# Alector Corporate Overview

November 2024

# 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, including the sufficiency of cash to fund operations through 2026; results of operations; business strategy and plans; the beneficial characteristics, safety, efficacy, and therapeutic effects of our product candidates; our 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; expectations regarding the timing and financial benefit of our collaborations; and objectives of management for future operations, as well as statements regarding industry trends.

We, Alector, Inc. (“Alector”), 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 its research programs and the development and manufacturing of its product candidates and blood-brain barrier technology platform; the ability of Alector’s clinical trials to demonstrate safety and efficacy of its product candidates, and other positive results; the timing and focus of Alector’s clinical trials, and the reporting of data from those trials, including the anticipated timing and detail regarding the release of data for INVOKE-2; Alector's plans relating to commercializing its product candidates, if approved, including the geographic areas 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, the European Union and world-wide 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 and future regulations and regulatory developments in the United States and other jurisdictions; Alector’s reliance on third parties to conduct clinical trials of its product candidates, and for the manufacture of its product candidates for preclinical studies and clinical trials; the impact of worldwide economic conditions, including macroeconomic downturns stemming from increased inflation, supply chain and other economic impacts of the coronavirus (COVID-19) pandemic and geopolitical events on our business; 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 product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects.

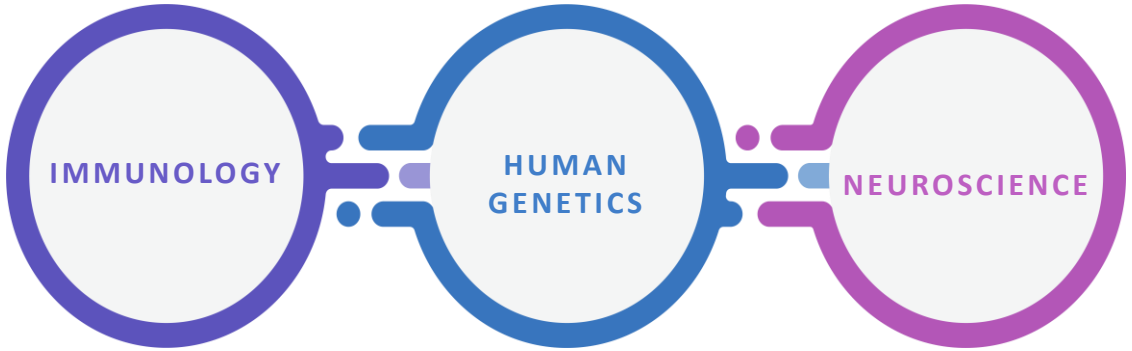
This presentation discusses certain investigational therapeutic agents which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of our product candidate for the therapeutic use for which it is being studied.

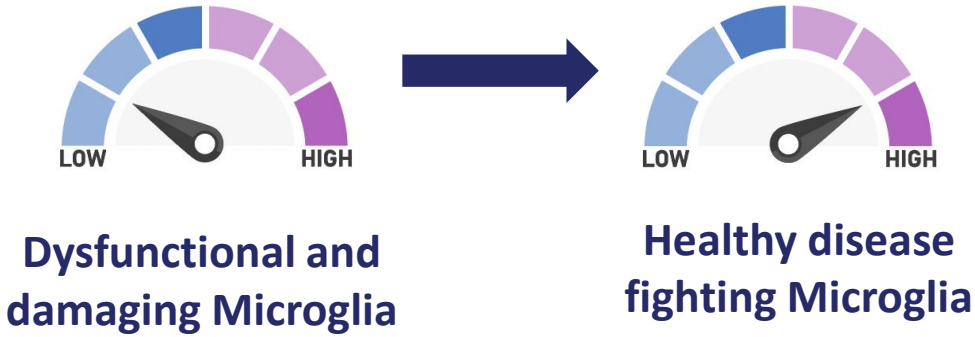
This presentation contains statistical data based on independent industry publications or other publicly available information, as well as other information based on our internal sources. We have not independently verified the accuracy or completeness of the data contained in these industry publications and other publicly available information. Accordingly, we make no representations as to the accuracy or completeness of that data.

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.

# Alector Value Proposition: Pioneering Immuno-neurology

| | |
|---|---|
| **BOLD VISION** | Realize a world where we made brain disorders history |
| **INNOVATIVE SCIENCE** | Proprietary pipeline of novel immuno-neurology drugs |
| **ANTICIPATED DATA** | AL002 INVOKE-2 Phase 2 data readout for early AD in Q4 2024 |
| **WELL RESOURCED** | Experienced team, global partnerships and financial resources |



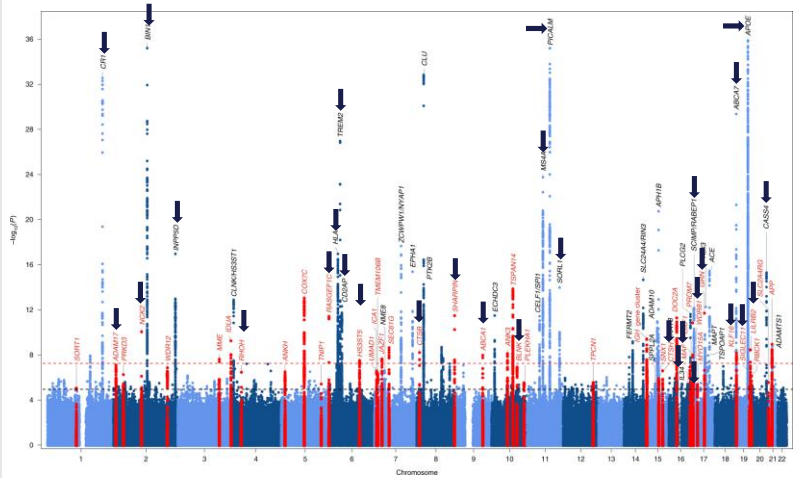

**Dysfunctional and damaging Microglia**

**Healthy disease fighting Microglia**

# Science: Rationale for Developing Microglia Immuno-modulatory Therapies for Dementia

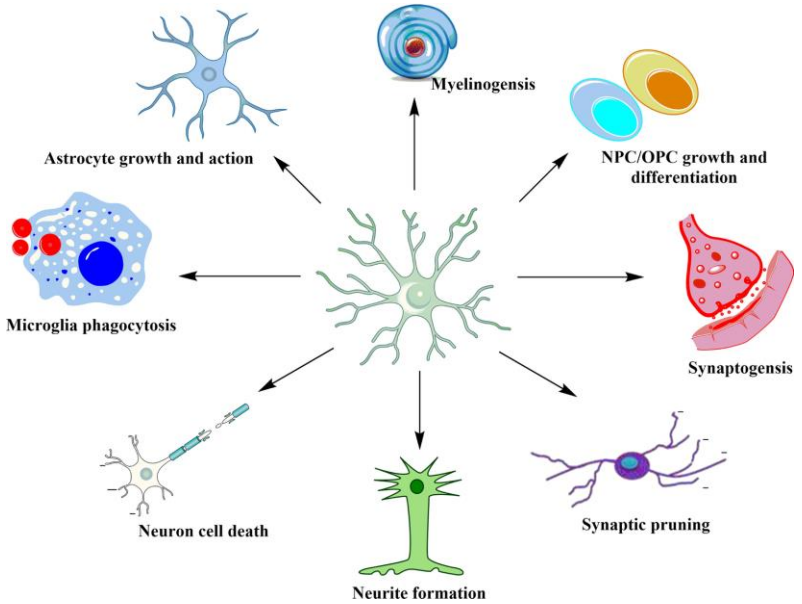
## HUMAN GENETICS

### MANY GENE MUTATIONS ASSOCIATED WITH NEURODEGENERATIVE DISEASE ARE IMMUNE RELATED[1]



## IMMUNOLOGY

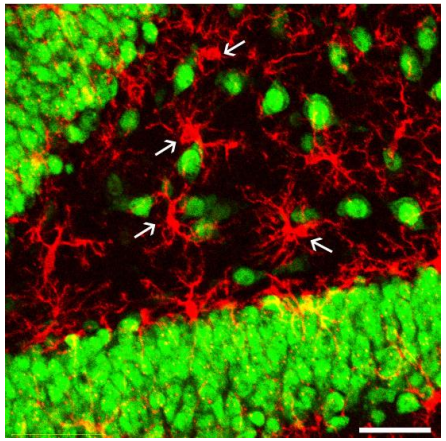
### THE MICROGLIA BRAIN IMMUNE SYSTEM IS ESSENTIAL FOR BRAIN FUNCTION AND HEALTH[2]



