Harnessing the Immune System to Cure Neurodegeneration

November 2020

ALECTOR
Forward Looking Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation, including statements regarding our future financial condition, results of operations, business strategy and plans, and objectives of management for future operations, as well as statements regarding industry trends, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potentially,” “predict,” “should,” “target,” “will” or the negative of these terms or other similar expressions.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: 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; 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 who suffer from the diseases we are targeting; our ability to expand our product candidates into additional indications and patient populations; the beneficial characteristics, safety, efficacy, and therapeutic effects of our product candidates; our plans relating to the further development and manufacturing of our product candidates, including additional indications we may pursue; 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 trials; our plans and ability to obtain or protect intellectual property rights; the accuracy of our estimates regarding expenses, future revenue, capital requirements, and needs for additional financing; our financial performance; and the sufficiency of our existing cash and cash equivalents to fund our future operating expenses and capital expenditure requirements. These risks are not exhaustive. New risk factors emerge from time to time and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements, as discussed in greater detail in our filings with the Securities and Exchange Commission (SEC), including without limitation in our Quarterly Report on Form 10-Q, as filed on November 10, 2020 with the Securities and Exchange Commission (“SEC”). You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation.

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Pioneering immuno-neurology

IMMUNO NEUROLOGY

Recruiting the brain’s immune system to cure neurodegeneration

Our therapeutics are genetically validated regulators of the brain’s immune system

Genetically defined patient populations and biomarkers enhance probability of success

Human Genetics  Immunology  Neuroscience
Human genetics has enabled a new therapeutic strategy

22/29

of AD risk genes are microglia specific (red)
Our differentiated approach: Combining human genetics with our understanding of immunology and neurodegeneration

Our therapies are designed to restore the function of the microglia to treat these multiple parallel pathologies in order to slow or stop the progression of neurodegenerative disease

Alector’s Immuno-Neurology Approach
Rapidly translating scientific leadership into emerging portfolio of first-in-class programs

Multiple first-in-class clinical programs
- Advanced **4 candidates** into the clinic since our founding
- **Advanced AL001 from preclinical to a Ph 3 study** in less than two years
- **Two immuno-neurology programs for Alzheimer’s disease**, advancing to Ph 2
- **3 additional clinical ready** programs progressing forward

Robust discovery pipeline
- >120 immune system targets
- Progressed **14 programs** into R&D development
- **>200 patent applications**, 38 patent families and 6 issued U.S. patents

Current cash and equivalents of $461.7M* expected to fund operations through 2022

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*As of 3Q 2020

** FIH: first-in-human trials
Robust portfolio of product candidates targeting the innate immune system

<table>
<thead>
<tr>
<th>PROGRAM</th>
<th>CANDIDATE</th>
<th>RESEARCH</th>
<th>PRE-CLINICAL</th>
<th>PHASE 1</th>
<th>PHASE 2</th>
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Portfolio optimized for enhanced clinical success

Each development program incorporates:

- Proven, genetically validated targets
- Biomarkers
- Defined patient populations
FTD-GRN represents our initial indication from our first-in-class progranulin program

MRI of frontal and temporal atrophy in FTD

• Frontotemporal dementia (FTD) is a devastating and rapidly progressive form of dementia
• Early onset under the age of 60
• Life expectancy 7 - 10 years
• 170,000 FTD patients in (US + EU)
  – 15,000 patients with PGRN mutations (FTD-GRN)
AL001 scientific rationale: PGRN deficiency causal for FTD

**Homozygous mutations (100% LOF)**
- 100% decrease in PGRN levels
- Dementia, vision loss, epilepsy, death\(^1\)

**Heterozygous mutations (50% LOF)**
- >50% decrease in PGRN levels
- FTD with >90% penetrance
- Dementia, death within 7 - 10 years

**Regulatory mutations (~20% LOF)**
- ~20% decrease in PGRN levels
- Risk factor for Alzheimer’s\(^3\), Parkinson’s diseases\(^3\)

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Note: LOF - loss of function.

