Forward-Looking Statement

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation 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,” “will” or the negative of these terms or other similar expressions. Forward-looking statements contained in this presentation also include, but are not limited to, statements regarding: our future financial condition, results of operations, business strategy and plans, plans, timelines and expectations related to our product candidates and our other clinical and pre-clinical programs, including with respect to the availability of data, the initiation of future clinical trials and plans and expectations regarding planned regulatory filings with respect to such programs; and objectives of management for future operations, as well as statements regarding industry trends.

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: Alector’s plans relating to the development and manufacturing of its product candidates and research programs; the ability of Alector, Inc.’s (“Alector”) clinical trials to demonstrate safety and efficacy of its product candidates, and other positive results; the timing and focus of Alector’s future clinical trials, and the reporting of data from those trials; Alector’s plans relating to commercializing its product candidates, if approved, including any geographic allocation of focus and sales strategy; the expected potential benefits of strategic collaborations with third parties and Alector’s ability to attract collaborators with development, regulatory and commercialization expertise; Alector’s estimates of the number of patients in the United States who suffer from the diseases it is targeting and the number of patients that will enroll in its clinical trials; the size of the market opportunity for Alector’s product candidates in each of the diseases it is targeting; Alector’s ability to expand its 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 Alector’s product candidates; the timing or likelihood of regulatory filings and approvals, including Alector’s expectation to seek special designations, such as orphan drug designation, for its product candidates for various diseases; Alector’s ability to obtain and maintain regulatory approval of its product candidates; Alector’s plans relating to the further development and manufacturing of its product candidates, including additional indications that it may pursue; existing regulations and regulatory developments in the United States and other jurisdictions; Alector’s continued reliance on third parties to conduct additional clinical trials of its product candidates, and for the manufacture of its product candidates for preclinical studies and clinical trials; and the other risks, uncertainties and assumptions discussed in the public filings we have made and will make with the Securities and Exchange Commission (“SEC”). 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. 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.

This presentation also contains results based on data from our clinical trials. These clinical trials are ongoing and this presentation does not speak to, and you should make no assumptions about, any additional data. In addition, the information we have chosen to publicly disclose regarding our product candidates has been selected from a more extensive amount of available information. You or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise. If the initial data that we report differ from updated, late, final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize our other product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects.

Except as required by law, we undertake no obligation to update any statements in this presentation for any reason after the date of this presentation.

We have filed Current Reports on Form 8-K, Quarterly Reports on Form 10-Q, Annual Reports on Form 10-K, and other documents with the SEC. You should read these documents for more complete information about us. You may obtain these documents for free by visiting EDGAR on the SEC website at www.sec.gov.

This presentation discusses certain investigational therapeutic agents, which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of our product candidate for the therapeutic use for which it is being studied.

This presentation contains statistical data based on independent industry publications or other publicly available information, as well as other information based on our internal sources. We have not independently verified the accuracy or completeness of the data contained in these industry publications and other publicly available information. Accordingly, we make no representations as to the accuracy or completeness of that data.
Translating Scientific Insights into a Broad Portfolio of First-in-Class Programs

**NOVEL APPROACH**
- Founded to pioneer a new field of research: Immuno-neurology
- Informed by neuroscience, human genetics and immunology
- Substantial IP portfolio established: 41 issued patents, 500+ patent applications

**MULTIPLE CLINICAL TRIALS**
- PGRN Phase 3 Program for FTD-GRN
- TREM2 Phase 2 Program for Early AD
- PGRN Phase 2 Program for FTD-C9orf72
- MS4A Phase 1 Program for AD
- Pre-Clinical Portfolio and Discovery Platform
  - Multiple immuno-neurology and oncology opportunities

**WORLD CLASS PARTNERS**
- $700M upfront
- $1.5B+ milestone
- 50-50 U.S. profit share
- Tiered double-digit royalties ex-U.S.
- $205M upfront payment
- $20M equity investment
- $986M milestone payments
- Global 50-50 profit share