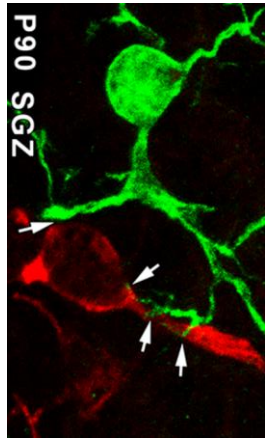

## NEUROSCIENCE

### HEALTHY MICROGLIA NOURISH, PROTECT AND OPTIMIZE THE FUNCTION OF NERVE CELLS[3]

Microglia (red) contact neurons (green)



Microglia (green) contact neurons (red)





1. Bellenguez C, et al. *Nature Genetics*. 2022;54:412-436.; ©2022 Bellenguez C et all. Originally published in *Nature Genetics*.
2. Wang, H., et al. Microglia in depression: an overview of microglia in the pathogenesis and treatment of depression. *J Neuroinflammation* 19, 132 (2022).
3. Liaury, K., et al. Morphological features of microglial cells in the hippocampal dentate gyrus of Gunn rat: a possible schizophrenia animal model. *J Neuroinflammation* 9, 56 (2012).; Cserép C., et al. Microglial control of neuronal development via somatic purinergic junctions. *Cell Rep*. 2022 Sep 20;40(12):111369.

# Well Resourced: Advancing Novel First-in-Class[1] Programs in Collaboration with Established Global Partners

| TARGET | CANDIDATE | RESEARCH | PRECLINICAL | PHASE 1 | PHASE 2 | PHASE 3 | ALECTOR'S COMMERCIAL OWNERSHIP | RIGHTS |
|---|---|---|---|---|---|---|---|---|
| PGRN | Latozinemab | FTD-*GRN* | | | | | U.S. 50-50 profit share with co-promote and tiered double-digit royalties ex-U.S. | GSK |
| | AL101 | AD | | | | | | GSK |
| TREM2 | AL002 | AD | | | | | Global 50-50 profit share with opt-in | abbvie |
| GPNMB | ADP027-ABC | PD | | | | | | alector |
| GCase | ADP050-ABC | PD, LBD | | | | | | alector |
| | Undisclosed-ABC | AD, PD | | | | | | alector |
| | Undisclosed-ABC | ALS, AD, PD | | | | | | alector |
| | Undisclosed-ABC | AD | | | | | | alector |

IP portfolio across all programs contains 60+ patent families, which include 120 issued patents and >500 pending patent applications directed to more than 20 targets and/or technologies

$457.2 MILLION[2] IN CASH PROVIDES RUNWAY THROUGH 2026

1. Alector is not aware of any other TREM2-activating candidates in a Phase 2 or a Phase 3 trial for AD, PGRN-elevating candidates in a Phase 3 trial for FTD, or PGRN-elevating candidates in a Phase 2 or Phase 3 trial for AD as of Nov. 2024.
2. Cash, cash equivalents, and marketable securities as of September 30, 2024, were $457.2 million.

FTD-*GRN* = frontotemporal dementia with a progranulin gene mutation, AD = Alzheimer's disease, PD= Parkinson's disease, ALS = amyotrophic lateral sclerosis, LBD = Lewy body dementia, ABC = Alector Brain Carrier, UD = undisclosed

# AL002 (TREM2 Activator): Promising Immuno-neurology Candidate for Early AD

| THE HYPOTHESIS | POTENTIAL THERAPEUTIC BENEFITS* | |
|---|---|---|
| Increased TREM2 signaling may recruit microglia to broadly counteract progression of AD | Broad mechanism suggests potential for superior stand-alone therapy | Potential for clinical efficacy at multiple disease stages |
| | Potential for superior clinical efficacy in combination with anti-Aβ antibodies | Potential for clinical efficacy independent of Aβ removal |

## AL002 STATUS

- Completed enrollment in Phase 2 trial
- Data expected in Q4 2024
- 98% of eligible participants who completed the planned treatment period have elected to roll over into the LTE
- Most advanced TREM2-activating candidate in clinical development for AD[1]
- Modulates multiple biomarkers of microglia activity
- Treatment-emergent ARIA-like MRI findings
- Potential AbbVie opt-in decision with $250M payment if exercised

alector

*Pending further research and clinical validation

1. Alector is not aware of any other TREM-2 activating candidates in a Phase 2 or Phase 3 trial for AD as of November 2024.

# Reimagining Care: Significant Need Remains in Alzheimer's Disease

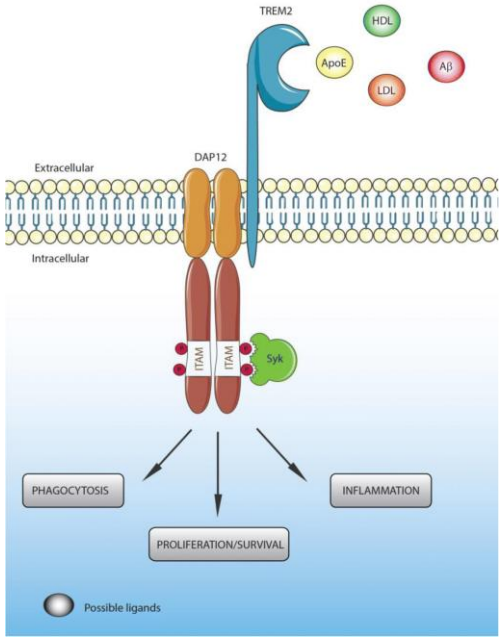
| Increasing Need | | Scientific Advancements | | Opportunity |
|---|---|---|---|---|
| **Aging Population** | **2.1 Billion Age 60+ by 2050**<br>In 2019, the number of people aged 60 years and older was 1 billion. This number is expected to increase to 1.4 billion by 2030 and 2.1 billion by 2050.[1] | **Diagnostic Advances** | **PET, MRI & Biomarkers**<br>Recent innovations in neuro-imaging and fluid biomarkers have improved early-stage detection of AD. These have also enabled more accurate monitoring of disease progression and response to treatment. | Wall Street estimates that the approved anti-Aβ antibodies, lecanemab and donanemab represent multi-billion-dollar peak sales opportunities.[4] |
| **Alzheimer's Disease** | **139 Million by 2050**<br>Currently, 35 million people worldwide are living with AD.[2] By 2050, the WHO predicts 139 million people worldwide will be living with AD or other dementias.[3] | **Treatment Advances** | **Better Approaches**<br>Traditional treatments primarily focused on managing symptoms. New therapeutics are designed to target the underlying AD mechanisms. | With advances in treatments and diagnostics, there is a growing opportunity to reach more AD patients. |

