% of the outstanding shares of our common stock as of the last day of the immediately preceding fiscal year; or
- such other amount as our board of directors may determine.

If an award expires or becomes unexercisable without having been exercised in full, is surrendered pursuant to an exchange program, or, with respect to restricted stock, restricted stock units, performance units or performance shares, is forfeited to or repurchased by us due to failure to vest, the unpurchased shares (or for awards other than stock options or stock appreciation rights, the forfeited or repurchased shares) will become available for future grant or sale under the 2019 Plan (unless the 2019 Plan has terminated). With respect to stock appreciation rights, only the net shares actually issued will cease to be available under the 2019 Plan and all remaining shares under stock appreciation rights will remain available for future grant or sale under the 2019 Plan (unless the 2019 Plan has terminated). Shares that have actually been issued under the 2019 Plan will not be returned to the 2019 Plan except if shares issued pursuant to awards of restricted stock, restricted stock units, performance shares, or performance units are repurchased by or forfeited to us, such shares will become available for future grant under the 2019 Plan. Shares used to pay the exercise price of an award or satisfy the tax withholding obligations related to an award will become available for future grant or sale under the 2019 Plan. To the extent an award is paid out in cash rather than shares, such cash payment will not result in a reduction in the number of shares available for issuance under the 2019 Plan.

Plan Administration. Our board of directors or one or more committees appointed by our board of directors will administer our 2019 Plan. The compensation committee of our board of directors will administer our 2019 Plan. In addition, if we determine it is desirable to qualify transactions under our 2019 Plan as exempt under Rule 16b-3 of the Exchange Act, such transactions will be structured to satisfy the requirements for exemption under Rule 16b-3. Subject to the provisions of our 2019 Plan, the administrator has the power to administer our 2019 Plan and make all determinations deemed necessary or advisable for administering the 2019 Plan, including

but not limited to, the power to determine the fair market value of our common stock, select the service providers to whom awards may be granted, determine the number of shares covered by each award, approve forms of award agreements for use under the 2019 Plan, determine the terms and conditions of awards (including, but not limited to, the exercise price, the time or times at which awards may be exercised, any vesting acceleration or waiver or forfeiture restrictions and any restriction or limitation regarding any award or the shares relating thereto), construe and interpret the terms of our 2019 Plan and awards granted under it, prescribe, amend and rescind rules relating to our 2019 Plan, including creating sub-plans, modify, or amend each award, including but not limited to the discretionary authority to extend the post-termination exercisability period of awards (except no option or stock appreciation right will be extended past its original maximum term), and allow a participant to defer the receipt of payment of cash or the delivery of shares that would otherwise be due to such participant under an award. The administrator also has the authority to allow participants the opportunity to transfer outstanding awards to a financial institution or other person or entity selected by the administrator and to institute an exchange program by which outstanding awards may be surrendered or cancelled in exchange for awards of the same type, which may have a higher or lower exercise price and/or different terms, awards of a different type, and/or cash or by which the exercise price of an outstanding award is increased or reduced. The administrator's decisions, interpretations, and other actions are final and binding on all participants.

Stock Options. Stock options may be granted under our 2019 Plan. The exercise price of options granted under our 2019 Plan must at least be equal to the fair market value of our common stock on the date of grant. The term of an option may not exceed ten years. With respect to any participant who owns more than 10% of the voting power of all classes of our (or any parent or subsidiary of ours) outstanding stock, the term of an incentive stock option granted to such participant must not exceed five years and the exercise price must equal at least 110% of the fair market value on the grant date. The administrator will determine the methods of payment of the exercise price of an option, which may include cash, shares or other property acceptable to the administrator, as well as other types of consideration permitted by applicable law. After the termination of service of an employee, director, or consultant, he or she may exercise his or her option for the period of time stated in his or her option agreement. In the absence of a specified time in an award agreement, if termination is due to death or disability, the option will remain exercisable for 12 months following the termination of service. In all other cases, in the absence of a specified time in an award agreement, the option will remain exercisable for three months following the termination of service. An option, however, may not be exercised later than the expiration of its term. Subject to the provisions of our 2019 Plan, the administrator determines the other terms of options.

Stock Appreciation Rights. Stock appreciation rights may be granted under our 2019 Plan. Stock appreciation rights allow the recipient to receive the appreciation in the fair market value of our common stock between the exercise date and the date of grant. Stock appreciation rights may not have a term exceeding ten years. After the termination of service of an employee, director, or consultant, he or she may exercise his or her stock appreciation right for the period of time stated in his or her stock appreciation rights agreement. In the absence of a specified time in an award agreement, if termination is due to death or disability, the stock appreciation rights will remain exercisable for 12 months following the termination of service. In all other cases, in the absence of a specified time in an award agreement, the stock appreciation rights will remain exercisable for three months following the termination of service. However, in no event may a stock appreciation right be exercised later than the expiration of its term. Subject to the provisions of our 2019 Plan, the administrator determines the other terms of stock appreciation rights, including when such rights become exercisable and whether to pay any increased appreciation in cash or with shares of our common stock, or a combination thereof, except that the per share exercise price for the shares to be issued pursuant to the exercise of a stock appreciation right will be no less than 100% of the fair market value per share on the date of grant.

Restricted Stock. Restricted stock may be granted under our 2019 Plan. Restricted stock awards are grants of shares of our common stock that vest in accordance with terms and conditions established by the administrator. The administrator will determine the number of shares of restricted stock granted to any employee, director, or consultant and, subject to the provisions of our 2019 Plan, will determine the terms and conditions of such awards. The administrator may impose whatever vesting conditions it determines to be appropriate (for example,

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the administrator may set restrictions based on the achievement of specific performance goals or continued service to us), except the administrator, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed. Recipients of restricted stock awards generally will have voting and dividend rights with respect to such shares upon grant without regard to vesting, unless the administrator provides otherwise. Shares of restricted stock that do not vest are subject to our right of repurchase or forfeiture.

Restricted Stock Units. Restricted stock units may be granted under our 2019 Plan. Restricted stock units are bookkeeping entries representing an amount equal to the fair market value of one share of our common stock. Subject to the provisions of our 2019 Plan, the administrator determines the terms and conditions of RSUs, including the vesting criteria and the form and timing of payment. The administrator may set vesting criteria based upon the achievement of company-wide, divisional, business unit or individual goals (including, but not limited to, continued employment or service), applicable federal or state securities laws or any other basis determined by the administrator in its discretion. The administrator, in its sole discretion, may pay earned restricted stock units in the form of cash, in shares or in some combination thereof. In addition, the administrator, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed.

Performance Units and Performance Shares. Performance units and performance shares may be granted under our 2019 Plan. Performance units and performance shares are awards that will result in a payment to a participant only if performance objectives established by the administrator are achieved or the awards otherwise vest. The administrator will establish performance objectives or other vesting criteria in its discretion, which, depending on the extent to which they are met, will determine the number or the value of performance units and performance shares to be paid out to participants. The administrator may set performance objectives based on the achievement of company-wide, divisional, business unit, or individual goals (including, but not limited to, continued employment or service), applicable federal or state securities laws or any other basis determined by the administrator in its discretion. After the grant of a performance unit or performance share, the administrator, in its sole discretion, may reduce or waive any performance objectives or other vesting provisions for such performance units or performance shares. Performance units will have an initial value established by the administrator on or prior to the grant date. Performance shares will have an initial value equal to the fair market value of our common stock on the grant date. The administrator, in its sole discretion, may pay out earned performance units or performance shares in cash, shares, or in some combination thereof.

Outside Directors. All outside (non-employee) directors will be eligible to receive all types of awards (except for incentive stock options) under our 2019 Plan. To provide a maximum limit on the cash compensation and equity awards that can be made to our outside directors, our 2019 Plan provides that in any given fiscal year, an outside director will not be granted cash compensation and equity awards with an aggregate value greater than \$750,000 (increased to \$1,000,000 in the fiscal year of his or her initial service as an outside director), with the value of each equity award based on its grant date fair value as determined according to GAAP for purposes of this limit. Any cash compensation paid or awards granted to an individual for his or her services as an employee or consultant (other than as an outside director) will not count toward this limit.

Non-Transferability of Awards. Unless the administrator provides otherwise, our 2019 Plan generally does not allow for the transfer of awards and only the recipient of an award may exercise an award during his or her lifetime. If the administrator makes an award transferrable, such award will contain such additional terms and conditions as the administrator deems appropriate.

Certain Adjustments. In the event of certain changes in our capitalization, to prevent diminution or enlargement of the benefits or potential benefits available under our 2019 Plan, the administrator will adjust the number and class of shares that may be delivered under our 2019 Plan and/or the number, class, and price of shares covered by each outstanding award and the numerical share limits set forth in our 2019 Plan.

Dissolution or Liquidation. In the event of our proposed liquidation or dissolution, the administrator will notify participants as soon as practicable and, to the extent not exercised, all awards will terminate immediately prior to the consummation of such proposed transaction.

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Merger or Change in Control. Our 2019 Plan provides that in the event of a merger or change in control, as defined under our 2019 Plan, each outstanding award will be treated as the administrator determines, without a participant's consent. The administrator is not required to treat all awards, all awards held by a participant or all awards of the same type similarly.