**STRONG FINANCIALS**
- $758 MILLION IN CASH: RUNWAY THROUGH 2025

---

FTD = Frontotemporal dementia, PD = Parkinson’s Disease, AD = Alzheimer’s Disease
Note: As of September 30, 2022, Alector’s cash, cash equivalents and investments totaled $758.3 million.
Recruiting microglia, the brain’s immune system, to potentially cure neurodegeneration

**Immuno-neurology Therapeutics**

Ineffective and damaging microglia  
→  
Effective and beneficial microglia

**Alector is applying the immuno-oncology concept of harnessing the immune system as a broad and potentially effective and long-lasting therapeutic approach**

**Human Genetics**
Develop drugs targeting risk genes for neurodegeneration to enhance protective functions of these risk genes

**Immunology**
Target checkpoint regulators on microglia and harness microglia as broad therapy for neurodegeneration

**Neuroscience**
Rejuvenate microglia and harness their physiological role as guardians of brain health

**Multiple first-in-class programs are in or entering the clinic for neurodegenerative diseases**
Genetic Rationale for Immuno-Neurology: Many Familiar Risk Genes for Alzheimer’s Disease are Checkpoint Proteins for the Microglia Brain Innate-Immune System

Most AD risk genes are microglia regulators (Arrows)
Biological Rationale for Immuno-Neurology: Microglia are Essential for Brain Health in Humans

Loss of microglia due to CSF1R mutations leads to neurodegeneration “Adult-Onset Leukoencephalopathy”

Patients experience range of psychiatric, neurocognitive, and motor symptoms

Results in microglial dysfunction, damage to white matter, high levels of NfL, rapid cognitive decline and early death

Average age of onset is ~43; Patients are disabled within ~4 years and die in ~5-6 years

Rapid brain tissue loss

~ 6 Year Survival Rate

Rapid Cognitive Decline

IDENTIFY FAMILIAL GENETIC RISK VARIANTS FOR NEURO-DEGENERATION
Germline genetics of Alzheimer’s, Parkinson’s, FTD, ALS, MS

DETERMINE GENE AND PROTEIN EXPRESSION SIGNATURES & KO/KI PHENOTYPE
7k Proteins, 20K genes, IPSC, CRISPR AI in house & public databases

TEST DRUGS IN DISEASE MODELS
Efficacy & safety

SELECT SUBSET THAT REGULATE IMMUNE SYSTEM
RNAseq, KO in models, IPSC, CRISPR AI

DEVELOP DRUGS THAT MIMIC THE SIGNATURE & FUNCTION OF THE PROTECTIVE GENETIC VARIANT
Drugs expression signature and phenotype

Alector’s Discovery Platform for Genetically Validated Microglia Checkpoint Targets
Alector’s Checkpoint Therapies Anticipated to Act Independently and in Combination

Our therapies seek to harness microglia to improve the functionality of neurons, oligodendrocytes, astrocytes, endothelial cells and blood vessels, and to remove debris, misfolded proteins and recycle damaged synapses.

Anti-Aβ-antibodies (or Abs against Tau, α-Synuclein, TDP43) mark misfolded aggregates and recruit microglia to remove them.

Our therapies are expected to enhance microglia’s ability to remove misfolded proteins in conjunction with Abs that tag these proteins.
Latozinemab (AL001) and AL101 elevate progranulin, a risk gene for FTD, AD, PD, and ALS, which promotes neuronal survival and enhances lysosomal activity, potentially improving degradation of misfolded proteins as well as the overall function of microglia and protecting neurons.

AL002 elevates signaling by TREM2, a risk gene for AD, which promotes microglia proliferation, survival and functionality to potentially improve the degradation of misfolded proteins and the functionality of multiple cell types in the brain.