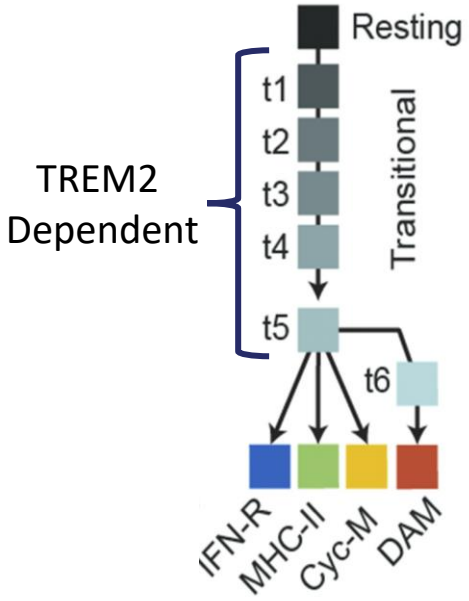
1. World Health Organization. Ageing. 2. Anstey KJ, Cherbuin N, Herath PM. (2013) "Development of a new method for assessing global risk of Alzheimer's disease for use in population health approaches to prevention." Prev Sci. 2013 Aug;14(4):411-21.; 3. Alzheimer's Disease International. (2024). World Alzheimer Report 2024. ; 4. Novel Amyloid β Targeting Therapies Mark Major Advance in Treating Alzheimer's Disease, Sept. 2023.

# TREM2: Immuno-modulatory Receptor For Microglia

## TREM2 IS A KEY MICROGLIA SIGNALING RECEPTOR

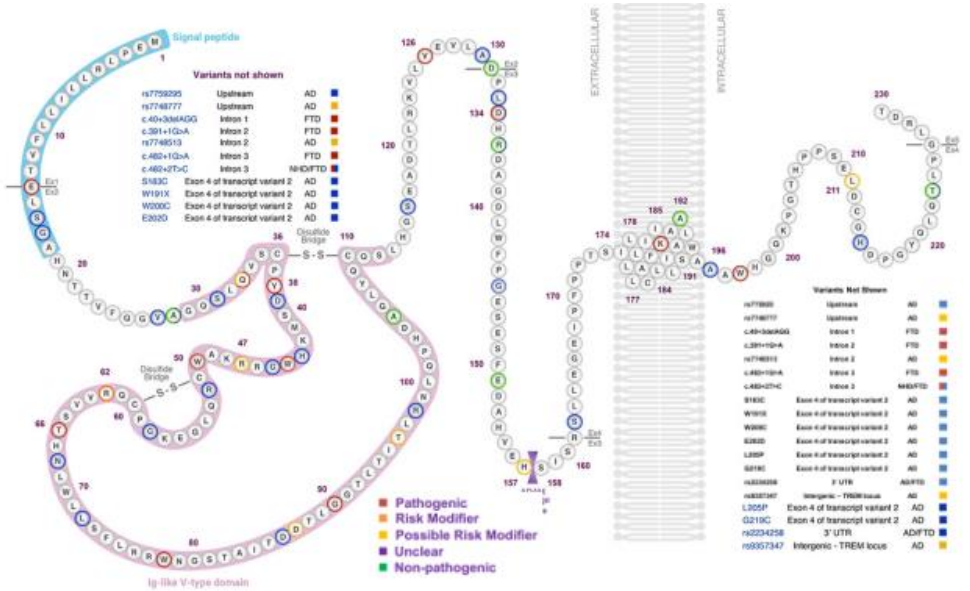
- TREM2 is a damage-sensing receptor[1]
- Responds to cellular damage and debris, and misfolded proteins [1]
- Regulates microglia survival proliferation, migration, function[1]




## TREM2 LOF IS A KEY GENETIC RISK FOR AD

- Homozygous mutations cause dementia (NHD, FTD)[2]
- Heterozygous mutations increase risk for AD by 3-fold[2]
- 40 TREM2 mutations related to AD have been identified[2]




1. Gratuze, M, et al., New insights into the role of TREM2 in Alzheimer's disease. *Mol Neurodegeneration* 13, 66 (2018).