If a successor corporation does not assume or substitute for any outstanding award, then the participant will fully vest in and have the right to exercise all of his or her outstanding options and stock appreciation rights, all restrictions on restricted stock and restricted stock units will lapse, and for awards with performance-based vesting, unless specifically provided for otherwise under the applicable award agreement or other agreement or policy applicable to the participant, all performance goals or other vesting criteria will be deemed achieved at 100% of target levels and all other terms and conditions met. If an option or stock appreciation right is not assumed or substituted in the event of a change in control, the administrator will notify the participant in writing or electronically that such option or stock appreciation right will be exercisable for a period of time determined by the administrator in its sole discretion and the option or stock appreciation right will terminate upon the expiration of such period.

For awards granted to an outside director, in the event of a change in control, the outside director will fully vest in and have the right to exercise all of his or her outstanding options and stock appreciation rights, all restrictions on restricted stock and restricted stock units will lapse and, for awards with performance-based vesting, unless specifically provided for otherwise under the applicable award agreement or other agreement or policy applicable to the participant, all performance goals or other vesting criteria will be deemed achieved at 100% of target levels and all other terms and conditions met.

Clawback. Awards will be subject to any clawback policy of ours, and the administrator also may specify in an award agreement that the participant's rights, payments, and/or benefits with respect to an award will be subject to reduction, cancellation, forfeiture, and/or recoupment upon the occurrence of certain specified events. Our board of directors may require a participant to forfeit, return, or reimburse us all or a portion of the award and/or shares issued under the award, any amounts paid under the award, and any payments or proceeds paid or provided upon disposition of the shares issued under the award in order to comply with such clawback policy or applicable laws.

Amendment; Termination. The administrator has the authority to amend, alter, suspend, or terminate our 2019 Plan, provided such action does not materially impair the rights of any participant. Our 2019 Plan automatically will terminate in 2029, unless we terminate it sooner.

2017 Stock Option and Grant Plan

Our 2017 Plan was adopted by our board of directors and approved by our stockholders approved in 2017 and was most recently amended in November 2018. Our 2017 Plan permitted the grant of incentive stock options, within the meaning of Section 422 of the Code, to our employees and our subsidiary corporations' employees, and the grant of nonstatutory stock options, restricted stock awards, unrestricted stock awards, and restricted stock units to officers, employees, directors, consultants, and key employees of ours and any of our subsidiary corporations.

Authorized Shares. Our 2017 Plan was terminated in connection with our initial public offering, and accordingly, no new awards will be granted under the 2017 Plan. Our 2017 Plan continues to govern outstanding awards granted thereunder. As of September 30, 2019, options to purchase 4,822,524 shares of our common stock and 1,191,750 shares of unvested restricted stock remained outstanding under our 2017 Plan.

Plan Administration. Our board of directors or a committee appointed by our board of directors administers our 2017 Plan. Subject to the provisions of our 2017 Plan, the administrator has the powers and discretion necessary or appropriate to administer the 2017 Plan and to control its operation. The administrator's powers

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include the power to modify the terms and conditions of any award, not inconsistent with the terms of the 2017 Plan including the number of shares to be covered, price, exercise price, conversion ratio or other price relating thereto, any vesting acceleration or waiver of forfeiture restrictions, and any restriction or limitation regarding any award. The administrator may at any time adopt, alter and repeal such rules, guidelines and practices for administration of the 2017 Plan and for its own acts and proceedings as it deems advisable; interpret the terms and provisions of the 2017 Plan and any award (including award agreements); make all determinations it deems advisable for the administration of the 2017 Plan; and decide all disputes arising in connection with the 2017 Plan. In addition, the administrator may modify the terms and procedures relating to the 2017 Plan and establish sub-plans for the purpose of satisfying applicable foreign laws. The administrator also has the authority to allow participants the opportunity to transfer outstanding awards to a financial institution or other person or entity selected by the administrator and to institute an exchange program by which outstanding awards may be surrendered or cancelled in exchange for awards of the same type, which may have a higher or lower exercise price and/or different terms, awards of a different type and/or cash, or by which the exercise price of an outstanding award is increased or reduced. The administrator's decisions and interpretations are final and binding on all persons, including us, all participants, and any other persons holding awards.

Options. Stock options were granted under our 2017 Plan. The exercise price of options granted under our 2017 Plan must have been at least equal to the fair market value of our common stock on the date of grant. The term of an incentive stock option could not exceed 10 years, except that with respect to any employee who owned more than 10% of the voting power of all classes of our (or any subsidiary of ours) outstanding stock, the term could not exceed five years, and the exercise price must have been equal to at least 110% of the fair market value on the grant date. Subject to the provisions of our 2017 Plan, the administrator will determine the methods of payment of the exercise price of an option. After termination of the participant's service, a participant may exercise any portion of his or her vested or exercisable option for the period of time as determined by the administrator and specified in the applicable option agreement. If termination is due to death or disability, the option generally will remain exercisable for at least twelve months. In all other cases, the option will generally remain exercisable for at least three months. However, an option agreement may provide that the option will terminate immediately upon the termination of the participant's service for cause (as defined in the 2017 Plan), and in no event may an option be exercised later than the expiration of its term. Subject to the provisions of our 2017 Plan, the administrator determines the other terms of options.

Restricted Stock Awards. Restricted stock awards were granted under our 2017 Plan. Restricted stock awards are grants of shares of our common stock that vest in accordance with terms and conditions established by the administrator. The administrator determined the number of shares of restricted stock granted to any employee, director, or consultant and, subject to the provisions of our 2017 Plan, determined the terms and conditions of such awards. The administrator could impose whatever conditions for lapse of the restriction on the shares it determined to be appropriate (for example, the administrator could set restrictions based on the achievement of pre-established performance goals or continued service to us), except the administrator, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed. Recipients of restricted stock awards generally have voting and dividend rights with respect to such shares upon grant without regard to the restriction, unless the administrator provided otherwise. Shares of restricted stock as to which the restrictions have not lapsed are subject to our right of repurchase or forfeiture.

Non-Transferability of Awards. Unless the administrator provides otherwise, our 2017 Plan generally does not allow for the transfer of awards other than by will or the laws of descent and distribution, and only the recipient of an award may exercise an award during his or her lifetime.

Certain Adjustments. In the event of certain changes in our capitalization, the administrator will make an appropriate and proportional adjustment to the number of shares that may be delivered under our 2017 Plan and the number, kind, and price of shares covered by each outstanding award.

Sale Events. Our 2017 Plan provides that in the event of a sale event, as defined under the 2017 Plan, (1) the 2017 Plan and all outstanding options will terminate upon the effective time of the sale event, and (2) all

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unvested restricted stock and restricted stock unit awards will be forfeited prior to the effective time of the sale event, in each case unless such awards are assumed or continued by the successor entity, or new stock awards of the successor entity or parent thereof are substituted therefore. In the event of termination of the 2017 Plan and all outstanding options pursuant to a sale event, each optionholder will be permitted, within a period of time prior to the sale event as specified by the administrator, to exercise all such options which are then exercisable or will become exercisable as of the effective time provided that the exercise of options not exercisable prior to the sale event shall be subject to the consummation of the sale event. In the event of forfeiture of restricted stock pursuant to a sale event, such restricted stock will be purchased from the holder at a price per share equal to the original per share purchase price paid by the holder. In the event of a sale event, the company will have the right, but not the obligation, to make a cash payment to a holder of an award, without the consent of the holder, in exchange for the cancellation of such award, in an amount equal to (1) the number of shares subject to the award multiplied by the value as determined by the administrator of the consideration payable per share of our common stock under the sale event, minus (2) the aggregate exercise price for such shares (if any).

Amendment; Termination. Our board of directors has the authority to amend or alter the 2017 Plan, provided such action will not impair the existing rights of any participant without the consent of the participant. As noted above, our 2017 Plan has been terminated and no further awards will be granted thereunder. All outstanding awards will continue to be governed by their existing terms.

2019 Employee Stock Purchase Plan

Our board of directors has adopted, and our stockholders have approved, our 2019 ESPP. We believe that allowing our employees to participate in our 2019 ESPP provides them with a further incentive towards promoting our success and accomplishing our corporate goals.

Authorized Shares. A total of 1,478,492 shares of our common stock are available for sale under our 2019 ESPP. The number of shares of our common stock that will be available for sale under our 2019 ESPP also includes an annual increase on the first day of each fiscal year beginning with our 2020 fiscal year, equal to the least of:

- 591,397 shares;
- 1% of the outstanding shares of our common stock as of the last day of the immediately preceding fiscal year; or
- such other amount as the administrator may determine.

2019 ESPP Administration. The compensation committee of our board of directors administers our 2019 ESPP and has exclusive discretionary authority to construe, interpret, and apply the terms of the 2019 ESPP, delegate ministerial duties to any of our employees, designate separate offerings under the 2019 ESPP, designate our subsidiaries and affiliates as participating in the 2019 ESPP, determine eligibility, adjudicate all disputed claims filed under the 2019 ESPP, and establish procedures that it deems necessary for the administration of the 2019 ESPP, including, but not limited to, adopting such procedures and sub-plans as are necessary or appropriate to permit participation in the 2019 ESPP by employees who are foreign nationals or employed outside the United States. The administrator's findings, decisions and determinations are final and binding on all participants to the full extent permitted by law.