(1) Sci Transl Med. 2017 Apr 12;9(385)
**AL001 for FTD-GRN:** Targeting progranulin to restore function of microglia

**MECHANISM OF ACTION**
- Increases the half-life of PGRN by blocking Sortilin, a degradation receptor, in order to restore PGRN to normal levels

**PHASE 1/2 DATA**
- AL001 was safe and well tolerated in healthy volunteers and patients and showed target engagement and restoration of PGRN

**STATUS**
- Pivotal Phase 3 study initiated in July 2020

**REGULATORY**
- Orphan Drug and Fast Track Designation
AL001 Phase 1 study design

In the Phase 1 study, AL001 was generally safe and well tolerated with no SAEs or DLTs reported

**Phase 1a Dose Escalation (N = 50)**

| Healthy Volunteers | AL001 dose escalation | N = 50 |

**Phase 1b Open Label (N = 14)**

| Asymptomatic FTD-GRN | AL001 60 mg/kg 1 dose | N = 6 |
| Symptomatic FTD-GRN | AL001 30 mg/kg q2w x 3 doses | N = 8 |

**STUDY OBJECTIVES:** Safety and tolerability, Pharmacokinetic (PK), and pharmacodynamic (PD) markers in blood and CSF

**PRIMARY ENDPOINT:** Safety and tolerability

**SECONDARY ENDPOINT:** Pharmacokinetic (PK)

**EXPLORATORY:** Pharmacodynamic (PD) markers in blood and CSF
AL001 increased plasma progranulin in healthy volunteers

AL001 was generally safe and well tolerated

AL001 triples PGRN levels in plasma

N = 50
Phase 1 data shows AL001 restores PGRN levels back to the normal range

Sustained increase in CSF PGRN in AL001 Phase 1b study

Individual dots represent individual subjects. Horizontal line represents the median.
* One symptomatic subject did not have a reportable CSF PGRN baseline level which complied with Core lab SOP and was therefore excluded.

Healthy Volunteers (HV) 
(N = 33)

Asymptomatic (aFTD-GRN) 
Single dose (N = 6)

Symptomatic (FTD-GRN) 
3 doses every 2 weeks (N = 8)
AL001 counteracts disease protein signature by normalizing inflammatory and lysosomal biomarkers and demonstrates a decrease in NfL in Phase 1b

AL001 reduced CSF Osteopontin (SPP1), a marker of inflammation

- AL001 reduced CSF Chitotriosidase (CHIT1), a marker of gliosis

- AL001 increased CSF Cathepsin B (CTSB), a marker of lysosomal function

Trend in reduction of plasma Neurofilament (NfL) levels from baseline in Phase 1b\(^1,2\)

Note: * represents p<0.05
NfL = Neurofilament light chain
1 Alector Research and Development Day presentation, December 13, 2019
2 SEM: standard error of the mean
AL001 Phase 1b participants had the option to rollover into Phase 2

Phase 1b Open Label (N = 14)

Asymptomatic FTD-GRN | N = 6
Symptomatic FTD-GRN | N = 8

Participants could roll over to Phase 2

Asymptomatic FTD-GRN | N = 5
Symptomatic FTD-GRN | N = 7

Dosing discontinued

Phase 2 Open Label (expected enrollment up to N = 40)

Asymptomatic FTD-GRN* | AL001 60 mg/kg q4w for 96 weeks | N = 5 (5: Ph 1b rollovers)
Symptomatic FTD-GRN* | AL001 60 mg/kg q4w for 96 weeks | N = 10** (7: Ph 1b rollovers) (3: New patients)
Symptomatic FTD-C9orf72 | AL001 60 mg/kg q4w for 96 weeks | Enrollment on-going

AAIC Dataset (N = 15)