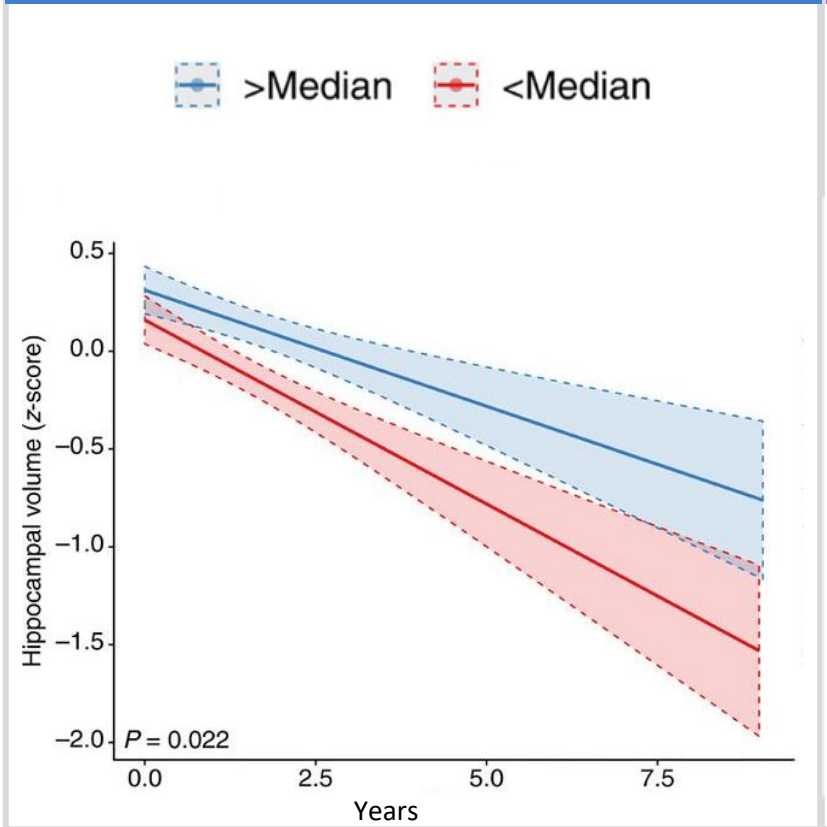
https://doi.org/10.1073/pnas.201774211

2. Mutations TREM2 | Alzforum. (n.d.). Retrieved November 29, 2023, from https://www.alzforum.org/mutations/trem2

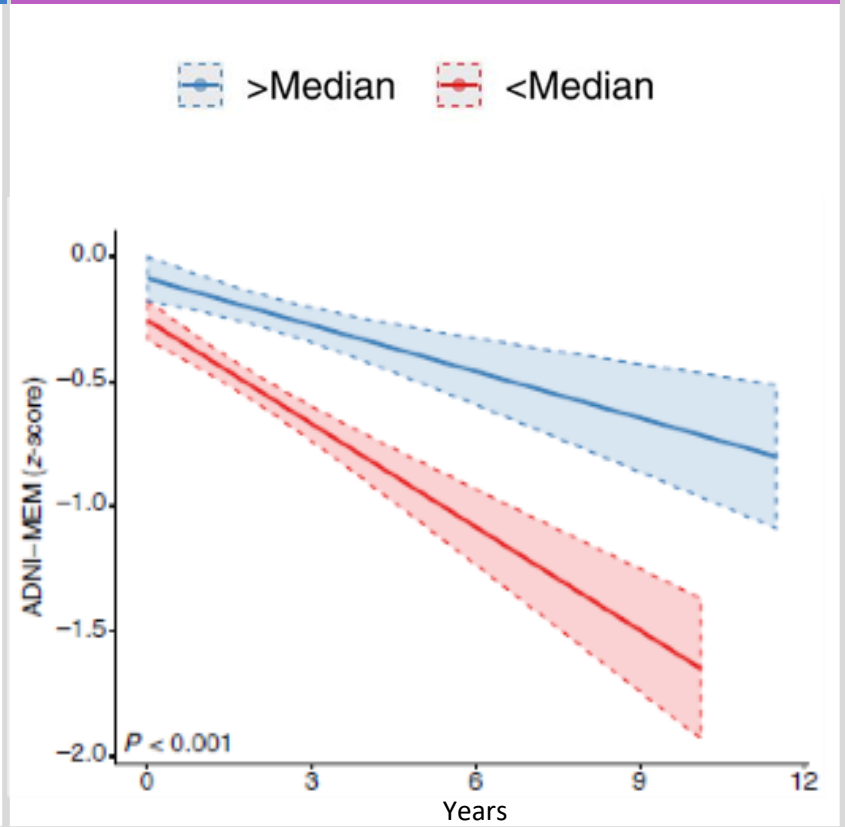
# High Levels of TREM2/sTREM2: Associated with Slower Cognitive Decline in AD

*Potential for TREM2 modulation to provide benefit in later stages of disease when tau is present*

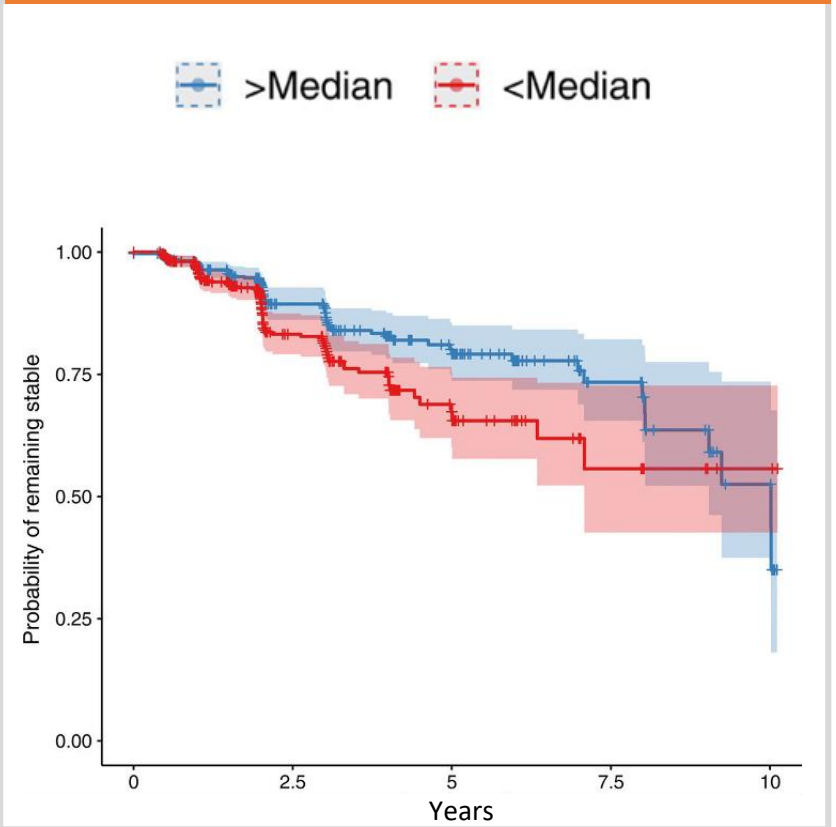
## HIGH TREM2/sTREM2 IS ASSOCIATED WITH DELAYED HIPPOCAMPAL ATROPHY IN MCI




## HIGH TREM2/sTREM2 IS ASSOCIATED WITH SLOWER DECLINE OF EPISODIC MEMORY IN MCI AND AD



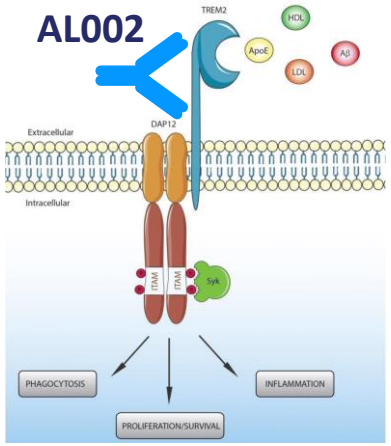

## HIGH TREM2/sTREM2 IS ASSOCIATED WITH SLOWER PROGRESSION FROM MCI TO AD



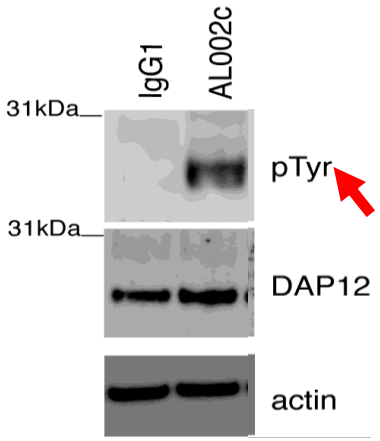

Ewers, M, et al., *Sci Transl Med*. 2019 Aug 28;11(507):eaav6221.
Requested from Publisher on 11/30/23.

# AL002: A TREM2-Activating Antibody That Shows Multiple Downstream Effects

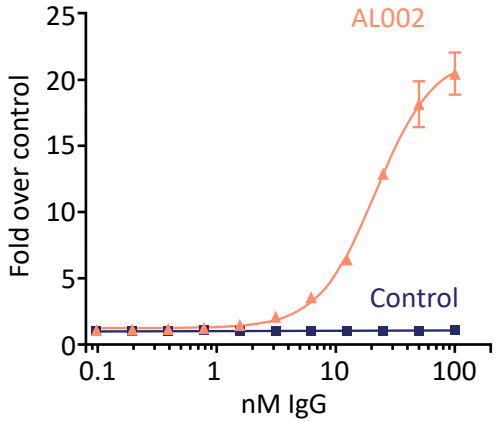
## AL002 Binds the Stalk Region[1]