Eligibility. Generally, all of our employees will be eligible to participate if they are customarily employed by us, or any participating subsidiary or affiliate, for at least 20 hours per week and more than five months in any calendar year. The administrator, in its discretion, may, prior to an enrollment date, for all options to be granted on such enrollment date in an offering, determine that an employee who (i) has not completed at least two years of service (or a lesser period of time determined by the administrator) since his or her last hire date, (ii) customarily works not more than 20 hours per week (or a lesser period of time determined by the

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administrator), (iii) customarily works not more than five months per calendar year (or a lesser period of time determined by the administrator), (iv) is a highly compensated employee within the meaning of Section 414(q) of the Code, or (v) is a highly compensated employee within the meaning of Section 414(q) of the Code with compensation above a certain level or is an officer or subject to disclosure requirements under Section 16(a) of the Exchange Act, is or is not eligible to participate in such offering period.

However, an employee may not be granted rights to purchase shares of our common stock under our 2019 ESPP if such employee:

- immediately after the grant would own capital stock and/or hold outstanding options to purchase such stock possessing 5% or more of the total combined voting power or value of all classes of capital stock of ours or of any parent or subsidiary of ours; or
- holds rights to purchase shares of our common stock under all employee stock purchase plans of ours or any parent or subsidiary of ours that accrue at a rate that exceeds \$25,000 worth of shares of our common stock for each calendar year in which such rights are outstanding at any time.

Offering Periods. Our 2019 ESPP includes a component that allows us to make offerings intended to qualify under Section 423 of the Code and a component that allows us to make offerings not intended to qualify under Section 423 of the Code to designated companies, as described in our 2019 ESPP. Our 2019 ESPP provides for consecutive, overlapping 6-month offering periods. The offering periods will be scheduled to start on the first trading day on or after June 1 and December 1 of each year, except the first offering period commenced on February 7, 2019 and will end on the first trading day on or before December 1, 2019, and the second offering period will commence on the last trading day on or after December 1, 2019.

Contributions. Our 2019 ESPP permits participants to purchase shares of our common stock through contributions (in the form of payroll deductions or otherwise to the extent permitted by the administrator) of up to 15% of their eligible compensation, which includes a participant's base straight time gross earnings but excludes payments for incentive compensation, bonuses, payments for overtime and shift premium, equity compensation income and other similar compensation. Unless otherwise determined by the administrator, a participant may make a one-time decrease (but not increase) to the rate of his or her contributions to 0% during an offering period.

Exercise of Purchase Right. Amounts contributed and accumulated by the participant will be used to purchase shares of our common stock at the end of each offering. A participant may purchase a maximum of 2,000 shares of our common stock during an offering period. The purchase price of the shares will be 85% of the lower of the fair market value of our common stock on the first trading day of the offering period or on the exercise date. Participants may end their participation at any time during an offering period and will be paid their accrued contributions that have not yet been used to purchase shares of our common stock. Participation ends automatically upon termination of employment with us.

Non-Transferability. A participant may not transfer contributions credited to his or her account nor any rights granted under our 2019 ESPP other than by will, the laws of descent and distribution or as otherwise provided under our 2019 ESPP.

Merger or Change in Control. Our 2019 ESPP provides that in the event of a merger or change in control, as defined under our 2019 ESPP, a successor corporation (or a parent or subsidiary of the successor corporation) will assume or substitute each outstanding purchase right. If the successor corporation refuses to assume or substitute for the outstanding purchase right, the offering period with respect to which the purchase right relates will be shortened, and a new exercise date will be set that will be before the date of the proposed merger or change in control. The administrator will notify each participant that the exercise date has been changed and that the participant's option will be exercised automatically on the new exercise date unless prior to such date the participant has withdrawn from the offering period.

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Amendment; Termination. The administrator has the authority to amend, suspend or terminate our 2019 ESPP. Our 2019 ESPP automatically will terminate in 2039, unless we terminate it sooner.

401(k) Plan

We maintain a 401(k) retirement savings plan for the benefit of our employees, including our named executive officers, who satisfy certain eligibility requirements. Under the 401(k) plan, eligible employees may elect to defer a portion of their compensation, within the limits prescribed by the Code, on a pre-tax or after-tax (Roth) basis, through contributions to the 401(k) plan. The 401(k) plan authorizes employer safe harbor contributions. The 401(k) plan is intended to qualify under Sections 401(a) and 501(a) of the Code. As a tax-qualified retirement plan, pre-tax contributions to the 401(k) plan and earnings on those pre-tax contributions are not taxable to the employees until distributed from the 401(k) plan, and earnings on Roth contributions are not taxable when distributed from the 401(k) plan.

Rule 10b5-1 Sales Plans

Certain of our directors and executive officers have adopted, and may adopt, written plans, known as Rule 10b5-1 plans, in which they have contracted or will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or executive officer when entering into the plan, without further direction from them. The director or executive officer may amend a Rule 10b5-1 plan in some circumstances and may terminate a plan at any time. Our directors and executive officers also may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material nonpublic information subject to compliance with the terms of our insider trading policy.

Limitation of Liability and Indemnification

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, and may indemnify our employees and other agents, to the fullest extent permitted by Delaware law. Delaware law prohibits our amended and restated certificate of incorporation from limiting the liability of our directors for the following:

- any breach of the director's duty of loyalty to us or to our stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- unlawful payment of dividends or unlawful stock repurchases or redemptions; and
- any transaction from which the director derived an improper personal benefit.

If Delaware law is amended to authorize corporate action further eliminating or limiting the personal liability of a director, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law, as so amended. Our amended and restated certificate of incorporation does not eliminate a director's duty of care and, in appropriate circumstances, equitable remedies, such as injunctive or other forms of non-monetary relief, remain available under Delaware law. This provision also does not affect a director's responsibilities under any other laws, such as the federal securities laws or other state or federal laws. Under our amended and restated bylaws, we will also be empowered to purchase insurance on behalf of any person whom we are required or permitted to indemnify.

In addition to the indemnification required in our amended and restated certificate of incorporation and amended and restated bylaws, we intend to enter into an indemnification agreement with each member of our board of directors and each of our officers prior to the completion of the offering. These agreements provide for the indemnification of our directors and officers for certain expenses and liabilities incurred in connection with

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any action, suit, proceeding, or alternative dispute resolution mechanism or hearing, inquiry, or investigation that may lead to the foregoing, to which they are a party, or are threatened to be made a party, by reason of the fact that they are or were a director, officer, employee, agent or fiduciary of our company, or any of our subsidiaries, by reason of any action or inaction by them while serving as an officer, director, agent or fiduciary, or by reason of the fact that they were serving at our request as a director, officer, employee, agent, or fiduciary of another entity. In the case of an action or proceeding by or in the right of our company or any of our subsidiaries, no indemnification will be provided for any claim where a court determines that the indemnified party is prohibited from receiving indemnification. We believe that these charter and bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against directors and officers, even though an action, if successful, might benefit us and our stockholders. Moreover, a stockholder's investment may be harmed to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers, and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable. There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

PRINCIPAL STOCKHOLDERS

The following table sets forth the beneficial ownership of our common stock as of November 1, 2019 by:

- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock;
- each of the named executive officers;
- each of our directors; and
- all of our current executive officers and directors as a group.

We have determined beneficial ownership in accordance with the rules of the SEC, and thus it represents sole or shared voting or investment power with respect to our securities. Unless otherwise indicated below, to our knowledge, the persons and entities named in the table have sole voting and sole investment power with respect to all shares that they beneficially owned, subject to community property laws where applicable. The information does not necessarily indicate beneficial ownership for any other purpose, including for purposes of Sections 13(d) and 13(g) of the Exchange Act.

We have based our calculation of the percentage of beneficial ownership prior to this offering on 68,923,730 shares of our common stock outstanding as of November 1, 2019. We have based our calculation of the percentage of beneficial ownership after this offering on _____ shares of our common stock outstanding immediately after the completion of this offering, assuming no exercise by the underwriters of their option to purchase additional shares. We have deemed shares of our common stock subject to stock options that are currently exercisable or exercisable within 60 days of November 1, 2019, to be outstanding and to be beneficially owned by the person holding the stock option for the purpose of computing the percentage ownership of that person. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person.

Unless otherwise indicated, the address of each beneficial owner listed in the table below is c/o Alector, Inc., 131 Oyster Point Boulevard, Suite 600, South San Francisco, California 94080.