Asymptomatic FTD-GRN | N = 5
Symptomatic FTD-GRN | N = 10**

PRIMARY ENDPOINT: Safety and tolerability
SECONDARY ENDPOINT: PK
EXPLORATORY: PD markers in blood and CSF, volumetric MRI (vMRI), Clinical Outcome Assessments

* Asymptomatic and Symptomatic FTD-GRN enrollment closed.
** Due to COVID-19 mediated site closures, 2/10 patients missed a dose and biomarker evaluations.
AL001 Phase 2: Generally safe and well tolerated in FTD-GRN participants

<table>
<thead>
<tr>
<th></th>
<th>aFTD-GRN (N=5)</th>
<th>n (%)</th>
<th>FTD-GRN (bvFTD and PPA) (N=10)</th>
<th>n (%)</th>
<th>Total (N=15)</th>
<th>n (%)</th>
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<tr>
<td>Any TEAE</td>
<td>4 (80.0)</td>
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<td>4 (40.0)</td>
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<td>8 (53.3)</td>
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<tr>
<td>Any Severe TEAE</td>
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<td></td>
<td>1* (10.0)</td>
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<td>1* (6.7)</td>
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<tr>
<td>Any Treatment-Related TEAE</td>
<td>1 (20.0)</td>
<td></td>
<td>0</td>
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<td>1 (6.7)</td>
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<tr>
<td>Any Treated-Related Severe TEAE</td>
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<td>0</td>
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<tr>
<td>Any SAE</td>
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<td>1* (6.7)</td>
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<td>Any TEAE Leading to Study Drug Discontinuation</td>
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<td>1* (10.0)</td>
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<tr>
<td>Any TEAE Leading to Study Discontinuation</td>
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</table>

* One participant had an unrelated severe SAEs (deep venous thrombosis) with onset date ~7 weeks after the last dose that led to treatment discontinuation. All other TEAEs were mild in severity.
Phase 2 data shows plasma PGRN restored to normal in FTD-GRN participants

Data cut-off: 14-May 2020
SEM: standard error of the mean
Solid circles represent the mean and the dashed bars represent the standard error of the mean.
*Due to COVID-19 mediated site closures, 2/10 patients missed a dose and biomarker evaluations.
Six out of eight participants in Phase 2 showed a decrease in NfL at their last measured timepoint

**Natural Log of Plasma Neurofilament Level Over Time**

Symptomatic FTD-GRN (N=8*)

**Plasma NfL levels – Symptomatic FTD-GRN (N=8*)**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Baseline</th>
<th>Last Measured Timepoint</th>
<th>% Change in NfL from Baseline</th>
<th>Last Measured Timepoint</th>
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<tr>
<td>1</td>
<td>82.9</td>
<td>39.9</td>
<td>(52%)</td>
<td>Day 29</td>
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<tr>
<td>2</td>
<td>11.2</td>
<td>8.0</td>
<td>(29%)</td>
<td>Day 200</td>
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<tr>
<td>3</td>
<td>22.9</td>
<td>16.4</td>
<td>(28%)</td>
<td>Day 85</td>
</tr>
<tr>
<td>4</td>
<td>19.8</td>
<td>15.8</td>
<td>(20%)</td>
<td>Day 58</td>
</tr>
<tr>
<td>5</td>
<td>68.0</td>
<td>64.8</td>
<td>(5%)</td>
<td>Day 122</td>
</tr>
<tr>
<td>6</td>
<td>148.8</td>
<td>141.2</td>
<td>(5%)</td>
<td>Day 85</td>
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<tr>
<td>7</td>
<td>46.3</td>
<td>55.1</td>
<td>19%</td>
<td>Day 122</td>
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<tr>
<td>8</td>
<td>39.7</td>
<td>76.1</td>
<td>92%</td>
<td>Day 117</td>
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</table>
AL001 case study: 47yo FTD-GRN patient with primary progressive aphasia