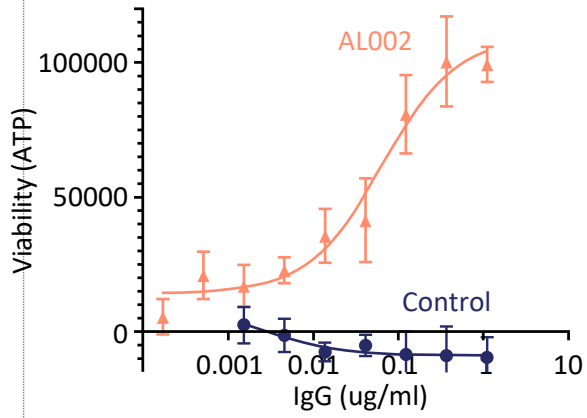

## Activates TREM2 Signaling



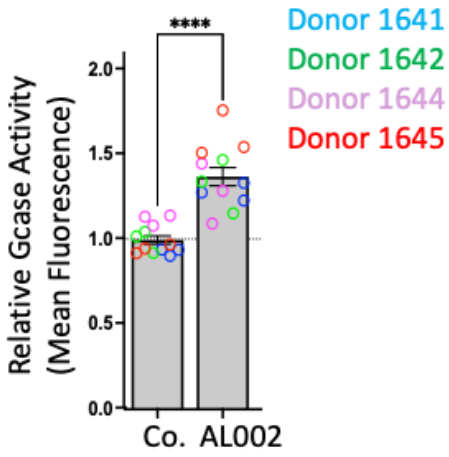

## Promotes Gene Expression



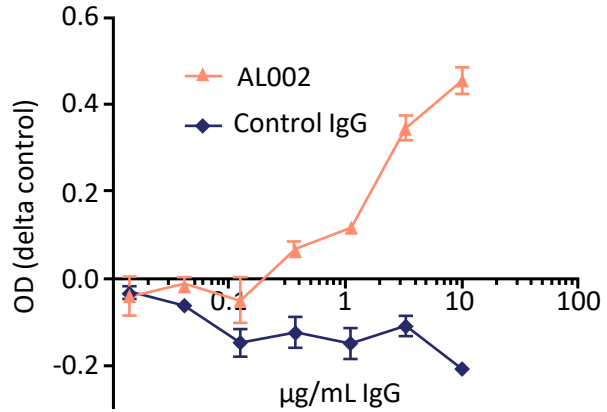

## Promotes Cell Viability



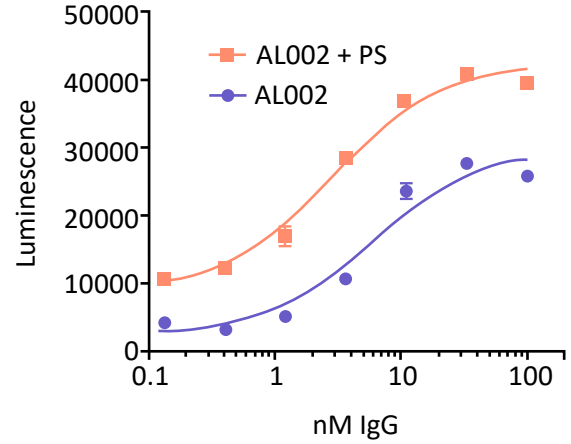

## Induces Lysosomal Enzymes




## Enhances Binding to APOE



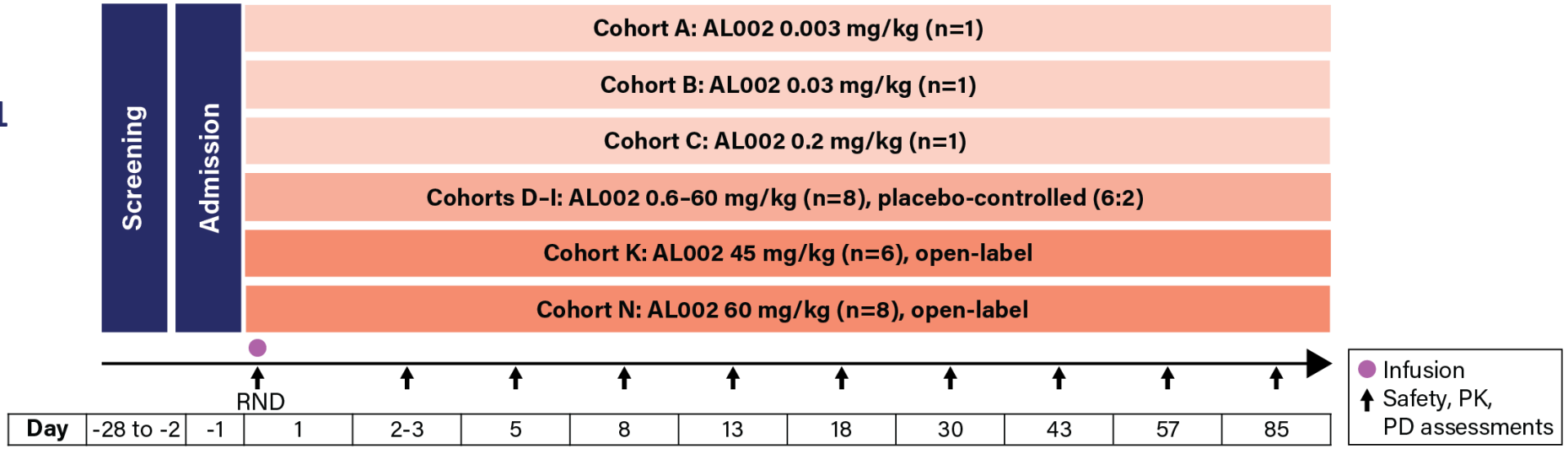

## Acts Additively with Phosphatidyl-Serine




Gratuze, M, et al., New insights into the role of TREM2 in Alzheimer's disease. *Mol Neurodegeneration* 13, 66 (2018).