<u>Name of Beneficial Owner</u>	<u>Shares Beneficially Owned Prior to this Offering</u>		<u>Shares Beneficially Owned After this Offering</u>	
	<u>Shares</u>	<u>Percentage</u>	<u>Shares</u>	<u>Percentage</u>
5% Stockholders:				
MRL Ventures Fund LLC(1)	3,545,719	5.1%		
Entities affiliated with OrbiMed Private Investments(2)	12,532,329	18.2%		
Entities affiliated with Polaris Venture Partners(3)	12,858,194	18.7%		
Named Executive Officers and Directors:				
Arnon Rosenthal, Ph.D.(4)	6,317,621	9.1%		
Robert King, Ph.D.(5)	617,525	*		
Robert Paul, M.D., Ph.D.(6)	481,885	*		
Tillman Gerngross, Ph.D.(7)	2,620,276	3.8%		
Louis J. Lavigne, Jr.(8)	42,634	*		
Terry McGuire(9)	11,666	*		
Richard Scheller, Ph.D.(10)	55,514	*		
David Wehner(11)	56,703	*		
Kristine Yaffe(12)	—	*		
All executive officers and directors as a group (11 persons)(13)	11,083,468	15.9%		

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- * Represents beneficial ownership of less than one percent (1%) of the outstanding shares of our common stock.
- (1) Based on information contained in a Schedule 13G filed on February 14, 2019. Consists of 3,545,719 shares held of record by MRL Ventures Fund LLC (MRL). All shares are held directly by MRL, which is a subsidiary of Merck Sharp & Dohme Corp. The address for MRL is 320 Bent Street, Cambridge, Massachusetts 02141.
 - (2) Based on information contained in a Schedule 13D/A filed on August 12, 2019. Consists of (a) 9,272,225 shares held of record by OrbiMed Private Investments IV-AL, LP (OrbiMed IV-AL), (b) 2,968,604 shares held of record by OrbiMed Private Investments IV-AL (Feeder), LP (OrbiMed IV-AL (Feeder)), (c) 203,200 shares held of record by OrbiMed Partners Master Fund Limited (OPM) and (d) 88,300 shares held of record by The Biotech Growth Trust PLC (BIOG). OrbiMed Capital GP IV LLC (OrbiMed GP), is the general partner of OrbiMed IV-AL and OrbiMed IV-AL (Feeder). OrbiMed Advisors LLC, or OrbiMed Advisors, is the managing member of OrbiMed GP. Dr. Carl Gordon is a managing partner at OrbiMed Advisors and is also a former member of our board of directors. OrbiMed Advisors exercises investment and voting power through a management committee comprised of Dr. Gordon, Sven H. Borho, and Jonathan T. Silverstein. Each of OrbiMed GP, OrbiMed Advisors, Dr. Gordon, Sven H. Borho, and Jonathan T. Silverstein disclaims beneficial ownership of the shares held by OrbiMed IV-AL and OrbiMed IV-AL (Feeder), except to the extent of its or his pecuniary interest therein, if any. OrbiMed Capital is the sole investment advisor of OPM and BIOG. OrbiMed Capital exercises investment and voting power through a management committee comprised of Carl L. Gordon, Sven H. Borho and Jonathan T. Silverstein. Each of OrbiMed Capital, Carl L. Gordon, Sven H. Borho and Jonathan T. Silverstein disclaims beneficial ownership of the shares held by OPM or BIOG, except to the extent of its or his pecuniary interest therein, if any. The address of the individuals and entities listed above is 601 Lexington Avenue, 54th Floor, New York NY 10022.
 - (3) Consists of (a) 9,350,877 shares held of record by Polaris Venture Partners VI (AIV), L.P. (PVP VI AIV), (b) 709,917 shares held of record by Polaris Venture Partners Founders' Fund VI, L.P. (PVPFF VI), (c) 498,468 shares held of record by Polaris Venture Partners VI, L.P. (PVP VI), and (d) 2,298,932 shares held of record by PVP VI (AIV) Feeder Corp. Holding Partnership, L.P. (PVP VI Feeder, and together with PVP VI AIV, PVPFF VI, and PVP VI, the Funds). Polaris Venture Management Co. VI, L.L.C. (PVM) is the general partner of the Funds and may be deemed to have sole power to vote and dispose of the shares held by the Funds. Amir Nashat, Brian Chee, David Barrett, Bryce Youngren, Jon Flint, and Terry McGuire are the managing members of PVM who collectively make voting and investment decisions with respect to the shares held by the Funds. The address of the individuals and entities listed above is One Marina Park Drive, 10th Floor, Boston, Massachusetts 02210.
 - (4) Consists of (a) 1,305,226 shares held of record by Dr. Rosenthal, of which 208,396 shares are subject to repurchase by us at the original purchase price as of November 1, 2019, (b) 712,500 shares held of record by Adi Rosenthal 2007 Trust dated March 27, 2007, for which Dr. Rosenthal serves as trustee, of which no shares are subject to repurchase by us at the original purchase price as of November 1, 2019, (c) 712,500 shares held of record by Noam Rosenthal 2007 Trust dated March 27, 2007, for which Dr. Rosenthal serves as trustee, of which no shares are subject to repurchase by us at the original purchase price as of November 1, 2019, (d) 712,500 shares held of record by Shani Rosenthal 2007 Trust dated March 27, 2007, for which Dr. Rosenthal serves as trustee, of which no shares are subject to repurchase by us at the original purchase price as of November 1, 2019, (e) 2,612,500 shares held of record by The Rosenthal Family Revocable Trust Dated November 4, 1994, as restated on June 9, 1999, for which Dr. Rosenthal serves as trustee, of which no shares are subject to repurchase by us at the original purchase price as of November 1, 2019, and (f) 775,000 shares subject to options held by Dr. Rosenthal, of which 262,395 shares are vested and exercisable within 60 days of November 1, 2019.
 - (5) Consists of (a) 537,317 shares held of record by Dr. King, of which 167,912 shares are subject to repurchase by us at the original purchase price as of November 1, 2019 and (b) 250,000 shares subject to options held by Dr. King, of which 80,208 shares are vested and exercisable within 60 days of November 1, 2019.

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- (6) Consists of (a) 333,719 shares held of record by Dr. Paul, of which 92,371 shares are subject to repurchase by us at the original purchase price as of November 1, 2019 and (b) 444,000 shares subject to options held by Dr. Paul, of which 148,166 shares are vested and exercisable within 60 days of November 1, 2019.
- (7) Consists of 2,608,610 shares held of record by Dr. Gerngross, of which no shares are subject to repurchase by us at the original purchase price as of November 1, 2019 and 20,000 shares subject to an option held by Dr. Gerngross, 11,666 of which shares are vested and exercisable within 60 days of November 1, 2019.
- (8) Consists of (a) 10,552 shares held of record by Lavrite, LLC, for which Mr. Lavigne serves as managing director, and (b) 90,000 shares subject to an option held by Mr. Lavigne, of which 32,082 shares are vested and exercisable within 60 days of November 1, 2019.
- (9) Consists of 20,000 shares subject to an option held by Mr. McGuire, of which 11,666 shares are vested and exercisable within 60 days of November 1, 2019. Mr. McGuire, who is one of our directors, is a managing member of PVM. Mr. McGuire has no voting or investment power over the shares held by the Funds described in Footnote 3 above. The address for Mr. McGuire is c/o PVM, One Marina Park Drive, 10th Floor, Boston, Massachusetts 02210.
- (10) Consists of (a) 19,981 shares held of record by Dr. Scheller, of which no shares are subject to repurchase by us at the original purchase price as of December 31, 2018 and (b) 101,834 shares subject to options held by Dr. Scheller, of which 35,533 shares are vested and exercisable within 60 days of November 1, 2019.
- (11) Consists of (a) 24,621 shares held of record by Mr. Wehner and (b) 90,000 shares subject to options held by Mr. Wehner, 32,082 of which shares are vested and exercisable within 60 days of November 1, 2019.
- (12) Consists of 40,000 shares subject to an option held by Dr. Yaffe, none of which shares are vested and exercisable within 60 days of November 1, 2019.
- (13) Consists of (a) 11,083,468 shares beneficially owned by our current executive officers and directors as of November 1, 2019, of which 718,609 shares may be repurchased by us at the original purchase price as of such date and (b) 724,230 shares subject to options vested and exercisable within 60 days of November 1, 2019.

DESCRIPTION OF CAPITAL STOCK

The following descriptions of our capital stock and certain provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the amended and restated certificate of incorporation and the amended and restated bylaws. Copies of these documents were filed with the SEC and referenced in the exhibits to our registration statement, of which this prospectus forms a part.

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.

Upon the completion of this offering and the issuance of _____ shares of common stock in this offering, there will be _____ shares of common stock outstanding. As of September 30, 2019, we had 50 stockholders of record. As of September 30, 2019, there were 5,918,124 shares of common stock subject to outstanding options.

Common Stock

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.

Fully Paid and Nonassessable

All of our outstanding shares of common stock are, and the shares of common stock to be issued in this offering, upon payment and delivery in accordance with the underwriting agreement, will be fully paid and nonassessable.

Preferred Stock

Our board of directors have 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. Upon closing of this offering, no shares of preferred stock will be outstanding, and we have no present plan to issue any shares of preferred stock.

Common Stock Options

As of September 30, 2019, we had outstanding options to purchase an aggregate of 5,918,124 shares of our common stock, with a weighted-average exercise price of \$10.84 per share, under our 2017 Plan and 2019 Plan.

Registration Rights

After the completion of this offering, 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

After the completion of this offering, certain holders of shares of our common stock will be entitled to certain demand registration rights. At any time beginning 180 days after the effective date of this offering, 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

After the completion of this offering, certain holders of shares of our common stock will be 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

After the completion of this offering, certain holders of shares of our common stock will be entitled to certain “piggyback” registration rights. If we propose to register the offer and sale of shares of our common stock

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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

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 will be 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 2023 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.

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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 will 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 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 will be 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 will 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.

Listing

Our common stock is listed on the NASDAQ Global Select Market under the symbol “ALEC.”

Transfer Agent and Registrar

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.

SHARES ELIGIBLE FOR FUTURE SALE

Sales of substantial amounts of common stock in the public market, including shares issued upon exercise of outstanding options, or the perception that such sales may occur, however, could adversely affect the market price of our common stock and also could adversely affect our future ability to raise capital through the sale of our common stock or other equity-related securities of ours at times and prices we believe appropriate.