AL044 modulates signaling by MS4A, a risk gene for AD, and elevates stTREM2 levels, which may promote microglia proliferation, survival and functionality in the context of disease signals.
First-in-Class Portfolio of Product Candidates Targeting the Innate Immune System

<table>
<thead>
<tr>
<th>TARGET</th>
<th>CANDIDATE</th>
<th>RESEARCH</th>
<th>PRECLINICAL</th>
<th>PHASE 1</th>
<th>PHASE 2</th>
<th>PHASE 3</th>
<th>COMMERCIAL RIGHTS</th>
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<tbody>
<tr>
<td>PGRN</td>
<td>AL001</td>
<td>FTD-GRN</td>
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<td>&gt;</td>
<td>GSK</td>
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<td>AL001</td>
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<td>FTD-C9orf72</td>
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<tr>
<td>AL001</td>
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<td>&gt;</td>
<td>GSK</td>
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<td>AL101</td>
<td>Healthy volunteers for AD and PD</td>
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<td></td>
<td>&gt;</td>
<td>GSK</td>
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<tr>
<td>TREM2</td>
<td>AL002</td>
<td>Alzheimer’s disease</td>
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<td>abbvie</td>
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<td>MS4A</td>
<td>AL044</td>
<td>Alzheimer’s disease</td>
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<td>AL044</td>
<td>Orphan neuro indication</td>
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<td>Multi-Siglec</td>
<td>AL009</td>
<td>Solid tumors</td>
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<tr>
<td>SIRP-alpha</td>
<td>AL008</td>
<td>Solid tumors</td>
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**Target indications include AD, PD, FTD, MS & cancer**

12+ programs

IP portfolio contains 50+ patent application families, which include 41 issued patents and >500 pending patent applications directed to more than 20 targets and/or technologies.

*In partnership with GSK, the company made a strategic, non-safety related decision to close enrollment in the ALS-C9orf72 Phase 2a biomarker trial and is currently evaluating plans for a new study.
Progranulin Franchise Programs
Latozinemab (AL001) – Phase 3
AL101 – Phase 1
**Latozinemab (AL001) and AL101: Raising Levels of Progranulin for Potential Benefit**

**Mechanism**
- Increases the half-life of PGRN by blocking Sortilin, a degradation receptor, in order to raise PGRN to normal levels

**Latozinemab (AL001) Status**
- Phase 1 studies of AL001 in healthy volunteers are complete
- Data presented from ongoing Phase 2 study in FTD-GRN and FTD-C9orf72
- Orphan Drug and Fast Track Designation
- Pivotal Phase 3 study in FTD-GRN actively enrolling

**AL101 Status**
- Phase 1 study of AL101 in healthy volunteers is complete
- Commencing preparatory work for Phase 2 in AD
Key biomarkers and clinical outcome assessments reflect underlying disease activity in FTD-GRN patients

<table>
<thead>
<tr>
<th>TARGET ENGAGEMENT</th>
<th>BIOMARKERS OF DISEASE ACTIVITY</th>
<th>CLINICAL BENEFIT</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGRN (plasma and CSF)</td>
<td>Lysosomal dysfunction</td>
<td>Clinical Outcome Assessments</td>
</tr>
<tr>
<td>PGRN</td>
<td>e.g. CTSD, LAMP1</td>
<td>e.g. C1QB</td>
</tr>
<tr>
<td>&gt; 50% reduction in PGRN levels causal for FTD</td>
<td>Dysfunctional lysosomes are hallmark of FTD-GRN</td>
<td>Pathological increases in complement proteins in FTD correlate with cognitive decline</td>
</tr>
</tbody>
</table>

**Trials of FTD-GRN with Latozinemab Make Use of Multiple Biomarkers Linked to Potential MoA and Efficacy**

CTSD = cathepsin D; LAMP1 = lysosomal associated membrane protein 1; C1QB = complement C1q B chain; GFAP = glial fibrillary acidic protein; NfL = neurofilament light chain;

CDR® plus NACC FTLD-SB: Clinical Dementia Rating (CDR) dementia staging instrument plus National Alzheimer’s Coordinating Center (NACC) behavior and language domains frontotemporal lobar degeneration (FTLD) sum of boxes (SB)
INFRONT-2: Latozinemab Restores PGRN in Plasma and CSF to Normal Levels in Symptomatic FTD-GRN

Data cut-off June 15, 2021
Mean +/- SEM
Source: AAIC 2021.
INFRONT-2: Use of Latozinemab Associated with Lowering of Mean Lysosomal and Inflammatory Biomarkers Towards Levels Seen in Control Subjects