# AL002: Phase 1 Study in Healthy Volunteers

## AL002 Phase 1 Study Design



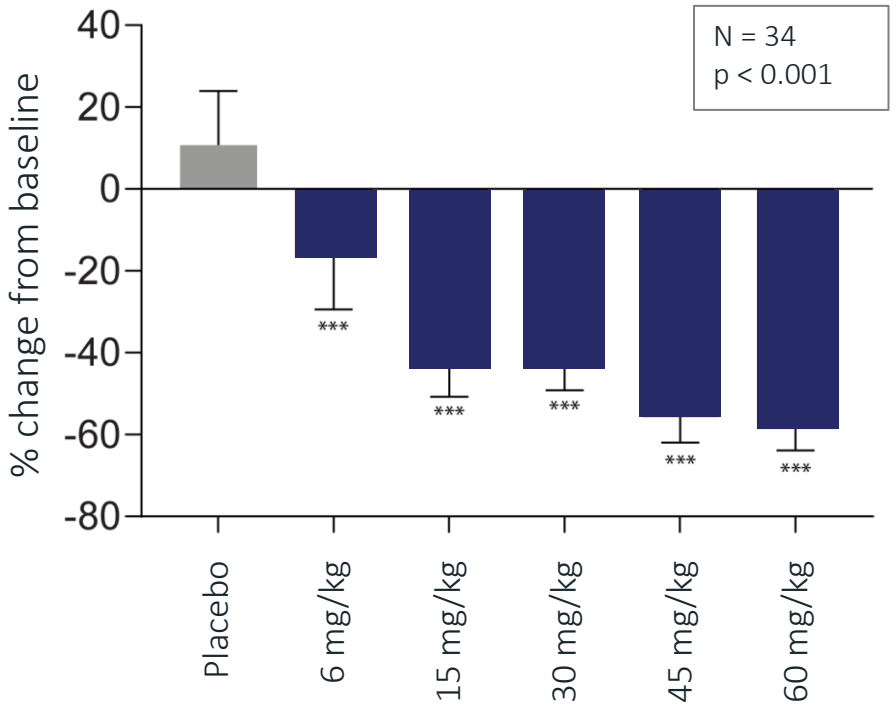

## Well Tolerated in Healthy Volunteers

| System Organ Class Preferred Term | AL002 0.003-0.2 mg/kg (n=3) n (%) | AL002 0.6 mg/kg (n=6) n (%) | AL002 2 mg/kg (n=6) n (%) | AL002 6 mg/kg (n=6) n (%) | AL002 15 mg/kg (n=6) n (%) | AL002 30 mg/kg (n=6) n (%) | AL002 45 mg/kg (n=6) n (%) | AL002 60 mg/kg (n=14) n (%) | Pooled Placebo (n=11) n (%) |
|---|---|---|---|---|---|---|---|---|---|
| **Participants with ≥1 TEAE** | 2 (66.7%) | 3 (50.0%) | 2 (33.3%) | 5 (83.3%) | 5 (83.3%) | 4 (66.7%) | 6 (100.0%) | 10 (71.4%) | 9 (81.8%) |
| **Participants with ≥1 treatment-related TEAE[b]** | 2 (66.7%) | 2 (33.3%) | 2 (33.3%) | 2 (33.3%) | 2 (33.3%) | 4 (66.7%) | 5 (83.3%) | 7 (50.0%) | 6 (54.5%) |
| **Treatment-related TEAEs in ≥5% of participants in the total AL002 group** | | | | | | | | | |
| Headache | 1 (33.3%) | 1 (16.7%) | 2 (33.3%) | 2 (33.3%) | 1 (16.7%) | 4 (66.7%) | 2 (33.3%) | 2 (14.3%) | 4 (36.4%) |
| Dizziness postural | 1 (33.3%) | 0 | 1 (16.7%) | 0 | 0 | 1 (16.7%) | 0 | 0 | 1 (9.1%) |
| Nausea | 0 | 0 | 1 (16.7%) | 1 (16.7%) | 0 | 0 | 1 (16.7%) | 6 (42.9%) | 2 (18.2%) |
| Vomiting | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 (21.4%) | 2 (18.2%) |
| **Any TEAE leading to study drug withdrawal** | 0 | 0 | 0 | 0 | 0 | 0 | 1 (16.7%) | 1 (7.1%) | 0 |

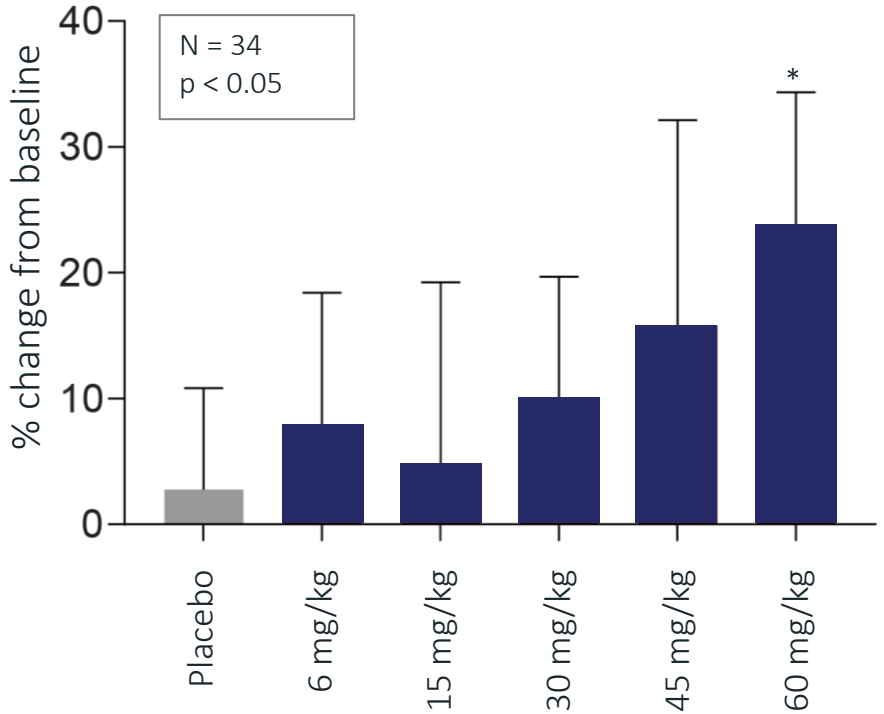
**No drug-induced or drug-related Serious Adverse Effects or Dose Limiting Toxicity occurred**