Upon completion of this offering, based on our shares outstanding as of September 30, 2019, _____ shares of our common stock will be outstanding, or _____ shares of common stock if the underwriters exercise their option to purchase additional shares in full. All of the shares of common stock expected to be sold in this offering will be freely tradable without restriction or further registration under the Securities Act unless held by our “affiliates,” as that term is defined in Rule 144 under the Securities Act. The remaining outstanding shares of our common stock will be deemed “restricted securities” as that term is defined under Rule 144. Restricted securities may be sold in the public market only if their offer and sale is registered under the Securities Act or if the offer and sale of those securities qualify for an exemption from registration, including exemptions provided by Rules 144 and 701 under the Securities Act, which are summarized below.

As a result of the lock-up agreements described below and the provisions of Rules 144 or 701 and no exercise of the underwriters’ option to purchase additional shares, the shares of our common stock that will be deemed “restricted securities” will be available for sale in the public market following the completion of this offering as follows:

- _____ shares will be eligible for sale on the date of this prospectus; and
- _____ shares will be eligible for sale upon expiration of the lock-up agreements and market stand-off provisions described below, beginning more than 90 days after the date of this prospectus.

Lock-Up Agreements

In connection with this offering, our executive officers, directors, and certain of our other stockholders affiliated with certain of our directors have entered into lock-up agreements with the underwriters, subject to certain exceptions, not to dispose of or hedge any of their common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus continuing through the date 90 days after the date of this prospectus, except with the prior consent of Morgan Stanley & Co. LLC and Goldman Sachs & Co. LLC. See the section titled “Underwriting” for additional information.

Rule 144

Rule 144, as currently in effect, generally provides that, once we have been subject to the public company reporting requirements of Section 13 or Section 15(d) of the Exchange Act for at least 90 days, a stockholder who is not deemed to have been one of our affiliates at any time during the preceding 90 days and who has beneficially owned the shares of our capital stock proposed to be sold for at least six months is entitled to sell such shares in reliance upon Rule 144 without complying with the volume limitation, manner of sale or notice conditions of Rule 144. If such stockholder has beneficially owned the shares of our capital stock proposed to be sold for at least one year, then such person is entitled to sell such shares in reliance upon Rule 144 without complying with any of the conditions of Rule 144.

Rule 144 also provides that a stockholder who is deemed to have been one of our affiliates at any time during the preceding 90 days and who has beneficially owned the shares of our common stock proposed to be sold for at least six months is entitled to sell such shares in reliance upon Rule 144 within any three month period beginning 90 days after the date of this prospectus a number of shares that does not exceed the greater of the following:

- 1% of the number of shares of our capital stock then outstanding, which will equal _____ shares immediately after the completion of this offering, assuming no exercise by the underwriters of their option to purchase additional shares; or

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- the average weekly trading volume of our common stock during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Sales of our capital stock made in reliance upon Rule 144 by a stockholder who is deemed to have been one of our affiliates at any time during the preceding 90 days are also subject to the current public information, manner of sale and notice conditions of Rule 144.

Rule 701

Rule 701 generally provides that, once we have been subject to the public company reporting requirements of Section 13 or Section 15(d) of the Exchange Act for at least 90 days, a stockholder who purchased shares of our common stock pursuant to a written compensatory benefit plan or contract and who is not deemed to have been one of our affiliates at any time during the preceding 90 days may sell such shares in reliance upon Rule 144 without complying with the current public information or holding period conditions of Rule 144. Rule 701 also provides that a stockholder who purchased shares of our common stock pursuant to a written compensatory benefit plan or contract and who is deemed to have been one of our affiliates during the preceding 90 days may sell such shares under Rule 144 without complying with the holding period condition of Rule 144.

Rule 10b5-1 Trading Plans

Certain of our executive officers and directors have adopted written plans, known as “Rule 10b5-1 trading plans,” under which they will contract with a broker to buy or sell shares of our common stock on a periodic basis to diversify their assets and investments. Under these 10b5-1 trading plans, a broker may execute trades pursuant to parameters established by the executive officer or director when entering into the plan, without further direction from such officer or director.

Registration Rights

After the completion of this offering, the holders of up to 59,809,220 shares of our common stock will be entitled to certain rights with respect to the registration of such shares under the Securities Act. The registration of these shares of our common stock under the Securities Act would result in these shares becoming eligible for sale in the public market without restriction under the Securities Act immediately upon the effectiveness of such registration, subject to the Rule 144 limitations applicable to affiliates. See the section titled “Description of Capital Stock—Registration Rights” for a description of these registration rights.

Registration Statement

We filed a registration statement on Form S-8 under the Securities Act to register all of the shares of our common stock subject to equity awards outstanding or reserved for issuance under our equity compensation plans. The shares of our common stock covered by such registration statement will be eligible for sale in the public market without restriction under the Securities Act immediately upon the effectiveness of such registration statement, subject to vesting restrictions, the conditions of Rule 144 applicable to affiliates, and any applicable market stand-off agreements and lock-up agreements.

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following is a summary of the material U.S. federal income tax consequences of the ownership and disposition of our common stock acquired in this offering by a “non-U.S. holder” (as defined below), but does not purport to be a complete analysis of all the potential tax considerations relating thereto. This summary is based upon the provisions of the Code, Treasury Regulations promulgated thereunder, administrative rulings and judicial decisions, all as of the date hereof. These authorities may be changed, possibly retroactively, so as to result in U.S. federal income tax consequences different from those set forth below. We have not sought, and do not intend to seek, any ruling from the Internal Revenue Service (IRS), with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS or a court will agree with such statements and conclusions.

This summary also does not address the tax considerations arising under the laws of any non-U.S., state, or local jurisdiction or under U.S. federal gift and estate tax rules, except to the limited extent set forth below. In addition, this discussion does not address tax considerations applicable to an investor’s particular circumstances or to investors that may be subject to special tax rules, including, without limitation:

- banks, insurance companies, regulated investment companies, real estate investment trusts, or other financial institutions;
- persons subject to the alternative minimum tax or the tax on net investment income;
- tax-exempt organizations;
- pension plans and tax-qualified retirement plans;
- controlled foreign corporations, passive foreign investment companies and corporations that accumulate earnings to avoid U.S. federal income tax;
- brokers or dealers in securities or currencies;
- traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;
- persons that own, or are deemed to own, more than five percent of our capital stock (except to the extent specifically set forth below);
- certain former citizens or long-term residents of the United States;
- persons who hold our common stock as a position in a hedging transaction, “straddle,” “conversion transaction,” or other risk reduction transaction;
- persons who hold or receive our common stock pursuant to the exercise of any option or otherwise as compensation;
- persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment); or
- persons deemed to sell our common stock under the constructive sale provisions of the Code.

In addition, if a partnership (including an entity or arrangement classified as a partnership or flow-through entity for U.S. federal income tax purposes) holds our common stock, the tax treatment of a partner in such partnership generally will depend on the status of the partner and upon the activities of the partnership. Partnerships holding our common stock and partners in such partnerships should consult their own tax advisors regarding the tax consequences of the ownership and disposition of our common stock.

You are urged to consult your tax advisor with respect to the application of the U.S. federal income tax laws to your particular situation, as well as any tax consequences of the purchase, ownership and disposition of our common stock arising under the U.S. federal gift or estate tax rules or under the laws of any state, local, non-U.S. or other taxing jurisdiction or under any applicable tax treaty.

Non-U.S. Holder Defined

For purposes of this discussion, you are a “non-U.S. holder” if you are a beneficial owner of our common stock that, for U.S. federal income tax purposes, is not a partnership or:

- an individual who is a citizen or resident of the United States;
- a corporation or other entity taxable as a corporation created or organized in the United States or under the laws of the United States or any political subdivision thereof, or otherwise treated as such for U.S. federal income tax purposes;
- an estate whose income is includible in gross income for U.S. federal income tax purposes regardless of its source; or
- a trust (x) whose administration is subject to the primary supervision of a U.S. court and that has one or more U.S. persons who have the authority to control all substantial decisions of the trust or (y) that has made a valid election under applicable Treasury Regulations to be treated as a U.S. person.

Distributions

As described in the section titled “Dividend Policy,” we have never declared or paid cash dividends on our common stock, and we do not anticipate paying any cash dividends on our common stock in the foreseeable future. However, if we do make distributions on our common stock, those payments will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed our current or accumulated earnings and profits, the excess will constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale or other disposition of our common stock as described under “—Gain on Disposition of Our Common Stock.”

Subject to the discussions below on effectively connected income, backup withholding and Foreign Account Tax Compliance Act (FATCA), any dividend paid to you generally will be subject to U.S. federal withholding tax either at a rate of 30% of the gross amount of the dividend or such lower rate as may be specified by an applicable income tax treaty between the United States and your country of residence. In order to receive a reduced treaty rate, you must provide us with an IRS Form W-8BEN or W-8BEN-E or other appropriate version of IRS Form W-8 certifying qualification for the reduced rate, and you will be required to update such forms and certifications from time to time as required by law. A non-U.S. holder of shares of our common stock eligible for a reduced rate of U.S. federal withholding tax pursuant to an income tax treaty may obtain a refund of any excess amounts withheld by filing an appropriate claim for refund with the IRS. If the non-U.S. holder holds our common stock through a financial institution or other agent acting on the non-U.S. holder’s behalf, the non-U.S. holder will be required to provide appropriate documentation to the agent, which then will be required to provide certification to us or our paying agent, either directly or through other intermediaries.