FLUID BIOMARKERS OF DISEASE ACTIVITY

Symptomatic FTD-GRN patients at 12 months

Normalization of lysosomal and inflammatory biomarkers

<table>
<thead>
<tr>
<th>Markers</th>
<th>Latozinemab Baseline (N=9)</th>
<th>Latozinemab 6 months (N=8)</th>
<th>Latozinemab 12 months (N=8)</th>
<th>Age-matched procured control (N=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTSD (fm/μL)</td>
<td>5.2 (1.16)</td>
<td>3.8 (0.57)</td>
<td>3.1 (0.21)</td>
<td>3.4 (0.08)</td>
</tr>
<tr>
<td>LAMP1 (fm/μL)</td>
<td>0.6 (0.12)</td>
<td>0.4 (0.06)</td>
<td>0.4 (0.043)</td>
<td>0.4 (0.01)</td>
</tr>
<tr>
<td>C1QB (fm/μL)</td>
<td>0.7 (0.12)</td>
<td>0.6 (0.07)</td>
<td>0.5 (0.02)</td>
<td>0.5 (0.02)</td>
</tr>
</tbody>
</table>

Mean +/- SEM
CTSD = cathepsin D protein
LAMP1 = lysosomal-associated membrane protein 1
C1QB = gene that encodes the B-chain polypeptide of serum complement subcomponent C1q
Source: AAIC 2021.
INFRONT-2: Latozinemab Treatment Decreases Glial Fibrillary Acidic Protein (GFAP) Levels Towards Range Seen in Asymptomatic Carriers of FTD-GRN Mutation

BIOMARKERS OF DISEASE ACTIVITY – ASTROGLIOSIS

GFAP Plasma Concentration

- Range in asymptomatic FTD-GRN: 101.17 – 228.63 pg/mL

GFAP CSF Concentration

- Range in asymptomatic FTD-GRN: 2.61 - 10.7 ng/mL

Data cut-off June 15, 2021
Mean ± SEM
1. Range is of baseline GFAP levels in asymptomatic FTD-GRN patients enrolled in INFRONT-2
Source: AAIC 2021.
Annual Delay in Disease Progression in Latozinemab-Treated Patients Compared to Matched Historical Controls

**CLINICAL BENEFIT**

**CDR® plus NACC FTLD-SB**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate¹</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual Change in GENFI2 (n=10)</td>
<td>6.4</td>
<td>[4.35,8.42]</td>
</tr>
<tr>
<td>Annual Change in Latozinemab (n=12)</td>
<td>3.3</td>
<td>[1.38,5.28]</td>
</tr>
<tr>
<td>Difference in Annual Change (GENFI2 – Latozinemab)</td>
<td>3.1</td>
<td>[0.24,5.88]</td>
</tr>
</tbody>
</table>

48% slowing of clinical progression (3.1 point change)

---

¹ Random Coefficient Model with Repeated Measurements including baseline & all available post-baseline measurements up to 12 months. Data cut-off Sep 8, 2021.

Phase 2 data presented at CTAD 2021 and ADPD 2022

NCT03987295

GENFI = The Genetic Frontotemporal Initiative

GENFI2 refers to the longitudinal FTD registry dataset

CDR® plus NACC FTLD-SB

GENFI2 clinical progression

Latozinemab clinical progression

Baseline | 3 Months | 6 Months | 9 Months | 12 Months
---|---|---|---|---

-3.0 | 0.0 | 2.5 | 5.0 | 7.5 | 10.0 | 12.5 | 15.0 | 17.5 | 20.0 | 22.5 | 25.0 | 27.5 | 30.0

Nominal Time (Months)
TBM = Tensor-based Morphometry (TBM) used for frontotemporal cortex and ventricles

Source: AAIC 2021.
Annual Delay in Disease Progression in Latozinemab-Treated FTD-C9orf72 Participants Compared to the ALLFTD Matched Historical Controls

**CLINICAL BENEFIT**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual Change in ALLFTD (n=10)¹</td>
<td>3.4</td>
<td>[1.30, 5.60]</td>
</tr>
<tr>
<td>Annual Change in latozinemab (n=10)²</td>
<td>1.6</td>
<td>[-0.63, 3.78]</td>
</tr>
<tr>
<td>Difference in Annual Change (ALLFTD – latozinemab)³</td>
<td>1.9</td>
<td>[-1.21, 4.95]</td>
</tr>
</tbody>
</table>