# AL002: Target Engagement and Evidence of Microglia Activation Observed in Phase 1

## Dose-Dependent Reduction in CSF sTREM2 (Mean +-SD), Associated with Target Engagement[1,2]



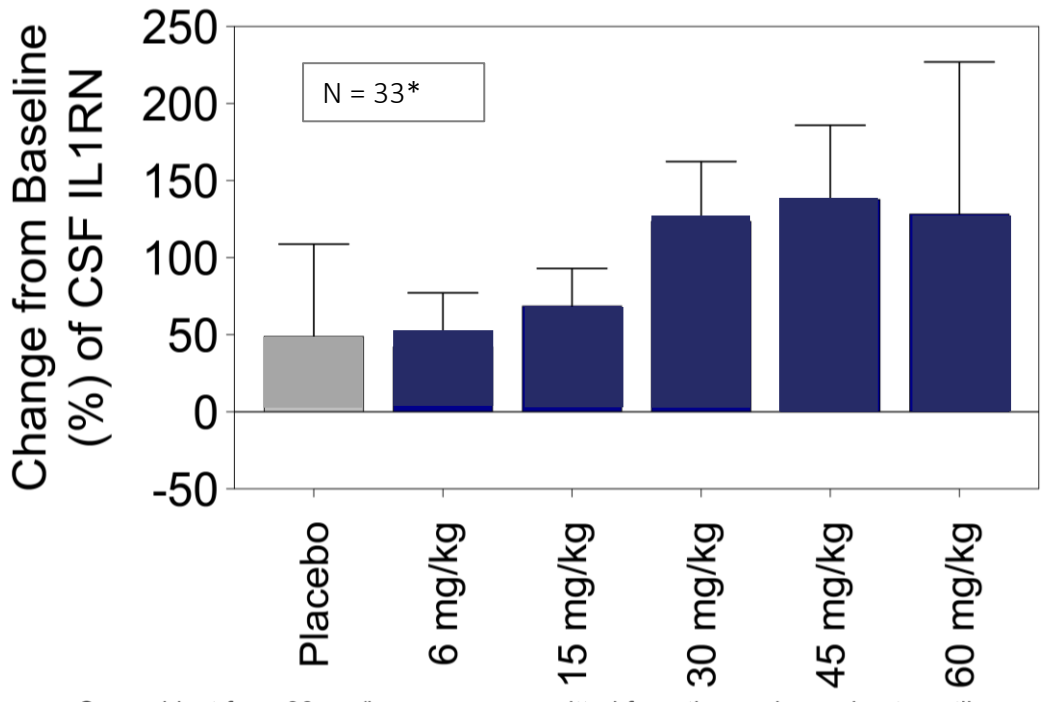

## Dose-Dependent Elevation in CSF sCSF-1R (Mean +-SD), Associated with Microglia Activation[1,2]



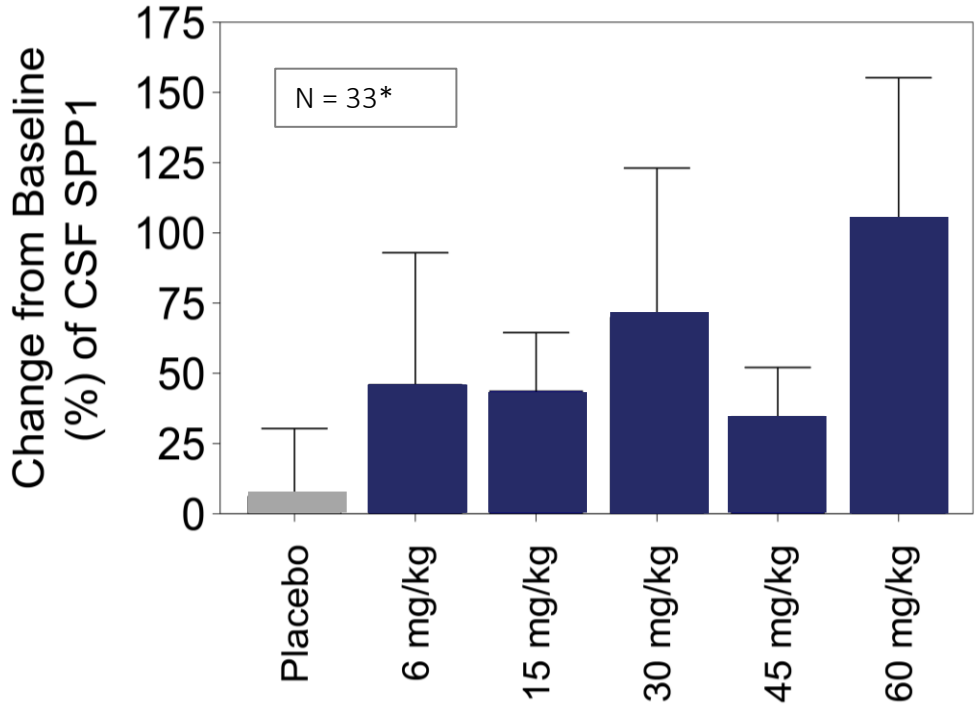

Data are presented as mean ±SD; cohort n = 6 (placebo, 6 mg/kg, 15 mg/kg, 30 mg/kg) and 5 (45 mg/kg, 60 mg/kg).
***P = 0.0001 for 6 mg/kg and P < 0.0001 for all other doses vs. pooled placebo control. *P = 0.026 at 60 mg/kg vs. pooled placebo.
[1]Phase 1 data presented at AAIC 2021; NCT03635047. [2]Wang S et al. *J Exp Med*. 2020;217(9):e 20200785.
**Consistent with preclinical results.

# AL002: Additional Evidence of Microglia Activation Observed in Phase 1

Dose-Dependent Elevation of IL1RN in CSF (Mean +-SD)




Dose Dependent Elevation of SPP1 in CSF (Mean +-SD)




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.

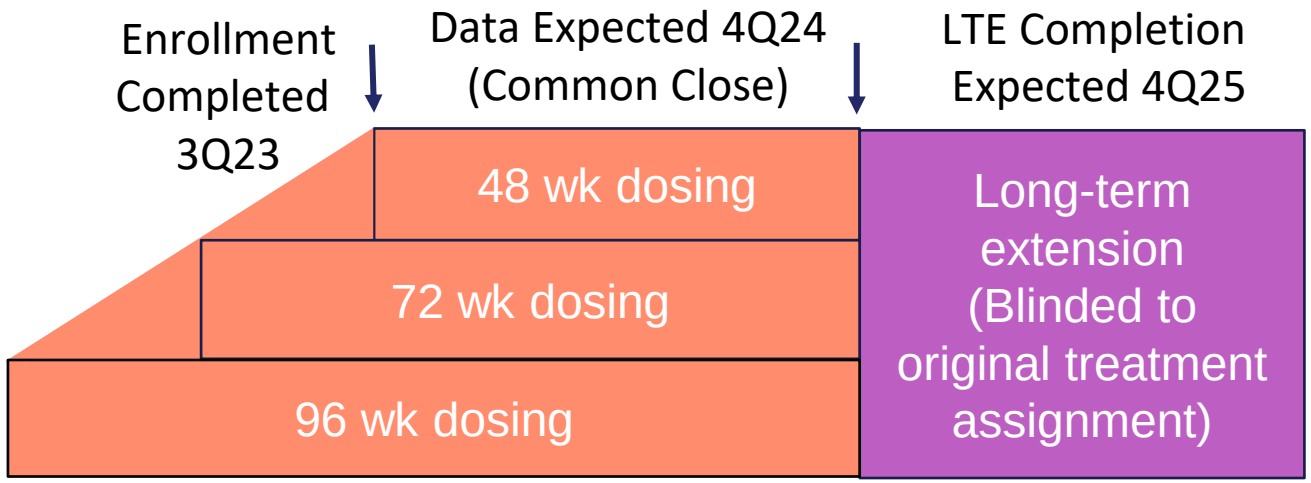
IL1RN = interleukin 1 receptor antagonist
SPP1 = secreted phosphoprotein 1
CSF = cerebrospinal fluid

# INVOKE-2: AL002 Phase 2 Study in Participants with Early Alzheimer's Disease

**Phase II Design: Randomized, double-blind, placebo-controlled 4-arm, common close study (48-96 weeks); randomized 381 participants (1:1:1:1) with early Alzheimer's disease**

## Treatment Arms

- AL002, 15mg/kg IV/q4w
- AL002, 40mg/kg IV/q4w
- AL002, 60mg/kg IV/q4w
- Placebo



# INVOKE-2: Clinical and Functional Outcome Measures

## PRIMARY OUTCOME MEASURE

- Clinical Dementia Rating Scale – Sum of Boxes
  - Primary endpoint of lecanemab Phase 3 trials

## SECONDARY CLINICAL AND FUNCTIONAL OUTCOME MEASURES

- RBANS
- ADAS-Cog 13
- ADCS-ADL-MCI
- MMSE

} Items extracted for the iADRS, the primary endpoint of the donanemab Phase 3 trial

## PROPORTIONAL ANALYSIS

- Enables using ALL of the data collected in this common close design trial

**Proportional constrained longitudinal data analysis models for clinical trials in sporadic Alzheimer's disease**


iADRS = Integrated Alzheimer's Disease Rating Scale
RBANs= Repeatable Battery for the Assessment of Neuropsychological Status
ADCS-ADL-MCI = Activities of Daily Living for Mild Cognitive Impairment
MMSE = Mini-Mental State Examination

# INVOKE-2: Biomarkers of Target Engagement, Microglial Signaling and AD Pathophysiology

| TARGET ENGAGEMENT AND MICROGLIAL SIGNALING | | ALZHEIMER'S DISEASE PATHOPHYSIOLOGY | | |
|---|---|---|---|---|
| CSF sTREM2 | CSF Markers of Microglial Signaling | Amyloid/Tau Pathology | Astrogliosis | Neuronal and Synaptic Injury |
| Reflects levels of TREM2 on microglial membrane<br><br>Lower levels of sTREM2 correlate with AL002 binding and receptor internalization | **CSF-1R:** Microglial proliferation<br><br>**OPN (SPP1):** Microglial phagocytosis<br><br>**IL1-RN:** Microglial immune regulation<br><br>Markers of microglial subtypes / activity | **Amyloid PET**<br>**Tau PET**<br><br>**Plasma pTau$^{217}$**<br>**CSF/Plasma pTau$^{MTBR}$**<br>**CSF/Plasma Aß 42/40** | **Plasma GFAP**<br>**CSF YKL40** | **NfL**<br>**Neurogranin**<br>**Total Tau**<br>**Volumetric MRI** |

OPN = osteopontin protein
CSF1R = colony stimulating factor 1 receptor
IL1RN = interleukin-1 receptor antagonist
GFAP = glial fibrillary acidic protein
AD = Alzheimer's disease

YKL40= protein named YKL-40 based on its three N-terminal amino acids tyrosine (Y), lysine (K) and leucine (L), and its molecular mass of 40 kDa 14.
NfL = neurofilament light chain
CDR-SB = Clinical Dementia Rating Sum Boxes

# ARIA: Treatment-related MRI Findings Resembling Amyloid Related Imaging Abnormalities Occurred in a Subset of Participants in the INVOKE-2 Trial