Dividends received by you that are treated as effectively connected with a U.S. trade or business conducted by you (and, if required by an applicable income tax treaty, that are attributable to a permanent establishment or fixed base maintained by you in the United States) are generally exempt from the 30% U.S. federal withholding tax, subject to the discussion below on backup withholding and FATCA withholding. In order to obtain this exemption, you must provide us with a properly executed IRS Form W-8ECI or other applicable IRS Form W-8 properly certifying such exemption. Such effectively connected dividends, although not subject to U.S. federal withholding tax, are taxed at the same graduated rates applicable to U.S. persons, net of certain deductions and credits. In addition, if you are a corporate non-U.S. holder, you may also be subject to a branch profits tax at a rate of 30% (or such lower rate as may be specified by an applicable income tax treaty between the United States and your country of residence) on our earnings and profits for the taxable year that are effectively connected with a U.S. trade or business conducted by you, as adjusted for certain items. You should consult your tax advisor regarding the tax consequences of the ownership and disposition of our common stock, including any applicable tax treaties that may provide for different rules.

Gain on Disposition of Our Common Stock

Subject to the discussion below regarding backup withholding and FATCA withholding, you generally will not be required to pay U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock unless:

- the gain is effectively connected with a U.S. trade or business conducted by you (and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by you in the United States);
- you are an individual who is present in the United States for a period or periods aggregating 183 days or more during the calendar year in which the sale or disposition occurs and certain other conditions are met; or
- our common stock constitutes a United States real property interest by reason of our status as a “United States real property holding corporation,” or USRPHC, for U.S. federal income tax purposes at any time within the shorter of the five-year period preceding your disposition of, or your holding period for, our common stock.

We believe that we are not currently and will not become a USRPHC for U.S. federal income tax purposes, and the remainder of this discussion so assumes. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property interests relative to the fair market value of our worldwide real property interests plus our other assets used or held for use in a trade or business, there can be no assurance that we will not become a USRPHC in the future. Even if we become a USRPHC, however, as long as our common stock is regularly traded on an established securities market, your common stock will be treated as U.S. real property interests only if you actually (directly or indirectly) or constructively hold more than five percent of such regularly traded common stock at any time during the shorter of the five-year period preceding your disposition of, or your holding period for, our common stock.

If you are a non-U.S. holder described in the first bullet above, you will be required to pay tax on the gain derived from the sale (net of certain deductions and credits) under regular graduated U.S. federal income tax rates applicable to U.S. persons, and a corporate non-U.S. holder described in the first bullet above also may be subject to the branch profits tax at a 30% rate, or such lower rate as may be specified by an applicable income tax treaty. If you are an individual non-U.S. holder described in the second bullet above, you will be subject to tax at 30% (or such lower rate specified by an applicable income tax treaty) on the gain derived from the sale, which gain may be offset by U.S. source capital losses for the year, provided you have timely filed U.S. federal income tax returns with respect to such losses. You should consult your tax advisor regarding any applicable income tax or other treaties that may provide for different rules.

Federal Estate Tax

Our common stock beneficially owned by an individual who is not a citizen or resident of the United States (as defined for U.S. federal estate tax purposes) at the time of their death will generally be includable in the decedent’s gross estate for U.S. federal estate tax purposes. Such stock, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax treaty provides otherwise.

Backup Withholding and Information Reporting

Generally, we must report annually to the IRS the amount of dividends paid to you, your name and address and the amount of tax withheld, if any. A similar report will be sent to you. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in your country of residence.

Payments of dividends on or of proceeds from the disposition of our common stock made to you may be subject to information reporting and backup withholding at the statutory rate (currently, 24%) unless you establish an exemption, for example, by properly certifying your non-U.S. status on a properly completed IRS

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Form W-8BEN or W-8BEN-E or another appropriate version of IRS Form W-8. Notwithstanding the foregoing, backup withholding and information reporting may apply if either we or our paying agent has actual knowledge, or reason to know, that you are a U.S. person.

Backup withholding is not an additional tax; rather, the U.S. federal income tax liability of persons subject to backup withholding will be reduced by the amount of tax withheld. If withholding results in an overpayment of taxes, a refund or credit may generally be obtained from the IRS, provided that the required information is furnished to the IRS in a timely manner.

Foreign Account Tax Compliance Act

Provisions of the Code commonly referred to as FATCA, Treasury Regulations issued thereunder and official IRS guidance generally impose a U.S. federal withholding tax of 30% on dividends on, and the gross proceeds from a sale or other disposition of our common stock, paid to a “foreign financial institution” (as specially defined under these rules), unless such institution enters into an agreement with the U.S. government to, among other things, withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding the U.S. account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners) or otherwise establishes an exemption. FATCA also generally imposes a U.S. federal withholding tax of 30% on dividends on and the gross proceeds from a sale or other disposition of our common stock paid to a “non-financial foreign entity” (as specially defined under these rules) unless such entity provides the withholding agent with a certification identifying the direct and indirect substantial U.S. owners of the entity and information with respect to such substantial U.S. owners, certifies that it does not have any such substantial U.S. owners, or otherwise establishes an exemption.

The withholding obligations under FATCA generally apply to dividends on our common stock and to the payment of gross proceeds of a sale or other disposition of our common stock. The withholding tax will apply regardless of whether the payment otherwise would be exempt from U.S. nonresident and backup withholding tax, including under the other exemptions described above. Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of such taxes. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this section. The U.S. Treasury Department recently released proposed regulations under FATCA which, if finalized in their present form, would eliminate the federal withholding tax of 30% applicable to gross proceeds of a sale or other disposition of our common stock, and has provided that such proposed regulations may be relied upon by taxpayers until final regulations are issued. Prospective investors should consult with their own tax advisors regarding the application of FATCA withholding to their investment in, and ownership and disposition of, our common stock.

The preceding discussion of U.S. federal tax considerations is for general information only. It is not tax advice to investors in their particular circumstances. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state and local, and non-U.S. tax consequences of purchasing, holding, and disposing of our common stock, including the consequences of any proposed change in applicable laws.

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We and our directors and executive officers, as well as certain of our other stockholders affiliated with certain of our directors, have agreed that, without the prior written consent of the representatives on behalf of the underwriters, we and they will not, during the period ending on and including the 90th day after the date of this prospectus (the restricted period):

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for shares of common stock;
- file any registration statement with the SEC relating to the offering of any shares of common stock or any securities convertible into or exercisable or exchangeable for common stock; or
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. In addition, we and each such person agrees that, without the prior written consent of the representatives on behalf of the underwriters, we or such other person will not, during the restricted period, make any demand for, or exercise any right with respect to, the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock.

The restrictions described in the immediately preceding paragraph do not apply to:

- a. the sale of shares to the underwriters;
- b. transactions by any person other than us relating to shares of common stock or other securities acquired in this offering or in open market transactions after the completion of this offering; provided that no filing under Section 16(a) of the Exchange Act is required or voluntarily made during the restricted period in connection with subsequent sales of the common stock or other securities acquired in such open market transactions;
- c. the transfer of shares of common stock or any security convertible into common stock (i) to an immediate family member of the lock-up signatory, or to a trust or other entity formed for estate planning for the benefit of the lock-up signatory or immediate family member, (ii) by bona fide gift, will or intestacy, (iii) if the lock-up signatory is a trust, to a trustor or beneficiary of the trust or to the estate of a beneficiary of such trust, or (iv) by bona fide gift to a charitable organization, provided that no filing under Section 16(a) of the Exchange Act or other public filing, report, or announcement reporting a reduction in beneficial ownership of shares of common stock or any security convertible into common stock shall be required or voluntarily made during the restricted period;
- d. if the lock-up signatory is a corporation, partnership, limited liability company, trust, or other business entity, transfers of common stock or any security convertible into common stock (i) to another corporation, partnership, limited liability company, trust, or other business entity that controls, is controlled by, manages, is managed by, or is under common control with the lock-up signatory or its affiliates or (ii) as part of a disposition, transfer, or distribution by the lock-up signatory to its stockholders, partners, members, or other equity holders; provided that no filing under Section 16(a) of the Exchange Act or other public filing, report, or announcement reporting a reduction in beneficial ownership of shares of common stock or securities convertible into common stock shall be required or voluntarily made during the restricted period (other than any required Form 5 filing);
- e. (i) the receipt by the lock-up signatory from us of shares of our common stock upon the exercise of options or the settlement of restricted stock units granted under a stock incentive plan or other equity award plan, as described in this prospectus, insofar as such option or restricted stock unit is outstanding as of the date of this prospectus, or (ii) the transfer of shares of common stock or other securities convertible into common stock to us upon a vesting event of our securities, the settlement of restricted

stock units, or the exercise of options to purchase our securities on a “cashless” or “net exercise” basis to the extent permitted by the instruments representing such options or restricted stock units (and any transfer to us necessary to generate cash needed for the payment of taxes due as a result of such vesting, settlement, or exercise) so long as such “cashless exercise” or “net exercise” is effected solely by the surrender of outstanding options or restricted stock units to us and our cancellation of all or a portion thereof. In the case of either (i) or (ii), no filing under Section 16(a) of the Exchange Act or other public announcement or filing shall be required or voluntarily made during the restricted period, and the underlying shares issued to the lock-up signatory shall continue to be subject to the terms of the lock-up agreement. For the purpose of (ii), filings under Section 16(a) of the Exchange Act shall be permissible if such filings relate solely to “net” or “cashless” exercises or settlements of stock options, restricted stock units, or other equity awards that would otherwise expire during the restricted period and any such filing includes a statement to the effect that such transfer is being made in connection with a “net” or “cashless” exercise or settlement of stock options, restricted stock units, or other equity awards, and the lock-up signatory provides written notice to the representatives no later than two business days prior to making any such filings;