- Analysis of propensity score-matched cohort demonstrated a delay in disease progression of 0.9 points [-1.35, 3.21], 36%

1: ALLFTD – one post-baseline timepoint at ~12 months
2: Latozinemab – all available post-baseline assessments (range from 3 to 12 months)
3: Model – Random coefficient model with repeated measurements

ALLFTD: historical observational cohort
Source: AD/PD 2022.
EXPLORATORY BIOMARKER – Glial Fibrillary Acidic Protein (GFAP)

GFAP Plasma Concentration

GFAP CSF Concentration

INFRONT-2: GFAP Levels in Plasma and CSF Are Decreased Over 12 Months in Latozinemab-treated FTD-C9orf72 Participants

Data cut-off June 15, 2021
Mean +/- SEM
Source: AD/PD 2022.
Enrollment Ongoing for Pivotal INFRONT-3 Phase 3 Study of AL001

Randomization
Randomized, Double Blinded, Placebo-Controlled Study
Target enrollment of 180 FTD-GRN carriers at risk for or symptomatic

Study Treatment
AL001 60 mg/kg IV q4w for 96 weeks

Study Completion Visit
8 weeks follow-up

Open-label extension

PRIMARY ENDPOINT
CDR® plus NACC FTLD-SB

SECONDARY CLINICAL OUTCOMES ASSESSMENTS:
CGI-S, CGI-I, FRS, RBANS

EXPLORATORY ENDPOINTS
vMRI, CSF and Plasma Biomarkers

Study taking place at clinical centers in US, Canada, Europe and Australia
Initial data read out after 96-week treatment period

“At risk” = GRN carriers who are pre-symptomatic and meet a pre-specified NfL threshold for enrollment in the Phase 3 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; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status
Latozinemab: Recent Updates and Considerations for Path Forward in FTD-GRN

- FTD-GRN remains a significant unmet need with no approved therapies
- INFRONT-3 is progressing as the largest and most comprehensive prospective, randomized study for FTD-GRN undertaken to date by any sponsor
- Recent FDA approvals signal a willingness to consider biomarker data supportive for neurodegenerative disease indications
- Progress in FTD biomarkers (fluid and vMRI) and the recently published familial FTD disease progression model may further advance how FTD-GRN clinical studies are conducted
AL101 Elevated Progranulin Levels in Plasma and CSF in Phase 1

Data supports development of AL101, which has higher potency and a longer half-life that enables the potential for lower and less frequent dosing, for larger indications such as Alzheimer’s disease.

Mean (±SD) Percentage Change from Baseline in Plasma (A) and CSF (B) Concentrations of Progranulin as a Function of Time After Multiple-Dose Administration of AL101

CSF = cerebrospinal fluid; IV = intravenous; MD = multiple-dose; PGRN = progranulin; SC = subcutaneous; SD = standard deviation

TREM2 Alzheimer’s Disease Program
AL002 – Phase 2
AL002: Designed to Activate TREM2 in Order to Enhance Microglia Function

Rationale

• TREM2 signaling controls critical microglial activity
• TREM2 is a prominent risk gene for Alzheimer’s disease
  • Homozygous mutations cause dementia (NHD, FTD)
  • Heterozygous mutations increase risk for Alzheimer’s disease by 3x
  • Ligands include APOE, an Alzheimer’s risk gene

Mechanism

• Activates TREM2 signaling with the intention of enhancing functionality of microglia to address pathology and protect neurons

Status

• INVOKE-2 Phase 2 double-blind, randomized, placebo-controlled clinical trial on-going

Intended to improve survival, proliferation, function of microglia
AL002 Demonstrated Biological Activity in Multiple *in vitro* Assays

**Receptor activation**

**Downstream effects**

**Macrophage function**

**Intracellular signaling**

AL002 promotes TREM2-mediated DAP12 phosphorylation

AL002 promotes TREM2-mediated NFAT activation in a reporter cell system in vitro

AL002 increases human macrophage survival under cellular stress

Alector data on file
TREM2 Activation Appears to Reduce Toxic Plaques and Neuronal Damage in a Mouse Model of AD