197 days of uninterrupted dosing shows a decrease in NfL

- Patient enrolled and completed Phase 1b, PGRN levels normalized and NfL decreased
- Patient had a 137-day gap between last dose in Phase 1b and enrollment in Phase 2, during which NfL increased by 37%
- After being on drug for 197 days in the Phase 2, without interruption, patient’s NfL decreased by 29%
AL001 program next steps

• FTD-C90rf72 patients will **continue the enrollment in Phase 2** (up to 20 total)

• **Present additional data** from the Phase 2 trial of AL001 in pre-symptomatic and symptomatic FTD-GRN participants and an additional cohort of FTD-C9orf72 patients in 2021

• Continue to **execute INFRONT-3 pivotal Phase 3**
AL001 next steps: Pivotal Phase 3 study initiated in July 2020

Approximately 50 clinical centers, including GENFI and ALLFTD registry sites, will be included in the global Phase 3 study

**Randomization**
- Randomized, Double Blinded, Placebo Controlled Study (N = 180)

**Individuals at Risk for or with FTD**

**PRIMARY ENDPOINT:** CDR® plus NACC FTLD-SB

**SECONDARY CLINICAL ENDPOINT:** CGI-S, CGI-I, FRS

**BIOMARKER ENDPOINTS:** vMRI, CSF, blood

**Study Treatment**
- AL001 60 mg/kg IV q4w for up to 96 weeks
- 8 weeks F/U

**Study Completion Visit**
- Open label extension

CDR® plus NACC FTLD-SB = Clinical Dementia Rating Dementia Staging Instrument PLUS National Alzheimer’s Disease Coordinating Center Frontotemporal Lobar Degeneration Behavior and Language Domains Sum of Boxes; CGI-S = Clinician’s Global Impression-Severity; CGI-I = Clinician’s Global Impression-Improvement; FRS = Frontotemporal Dementia Rating Scale
Targeting PGRN beyond FTD-GRN: Indication expansion

- On-going Phase 2 study includes FTD-C9orf72 cohort
- Additional indications include ALS and/or all FTD patients regardless of mutation

- Ongoing Phase 1 study assessing the safety and tolerability in healthy volunteers with data expected in 2021.

Note: Figure not to scale.
Alzheimer’s disease represents a significant unmet need

No disease modifying therapeutics available

Most common form of dementia\(^1\)

Initial onset in patients **over 65**\(^2\)

\(~5.7\) million\(^2\) cases in the U.S. in 2018 with projections to rise to nearly **14 million in 2050**\(^2\)

6th\(^3\) leading cause of death in the U.S.

60% to 70% of all cases\(^2\)

Past development programs focused on single pathology of disease, such as beta amyloid and tau proteins, which did not yield success.

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3. NIH National Institute of Aging, “Alzheimer’s Disease Fact Sheet”
TREM2 homozygous loss of function may cause neurodegeneration by age 40, with a lifespan of ~10 years following diagnosis.

TREM2 heterozygous loss of function increases risk for AD by 3x.

A SNP (rs9381040) associated with increased TREM2 expression is protective against AD.
**AL002 for AD:** Targeting TREM2 to recruit microglia to counteract disease pathologies

**MECHANISM OF ACTION**
- Antibody designed to activate TREM2 and enhance microglia activity

**PHASE 1 DATA**
- AL002 successfully achieved its primary and secondary endpoints in the Phase 1 study

**STATUS**
- Initiating Phase 2 in 2020

**PARTNER**
- Global 50/50 profit and cost share partnership with AbbVie

"Improve survival, proliferation, function of microglia"
AL002 recruits microglia to counteract pathologies in AD mouse model

**AL002 strongly increases a marker of microglial proliferation**

**AL002s recruit microglia to plaques**

**AL002s reduces area occupied by plaques**

**** indicates a p-value < 0.0001 by T-test.
(1) Data generated by D. Wilcock, University of Kentucky
Target engagement and proof-of-mechanism in CSF achieved in Phase 1