- f. the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that (i) such plan does not provide for the transfer of common stock during the restricted period and (ii) to the extent a public announcement or filing under the Exchange Act, if any, is required or voluntarily made regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of common stock may be made under such plan during the restricted period;
- g. the transfer of shares of common stock or securities convertible into common stock to us pursuant to agreements under which we or any of our equityholders have the option to repurchase such shares of common stock or other securities convertible into common stock upon termination of service of the lock-up signatory;
- h. the transfer of shares of common stock or other securities convertible into common stock pursuant to a bona fide third party tender offer, merger, consolidation, or other similar transaction made to all holders of our capital stock involving a “change of control”, after the completion of this offering, that has been approved by our board of directors, provided that in the event that such transaction is not completed, the lock-up signatory’s shares of common stock or securities convertible into common stock will remain subject to the terms of the lock-up agreement;
- i. the transfer of shares of common stock or securities convertible into common stock pursuant to a domestic order or in connection with a divorce settlement; or
- j. sale of shares of common stock under a trading plan pursuant to Rule 10b5-1 under the Exchange Act established prior to the execution of the relevant lock-up agreement and has been disclosed to the representatives, provided that any filing required by Section 16 of the Exchange Act that is made in connection with any such sales during the restricted period shall state that such sales have been executed pursuant to such trading plan.

In the case of any transfer pursuant to (c), (d) and (i) above, the donee, transferee, or distributee must agree in writing to be bound by the lock-up restrictions. In the case of (c) and (d) above, such transfer or distribution shall not involve a disposition for value. In the case of (g) and (i) above, no filing under Section 16(a) of the Exchange Act or other public filing, report, or announcement reporting a reduction in beneficial ownership of shares of common stock or securities convertible into common stock shall be voluntarily made during the restricted period. In the case of (g) and (i) above, if the lock-up signatory is required to file a report under Section 16(a) of the Exchange Act during the restricted period, the lock-up signatory shall include a statement to the effect that such transfer is to us in connection with the repurchase of shares of common stock or other securities convertible into common stock or pursuant to a qualified domestic order or in connection with a divorce settlement, as the case may be.

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The representatives, in their sole discretion, may release the common stock and other securities subject to the lock-up agreements described above in whole or in part at any time with or without notice.

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the option to purchase additional shares described above. The underwriters can close out a covered short sale by exercising such option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under such option. The underwriters may also sell shares in excess of such option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of common stock in the open market to stabilize the price of the common stock. These activities may raise or maintain the market price of the common stock above independent market levels or prevent or retard a decline in the market price of the common stock. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

A prospectus in electronic format may be made available on websites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The representatives may agree to allocate a number of shares of common stock to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters that may make Internet distributions on the same basis as other allocations.

Other Relationships

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for us, for which they received or will receive customary fees and expenses.

In addition, in the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investment and securities activities may involve our securities and instruments. The underwriters and their respective affiliates may also make investment recommendations or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

Selling Restrictions

Canada

The shares of our common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or

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subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares of our common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State) an offer to the public of any shares of our common stock may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any shares of our common stock may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- (a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- (b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or
- (c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares of our common stock in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of our common stock to be offered so as to enable an investor to decide to purchase any shares of our common stock, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State, and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

United Kingdom

Each underwriter has represented and agreed that:

- (a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000 (FSMA)) received by it in connection with the issue or sale of the shares of our common stock in circumstances in which Section 21(1) of the FSMA does not apply to us; and

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- (b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares of our common stock in, from or otherwise involving the United Kingdom.

Hong Kong

The shares of common stock have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation, or document relating to the shares of common stock has been or may be issued or has been or may be in the possession of any person for the purposes of issuance, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares of common stock which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Japan

No registration pursuant to Article 4, paragraph 1 of the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) (FIEL) has been made or will be made with respect to the solicitation of the application for the acquisition of the shares of common stock.

Accordingly, the shares of common stock have not been, directly or indirectly, offered or sold and will not be, directly or indirectly, offered or sold in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or re-sale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan except pursuant to an exemption from the registration requirements, and otherwise in compliance with, the FIEL and the other applicable laws and regulations of Japan.

For Qualified Institutional Investors (QII)

Please note that the solicitation for newly-issued or secondary securities (each as described in Paragraph 2, Article 4 of the FIEL) in relation to the shares of common stock constitutes either a “QII only private placement” or a “QII only secondary distribution” (each as described in Paragraph 1, Article 23-13 of the FIEL). Disclosure regarding any such solicitation, as is otherwise prescribed in Paragraph 1, Article 4 of the FIEL, has not been made in relation to the shares of common stock. The shares of common stock may only be transferred to QIIs.

For Non-QII Investors

Please note that the solicitation for newly-issued or secondary securities (each as described in Paragraph 2, Article 4 of the FIEL) in relation to the shares of common stock constitutes either a “small number private placement” or a “small number private secondary distribution” (each as is described in Paragraph 4, Article 23-13 of the FIEL). Disclosure regarding any such solicitation, as is otherwise prescribed in Paragraph 1, Article 4 of the FIEL, has not been made in relation to the shares of common stock. The shares of common stock may only be transferred en bloc without subdivision to a single investor.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or

invitation for subscription or purchase, of the shares of our common stock may not be circulated or distributed, nor may the shares of our common stock be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (SFA), (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares of our common stock are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (b) a trust (where the trustee is not an accredited investor) the sole purpose of which is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares of our common stock pursuant to an offer made under Section 275 of the SFA except:

- (a) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i) (B) of the SFA;
- (b) where no consideration is or will be given for the transfer;
- (c) where the transfer is by operation of law;
- (d) as specified in Section 276(7) of the SFA; or
- (e) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

LEGAL MATTERS

The validity of the issuance of our common stock offered in this prospectus will be passed upon for us by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. Davis Polk & Wardwell LLP, Menlo Park, California, is acting as counsel for the underwriters.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2018, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our consolidated financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of our common stock offered by this prospectus. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement, as permitted by the rules and regulations of the SEC. For further information with respect to us and our common stock, we refer you to the registration statement, including the exhibits filed as a part of the registration statement. Statements contained or incorporated by reference in this prospectus concerning the contents of any contract or any other document is not necessarily complete. If a contract or document has been filed as an exhibit to the registration statement, please see the copy of the contract or document that has been filed. Each statement in this prospectus relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit. The SEC also maintains an Internet website that contains the registration statement of which this prospectus forms a part, as well as the exhibits thereto. These documents, along with future reports, proxy statements, and other information about us, are available at the SEC's website, www.sec.gov.

We are subject to the information and reporting requirements of the Securities Exchange Act of 1934, as amended, and, in accordance with this law, will file periodic reports, proxy statements, and other information with the SEC. These periodic reports, proxy statements, and other information are available for inspection and copying at the SEC's public reference facilities and the website of the SEC referred to above. We also maintain a website at www.alector.com where these materials are available. You may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. Information contained on, or that can be accessible through, our website is not a part of this prospectus and the inclusion of our website address in this prospectus is an inactive textual reference only.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to “incorporate by reference” information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (File No. 001-38792):

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2018, filed with the SEC on March 26, 2019;
- our Quarterly Report on [Form 10-Q](#) for the quarter ended March 31, 2019, filed with the SEC on May 13, 2019;
- our Quarterly Report on [Form 10-Q](#) for the quarter ended June 30, 2019, filed with the SEC on August 12, 2019;
- our Quarterly Report on [Form 10-Q](#) for the quarter ended September 30, 2019, filed with the SEC on November 12, 2019;
- the information contained in our [Definitive Proxy Statement](#) on Schedule 14A, filed with the SEC on March 27, 2019, to the extent incorporated by reference in Part III of our Annual Report on Form 10-K for the fiscal year ended December 31, 2018;
- our Current Reports on Form 8-K filed with the SEC on (i) [February 11, 2019](#), (ii) [May 16, 2019](#), (iii) [June 13, 2019](#), and (iv) [August 12, 2019](#); and
- the description of our Common Stock set forth in our Registration Statement on [Form 8-A](#) (File No. 011-38792), filed with the SEC on February 1, 2019, including any amendments or reports filed for the purpose of updating such description.

Any statement contained in a document incorporated by reference into this prospectus shall be deemed to be modified or superseded for the purposes of this prospectus to the extent that a statement contained herein or in any subsequently filed document that is also incorporated by reference in this prospectus modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

Notwithstanding the statements in the preceding paragraphs, no document, report or exhibit (or portion of any of the foregoing) or any other information that we have “furnished” to the SEC pursuant to the Exchange Act shall be incorporated by reference into this prospectus.

We will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference in this prospectus, including exhibits to these documents. You should direct any requests for documents to Alector, Inc., Attn: Vice President, Legal, 131 Oyster Point Boulevard, Suite 600, South San Francisco, California 94080.

You also may access these filings on our website at www.alector.com. We do not incorporate the information on our website into this prospectus or any supplement to this prospectus and you should not consider any information on, or that can be accessed through, our website as part of this prospectus or any supplement to this prospectus (other than those filings with the SEC that we specifically incorporate by reference into this prospectus or any supplement to this prospectus).