- Filamentous Plaque is considered detrimental

**CV**- mice expressing WT human TREM2  

**R47H**- mice expressing R47H mutant TREM2

Studies conducted with AL002c, a murine version of AL002.
AL002 Shows Evidence of Target Engagement and Microglia Activation with Decreases in sTREM2 and Increases in IL1RN in the CSF of NHPs

Preclinical results consistent with subsequent human data

AL002 decreases sTREM2 in the CSF of non-human primates in a dose-dependent manner

AL002 increases IL1RN in the CSF of non-human primates in a dose-dependent manner
AL002 Target Engagement and Evidence of Microglia Activation Achieved in Phase 1

AL002 was generally well-tolerated and demonstrated dose-dependent target engagement and activation of microglia in healthy volunteers consistent with preclinical results1.

**Dose-Dependent Reduction in CSF sTREM2 (Mean ±-SD), Associated with Target Engagement**

![Graph showing dose-dependent reduction in CSF sTREM2](image)

- Placebo
- 6 mg/kg
- 15 mg/kg
- 30 mg/kg
- 45 mg/kg
- 60 mg/kg

% change from baseline

N = 34
p < 0.001

**Dose-Dependent Elevation in CSF sCSF-1R (Mean ±-SD), Associated with Microglia Activation**

![Graph showing dose-dependent elevation in CSF sCSF-1R](image)

- Placebo
- 6 mg/kg
- 15 mg/kg
- 30 mg/kg
- 45 mg/kg
- 60 mg/kg

% change from baseline

N = 34
p < 0.05

---

Data are presented as mean ±SD; cohort n = 6 (placebo, 6 mg/kg, 15 mg/kg, 30 mg/kg) and 5 (45 mg/kg, 60 mg/kg).

***P = 0.0001 for 6 mg/kg and P < 0.0001 for all other doses vs. pooled placebo control. *P = 0.026 at 60 mg/kg vs. pooled placebo.

AL002 Treatment in Phase 1 Also Caused an Increase in CSF Levels of IL1RN and SPP1, Indicating Further Evidence of Microglial Activation

At doses 6mg/kg – 45 mg/kg, N=6/cohort. N=14 in the 60 mg/kg cohort. Pooled placebo N=11.

*Outlier value (1280.3% above baseline at Day 3 from 1 participant in the 30 mg/kg dose group) were omitted from the graph.

Phase 1 data presented at AAIC 2021; NCT03635047.

Elevation of IL1RN in CSF (Mean +-SD) After Treatment with AL002

Elevation of SPP1 in CSF (Mean +-SD) After Treatment with AL002
INVOKE-2 Phase 2 AL002 Study in Individuals with Early Alzheimer’s Disease

**Randomization**
- Randomized, Double Blinded, Placebo-controlled Study (up to 96 weeks)
- Target enrollment of ~265 people with early Alzheimer’s disease

**Treatment**
- AL002 Dose 1 IV/q4w
- AL002 Dose 2 IV/q4w
- AL002 Dose 3 IV/q4w
- Placebo arm

**Study Completion Visit**
- 8 weeks safety F/U

**Primary Endpoint**
- CDR-SB

**Secondary Clinical Outcomes Assessments:**
- RBANS, ADAS-Cog13, ADCS-ADL-MCI

**Exploratory Endpoints**
- vMRI, CSF, Plasma Biomarkers and PET scans

*Common close design, while treatment is up to 96 weeks, the study is completed when the last patient reaches 48 weeks of therapy (plus 8 weeks of safety follow-up).*
### AL002: The Most Advanced Clinical Program Targeting TREM2

<table>
<thead>
<tr>
<th></th>
<th>2023</th>
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- **Enrollment Complete**
- **Top-line Data**
- **Potential AbbVie Opt-in $250M**

#### Key Points:

- Active engagement with sites and investigators (post removal of ApoE e4 homozygous population)
- Significant momentum in engagement (increasingly recognized as a program with transformative potential)
- ARIA events being actively monitored and managed (potential biomarker for amyloid modulation)
MS4A Alzheimer’s Disease Program
AL044 – Phase 1
Overview of MS4A Target and AL044 Candidate