AL002 was found to be generally safe and well-tolerated in 34 healthy volunteers

Dose-dependent reduction in soluble TREM2

Dose-dependent elevation in sCSF-1R, associated with microglia activation

N = 34*

p < 0.001

% change from baseline

N = 34*

p < 0.05

% change from baseline
AL002 next steps: Initiate Phase 2 in 2020

**Patients with prodromal-to-mild (early AD)**

**Randomized, Double Blinded, Placebo Controlled Study** *(48-96 weeks)*

**AL002 arms**

**Placebo arm**

**Primary Endpoint:** CDR-SB

**Secondary Clinical Outcome Assessments:**

RBANS, ADAS-Cog13, ADCS-ADL-MCI

* Number of active arms could change during the study
**AL003 for AD:** Increase activity of microglia by blocking SIGLEC 3

**MECHANISM OF ACTION**
- SIGLEC 3 is inhibitory receptor expressed on microglia
- AL003 blocks SIGLEC 3 in the same manner of a PD-1 inhibitor to allow immune system to work at fully capacity

**PHASE 1A DATA**
- AL003 successfully achieved its primary and secondary endpoints in the Phase 1a study

**STATUS**
- Phase 1b ongoing with data expected in 2021

**PARTNER**
- Global 50/50 profit and cost share partnership with AbbVie
SIGLEC 3 mutation a risk for Alzheimer’s disease

SIGLEC 3 is an inhibitory receptor for microglia

Prevalent risk allele in AD*:
- Reduces ability to clear A beta plaques**
- Leads to a smaller brain volume***

Protective SIGLEC 3 variant
- low A-beta

Risk SIGLEC 3 variant
- high A-beta

A-beta clearance

AA: Protective Allele  
CC: Risk Allele

SIGLEC 3 Expression

AA: Protective Allele  
CC: Risk Allele

A-beta clearance

MFI SIGLEC 3

AA  
AC  
CC

Della MFI

AA  
AC  
CC

***Neurobiol Aging. 2015 Apr;36(4):1765.e7-1765.e16
Target engagement and proof-of-mechanism in CSF achieved in Phase 1a
AL003 was found to be generally safe and well-tolerated in 21 healthy volunteers
AL003 demonstrated long lasting peripheral target engagement

The Phase 1b portion of the study continues to enroll with data expected in 2021
Latest prioritized product candidates moving towards the clinic

**AL014** for AD
- Designed to counteract the risk variants of MS4A4A and to functionally convert the risk variants of MS4A4A to the protective variant
- Goal: mimic and exceed the beneficial activity of the protective MS4A4A variant, which may potentially decrease the progression of AD
- First-in-human study expected to initiate in the next 12-18 months

**AL008** Oncology
- Novel antibody targeting the CD47-SIRP-alpha pathway
- Unique dual mechanism of action that relieves immune suppression (a “don’t eat me signal”) while also engaging Fc gamma to drive anti-tumor immunity

**ADP009** Oncology
- First-in-class multi-Siglec inhibitor that recruits innate immune cells to activate adaptive immunity
In 2021, we will continue to advance Alector’s broad clinical pipeline

| AL001          | • Continue progressing Phase 3 study of AL001 in FTD-GRN  
|               | • Phase 2 results in FTD-GRN                          |
| AL002          | • Continue progressing Phase 2 study of AL002 in AD (initiation expected in 2020) |
| AL003          | • Phase 1b results from AL003 in AD                    |
| AL101          | • Phase 1 results of AL101 in healthy volunteers       |
| AL014          | • Initiation of Phase 1 FiH study of AL014              |

Current cash and equivalents of $461.7M* expected to fund operations through 2022
“At Alector we envision a world where dementia and neurodegeneration are illnesses of the past, just as smallpox and polio have become.”

Arnon Rosenthal, PhD
Chief Executive Officer, Co-Founder
Harnessing the Immune System to Cure Neurodegeneration
AL001 counteracts the disease protein signature in FTD patients in Phase 1b

- AL001 reduces inflammatory markers of disease (blue)
- AL001 increases proteins associated with lysosomal function (red)