PART II**INFORMATION NOT REQUIRED IN THE PROSPECTUS****Item 13. Other Expenses of Issuance and Distribution**

The following table sets forth the expenses to be incurred in connection with the offering described in this Registration Statement, other than underwriting discounts and commissions, all of which will be paid by us. All amounts are estimates except the Securities and Exchange Commission's registration fee, the Financial Industry Regulatory Authority, Inc.'s filing fee, and the NASDAQ listing fee.

	Amount to be Paid
SEC Registration Fee	\$ *
FINRA filing fee	*
Printing and engraving expenses	*
Legal fees and expenses	*
Accounting fees and expenses	*
Transfer agent and registrar fees	*
Miscellaneous expenses	*
Total	<u>\$ *</u>

* To be provided by amendment.

Item 14. Indemnification of Directors and Officers

Section 145 of the Delaware General Corporation Law empowers a corporation to indemnify its directors and officers and to purchase insurance with respect to liability arising out of their capacity or status as directors and officers, provided that the person acted in good faith and in a manner the person reasonably believed to be in our best interests, and, with respect to any criminal action, had no reasonable cause to believe the person's actions were unlawful. The Delaware General Corporation Law further provides that the indemnification permitted thereunder shall not be deemed exclusive of any other rights to which the directors and officers may be entitled under the corporation's bylaws, any agreement, a vote of stockholders or otherwise. The certificate of incorporation of the registrant provides for the indemnification of the registrant's directors and officers to the fullest extent permitted under the Delaware General Corporation Law. In addition, the bylaws of the registrant require the registrant to fully indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding (whether civil, criminal, administrative or investigative) by reason of the fact that such person is or was a director or officer of the registrant, or is or was a director or officer of the registrant serving at the registrant's request as a director, officer, employee, or agent of another corporation, partnership, joint venture, trust, or other enterprise, against expenses (including attorney's fees), judgments, fines, and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit, or proceeding, to the fullest extent permitted by applicable law.

Section 102(b)(7) of the Delaware General Corporation Law permits a corporation to provide in its certificate of incorporation that a director of the corporation shall not be personally liable to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except (1) for any breach of the director's duty of loyalty to the corporation or its stockholders, (2) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (3) for payments of unlawful dividends or unlawful stock repurchases or redemptions or (4) for any transaction from which the director derived an improper personal benefit. The registrant's certificate of incorporation provides that the registrant's directors shall not be personally liable to it or its stockholders for monetary damages for breach of fiduciary duty as a director and that if the Delaware General Corporation Law is amended to authorize corporate action further eliminating or limiting

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the personal liability of directors, then the liability of the registrant's directors shall be eliminated or limited to the fullest extent permitted by the Delaware General Corporation Law, as so amended.

Section 174 of the Delaware General Corporation Law provides, among other things, that a director who willfully or negligently approves of an unlawful payment of dividends or an unlawful stock purchase or redemption may be held liable for such actions. A director who was either absent when the unlawful actions were approved, or dissented at the time, may avoid liability by causing his or her dissent to such actions to be entered in the books containing minutes of the meetings of the board of directors at the time such action occurred or immediately after such absent director receives notice of the unlawful acts.

As permitted by the Delaware General Corporation Law, the registrant has entered into separate indemnification agreements with each of the registrant's directors and certain of the registrant's officers which require the registrant, among other things, to indemnify them against certain liabilities which may arise by reason of their status as directors, officers, or certain other employees.

The registrant expects to obtain and maintain insurance policies under which its directors and officers are insured, within the limits and subject to the limitations of those policies, against certain expenses in connection with the defense of, and certain liabilities which might be imposed as a result of, actions, suits, or proceedings to which they are parties by reason of being or having been directors or officers. The coverage provided by these policies may apply whether or not the registrant would have the power to indemnify such person against such liability under the provisions of the Delaware General Corporation Law.

These indemnification provisions and the indemnification agreements intended to be entered into between the registrant and the registrant's officers and directors may be sufficiently broad to permit indemnification of the registrant's officers and directors for liabilities (including reimbursement of expenses incurred) arising under the Securities Act of 1933, as amended.

The underwriting agreement between the registrant and the underwriters to be filed as Exhibit 1.1 to this registration statement provides for the indemnification by the underwriters of the registrant's directors and officers and certain controlling persons against specified liabilities, including liabilities under the Securities Act with respect to information provided by the underwriters specifically for inclusion in the registration statement.

Item 15. Recent Sales of Unregistered Securities

The following list sets forth information regarding all unregistered securities sold by us since October 13, 2017. No underwriters were involved in the sales and the certificates representing the securities sold and issued contain legends restricting transfer of the securities without registration under the Securities Act or an applicable exemption from registration.

(1) In April 2018, July 2018, and October 2018, we issued 9,373,633 shares of our Series E preferred stock at \$14.2154 per share, for aggregate proceeds of \$133.2 million to a total of 32 accredited investors.

(2) From October 13, 2017 through the filing of our registration statement on Form S-1 on December 2, 2019, we granted stock options to purchase an aggregate of 8,824,155 shares of common stock upon the exercise of options under our 2017 Plan and 2019 Plan at exercise prices per share ranging from \$6.95 to \$21.00, for an aggregate exercise price of approximately \$111.8 million.

(3) On October 13, 2017, we completed a reorganization whereby we converted from a Delaware limited liability company, under the name Alector LLC, to a Delaware corporation under the name Alector, Inc. (the Conversion). In conjunction with the Conversion, (i) all of our outstanding common units converted on a 1-for-1 basis into 9,421,460 shares of common stock; (ii) all of our outstanding preferred units converted on a 1-for-1 basis into 36,001,203 shares of convertible preferred stock; and (iii) our unvested restricted units

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converted on a 1-for-1 basis into 202,924 shares of unvested restricted common stock. Prior to the Conversion, we had issued profit interest units to employees. Our vested profit interest units converted on a net issuance basis into 1,035,653 shares of common stock and our unvested profit interest units converted on a net issuance basis into 3,165,350 shares of restricted common stock.

The offers, sales, and issuances of the securities described in Item 15(1) were exempt from registration under the Securities Act under Section 4(a)(2) of the Securities Act or Regulation D promulgated thereunder as transactions by an issuer not involving a public offering. The recipients of securities in each of these transactions acquired the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the securities issued in these transactions. Each of the recipients of securities in these transactions was an accredited person and had adequate access, through employment, business, or other relationships, to information about the registrant.

The offers, sales, and issuances of the securities described in Items 15(2), 15(3), and 15(4) were exempt from registration under the Securities Act under either (1) Rule 701 in that the transactions were under compensatory benefit plans and contracts relating to compensation as provided under Rule 701 or (2) Section 4(a)(2) of the Securities Act as transactions by an issuer not involving any public offering. The recipients of such securities were the registrant's employees, consultants, or directors and received the securities under the registrant's 2017 Plan. The recipients of securities in each of these transactions represented their intention to acquire the securities for investment only and not with view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the securities issued in these transactions.

Item 16. Exhibit and Financial Statement Schedules

(a) Exhibits.

See the Exhibit Index immediately preceding the signature page hereto for a list of exhibits filed as part of this registration statement on Form S-1, which Exhibit Index is incorporated herein by reference.

(b) Financial Statement Schedules.

Schedules have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes thereto.

Item 17. Undertakings

The undersigned registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreements, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers, and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer, or controlling person of the registrant in the successful defense of any action, suit, or proceeding) is asserted by such director, officer, or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form

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of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933 shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

EXHIBIT INDEX

Number	Exhibit Title	Incorporated by Reference			Filed Herewith
		Form	File No.	Exhibit	
1.1*	Form of Underwriting Agreement, including Form of Lock-up Agreement.				
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	3.2	2/11/2019
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
5.1*	Opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation.				
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.	S-1	333-229152	10.11	1/7/2019
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

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<u>Number</u>	<u>Exhibit Title</u>	<u>Incorporated by Reference</u>			<u>Filed Herewith</u>
		<u>Form</u>	<u>File No.</u>	<u>Exhibit</u>	
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
21.1	List of subsidiaries of Registrant.	S-1	333-229152	21.1	01/07/2019
23.1*	Consent of Independent Registered Public Accounting Firm.				
23.2*	Consent of Wilson Sonsini Goodrich & Rosati, Professional Corporation (included in Exhibit 5.1).				
24.1*	Power of Attorney (see page II-6 to this Form S-1).				

* To be filed by amendment

+ 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.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of South San Francisco, State of California, on the day of _____.

ALECTOR, INC.

By: _____
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., Sabah Oney, Ph.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 (including post-effective amendments) to this registration statement and any and all additional registration statements pursuant to Rule 462(b) of the Securities Act of 1933, as amended, 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 Act of 1933, as amended, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
_____ Arnon Rosenthal, Ph.D.	Chief Executive Officer and Director (Principal Executive Officer)	
_____ Calvin Yu	Vice President, Finance (Principal Financial and Accounting Officer)	
_____ Tillman Gerngross, Ph.D.	Chairperson of the Board	
_____ Louis J. Lavigne, Jr.	Director	
_____ Terry McGuire	Director	
_____ Richard Scheller, Ph.D.	Director	
_____ David Wehner	Director	
_____ Kristine Yaffe, M.D.	Director	