- Member of ~22 membrane-tetra spanning 4A family, structurally related to CD20
- Expressed on microglia, CNS perivascular macrophages
- Regulates multiple aspects of AD risk and disease progression
- AL044, our drug candidate, functionally phenocopies and exceeds the activities of the protective MS4A variant
- AL044 regulates microglia, signaling, proliferation, survival, migration, lysosomal function, immune response and energetics
- Phase 1 study initiated in September 2022

Effects of MS4A on AD

<table>
<thead>
<tr>
<th>Protective Allele</th>
<th>Effects on AD</th>
<th>Risk Allele</th>
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<tbody>
<tr>
<td></td>
<td>AD Risk</td>
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<td></td>
<td>Rate of cognitive decline</td>
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<td>Ab Plaques &amp; CSF Tau</td>
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<td>Rate of brain Tissue Loss</td>
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<td></td>
<td>Rate of Conversion from MCI to AD</td>
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<tr>
<td></td>
<td>Age of onset and survival</td>
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<tr>
<td></td>
<td>CSF Soluble TREM2</td>
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<td></td>
<td>Protective Interactions with APOE4</td>
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</tbody>
</table>

Higher levels of sTREM2 are thought to represent higher activity of TREM2 signaling and better functioning microglia*.

**MS4A Regulates Level of Soluble TREM2 in the CSF**

**GWAS of CSF sTREM2 Level**

Manhattan and regional plot of the results from QTL analysis for CSF sTREM2 levels.

**Effect of MS4A SNPs on sTREM2 Expression**

Higher levels of sTREM2 are associated with protection from AD disease initiation and progression.

---

*The same SNPs that are associated with risk, survival, age of onset and levels of MS4A mRNA in AD are also associated with the levels of soluble TREM2 (sTREM2) in the human CSF. sTREM2 is considered a proxy for the level of membrane signaling TREM2.

AL044 Phenocopies and Exceeds the Elevation of Soluble and Membrane TREM2 by the Protective Allele

The protective allele of MS4A increases $s\text{TREM2}$ by ~20%

**sTREM2 Levels After Treatment with AL044 for 48 Hours**

- **Donor 1009**
  - EC50 (nM): 0.370 ± 0.068
  - Max response: 5.904 ± 1.770

**Membrane TREM2 Levels After Treatment with AL044 for 48 Hours**

- **Donor 1009**
  - EC50 (nM): 0.329 ± 0.014
  - Max response: 2.313 ± 0.223

Source: RTR-AL044-012

Note: Monocyte-derived macrophages. Treated for 48 hours. Membrane TREM2 measured by flow cytometry. Soluble TREM2 measured by MSD.
AL044: Targeting a Candidate Master Immune Checkpoint Regulator of Microglia

Disease Signals such as TREM2, CSF1R, Dectin ligands

AL044 is expected to ready microglia

Double trigger system

CSF1R  TREM2  Dectin-1

survival  proliferation  phagocytosis  migration  Lysosomes  metabolism  Innate immune memory

Clearing misfolded proteins  Resolve Inflammation  Removal damaged myelin  Removal damaged synapses  Lipid processing  Immunity to infection  Protect vasculature

Candidate Therapy for AD and other neurodegenerative disorders
Alector Oncology Overview
Neurodegeneration and Cancer Converge on Innate Immunity

Innate immunity plays critical role in both neurodegeneration and cancer

NEURODEGENERATION

Repolarizing and recruiting the aged microglia brain innate immune system to treat neurodegeneration

Tumor associated Macrophage (TAMs) Aging Microglia

Reprogramming tumor associated macrophages (TAMs) to treat cancer

CANCER

Aging microglia share gene expression signature with tumor associated macrophages (TAMs)

R = 0.188

Genes upregulated in aging microglia and tumor macrophages

Genes down regulated in aging microglia and tumor macrophages

Healthy vs Tumor macrophages
Cancer Remains a Large Unmet Medical Need with Less Than 20% of Cancers Meaningfully Responding to Immunotherapy

80% of cancers are still refractive to T-cell immunotherapy in part due to tumor associated macrophages (TAMs), innate immune cells which promote tumor growth, vascularization and metastasis, and suppress response to therapy.

Haslam A, Prasad V. Estimation of the Percentage of US Patients With Cancer Who Are Eligible for and Respond to Checkpoint Inhibitor Immunotherapy Drugs. JAMA Netw Open. 2019;2(5)

*N Engl J Med 2017; 377:2500-2501*
TAMs Lead to Poor Tumor Prognosis and Resistance to Immunotherapy in Cancer

Tumor Associated Macrophages (TAMs) or Myeloid Derived Immuno-Suppressor Cells (MDSCs) suppress immune response and immune therapy

Promote resistance to chemotherapy and radiotherapy

Promote tumor neo vascularization and growth

Promote tumor proliferation, invasion, migration and metastasis

Suppress infiltration, trafficking and activation of T-cell, stimulate resistance to CAR-T therapy
Alector’s Therapeutic Strategy is to Reprogram TAMs (Rather Than Blocking or Killing Them) by Targeting Genetically Validated TAM Immune Checkpoints

Reprogramming TAMs to potentially cure cancer

Alector innate Immuno-oncology therapeutics reprogram TAMs

Untreated TAMs

Activities in the cancer micro-environment

Stimulate anti tumor activity of T, B, natural killer, macrophages, dendritic cells

Suppress tumor growth, angiogenesis and metastasis

Augment T-cells checkpoint therapy, CAR-T, vaccine, chemo & radio-therapy

Re-program TAMs

“TAMs are highly malleable... Therefore, repolarization of TAMs appears to be a better means of treating tumors.”

Yang et al, Science Direct 2020
Alector’s Pipeline of Myeloid Cell Cancer Therapeutic Programs

*Anticipated to reprogram TAMs, resulting in slowing of tumor growth, increased T-cell infiltration and antigen presentation, suppression of metastasis and vascularization, and enhancement of checkpoint immunotherapy*

<table>
<thead>
<tr>
<th>Program</th>
<th>Target</th>
<th>Discovery Biology</th>
<th>Target Validation</th>
<th>Lead Selection</th>
<th>IND Enabling</th>
<th>Phase 1</th>
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<tbody>
<tr>
<td>AL009</td>
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Translating Scientific Insights into a Broad Portfolio of First-in-Class Programs

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<tr>
<th>NOVEL APPROACH</th>
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<tbody>
<tr>
<td>Founded to pioneer a new field of research: Immuno-neurology</td>
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<tr>
<td>Informed by neuroscience, human genetics and immunology</td>
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<tr>
<td>Substantial IP portfolio established: 41 issued patents, 500+ patent applications</td>
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<tr>
<th>MULTIPLE CLINICAL TRIALS</th>
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<tr>
<td>PGRN Phase 3 Program for FTD-GRN</td>
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<td>PGRN Phase 2 Program for FTD-C9orf72</td>
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<td>MS4A Phase 1 Program for AD</td>
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<tr>
<td>Pre-Clinical Portfolio and Discovery Platform</td>
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<tr>
<td>Multiple immuno-neurology and oncology opportunities</td>
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<tr>
<th>WORLD CLASS PARTNERS</th>
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<tr>
<td>$700M upfront</td>
</tr>
<tr>
<td>$1.5B+ milestone</td>
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<tr>
<td>50-50 U.S. profit share</td>
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<tr>
<td>Tiered double-digit royalties ex-U.S.</td>
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<tr>
<td>$205M upfront payment</td>
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<tr>
<td>$20M equity investment</td>
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<tr>
<td>$986M milestone payments</td>
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<td>Global 50-50 profit share</td>
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<th>STRONG FINANCIALS</th>
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<td>$758 MILLION IN CASH: RUNWAY THROUGH 2025</td>
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FTD = Frontotemporal dementia, PD = Parkinson’s Disease, AD = Alzheimer’s Disease
Note: As of September 30, 2022, Alector’s cash, cash equivalents and investments totaled $758.3 million.
Thank You