- MRI findings resemble ARIA reported with anti-amyloid antibodies regarding:
  - MRI features, incidence, timing of onset/resolution, relatedness to number of ApoE ε4 alleles
  - Frequency and spectrum of clinical manifestations
- ApoE ε4/ε4s were voluntarily excluded from study:
  - ARIA incidence and radiographic severity were reduced after exclusion of ApoE ε4/ε4
- Most participants with radiographic ARIA in the trial population (excludes ApoE ε4/ε4) have been asymptomatic and clinically serious cases have been uncommon.
- Data Monitoring Committee regularly reviews data

| ARIA-E | ApoE ε4/ε4† | Current Study Population (Non–ApoE ε4/ε4) |
|---|---|---|
| ARIA-E incidence, n/N (%) | 8/15 (71)* | 49/337 (19)* |
| Radiographic severity (scale of 1-5), mean (SD) | 2.5 (1.6) | 2.2 (1.3) |

| ARIA-H | ApoE ε4/ε4† | Current Study Population (Non–ApoE ε4/ε4) |
|---|---|---|
| ARIA-H incidence, n/N (%) | 8/15 (71)* | 57/337 (23)* |
| ARIA-H radiographic severity (%) | | |
| Mild | 1/8 (12.5) | 25/57 (44) |
| Moderate | 2/8 (25) | 16/57 (28) |
| Severe | 5/8 (62.5) | 16/57 (28) |

| Symptomatic ARIA in Current Trial Population† | |
|---|---|
| Total participants dosed (excluding ApoE ε4/ε4)† | 337 |
| Participants with ARIA-E (%) | 49 (19)* |
| Asymptomatic (%) | 43/49 (88) |
| Symptomatic (%) | 6/49 (12) |
| Clinically serious ARIA (%) | 2/337 (<1) |

This study remains blinded to treatment assignment.

*Placebo controlled; assumes all ARIA occurs in active treatment arms.

†Voluntarily discontinued APOE e4 homozygote trial participation.

# INVOKE-2 Baseline Characteristics: Data Confirm Intended Study Population for Testing Effects of AL002 in Early AD

## DEMOGRAPHIC AND BASELINE CHARACTERISTICS

| | |
|---|---|
| **Age, median (min, max), years** | 71.0 (51,85) |
| **Age group, n (%)**<br><65 years<br>65 to <75 years<br>≥75 years | <br>84 (22.0)<br>176 (46.2)<br>121 (31.8) |
| **Age ≥65 years, n (%)** | 297 (78.0) |
| **Female, n (%)** | 191 (50.1) |
| **Race, n (%)**<br>White<br>Asian<br>Black/African American<br>Multiple<br>Not reported/Missing/Unknown | <br>357 (93.7)<br>4 (1.0)<br>3 (0.8)<br>1 (0.3)<br>16 (4.2) |
| **Ethnicity**<br>Hispanic/Latino<br>Not Hispanic/Latino<br>Not reported/Missing/Unknown | <br>17 (4.5)<br>348 (91.3)<br>16 (4.2) |
| **Region, n (%)**<br>United States<br>Rest of world | <br>80 (21.0)<br>301 (79.0) |

## BASELINE CLINICAL CHARACTERISTICS

| | |
|---|---|
| **Clinical diagnosis, n (%)**<br>Mild cognitive impairment due to AD<br>Mild dementia due to AD | <br>256 (67.2)<br>125 (32.8) |
| ***APOE* genotype, n (%)**<br>ε2/ε3<br>ε2/ε4<br>ε3/ε3<br>ε3/ε4<br>ε4/ε4[a] | <br>5 (1.3)<br>6 (1.6)<br>137 (36.0)<br>218 (57.2)<br>15 (3.9) |
| **Amyloid PET Centiloids, mean (SD), (n=244)** | 100.1 (38.9) |
| **CDR-GS, n (%)**<br>0.5<br>1 | <br>297 (78.0)<br>84 (22.0) |
| **CDR-SB, mean (SD)** | 3.4 (1.4) |
| **MMSE, mean (SD)** | 24.5 (2.4) |
| **RBANS, mean (SD)** | 66.4 (12.1) |
| **ADAs-Cog13, mean (SD)** | 29.2 (8.6) |
| **ADCS-ADL-MCI, mean (SD)** | 40.3 (7.2) |
| **ADCOMS, mean (SD)** | 0.43 (0.16) |

alector

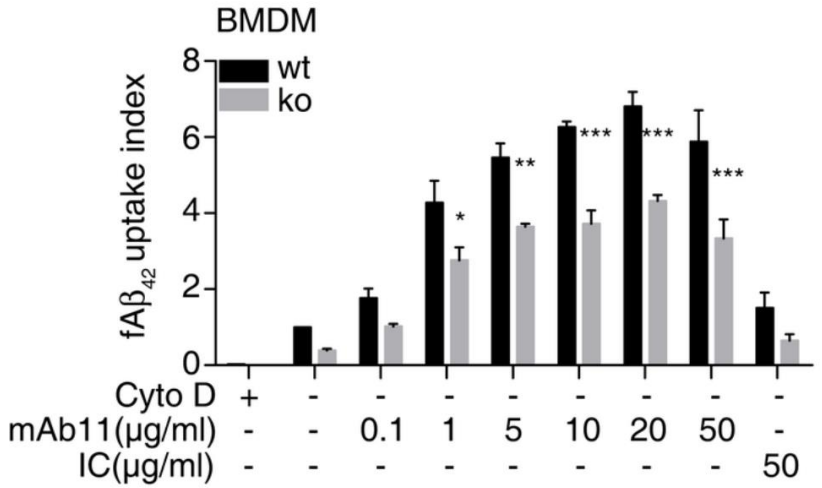
N=381 participants
Source: AAIC 2024.

[a]*APOE4* homozygotes were discontinued from the study.

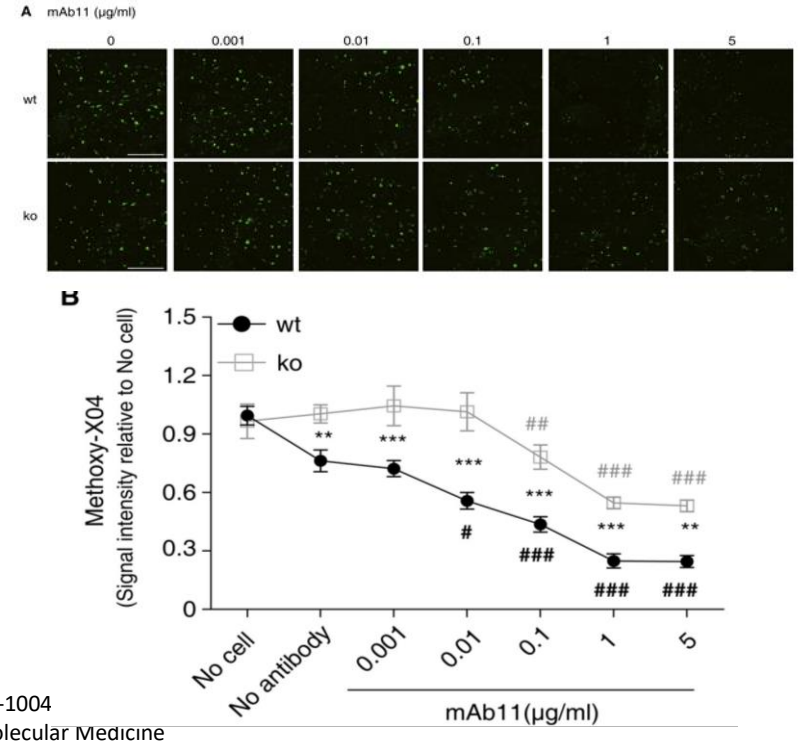
# Opportunity: Explore Combination with Anti-Amyloid Beta Antibodies

***"TREM2 deficiency reduces the efficacy of immunotherapeutic amyloid clearance"***
**EMBO Molecular Medicine, 2016**

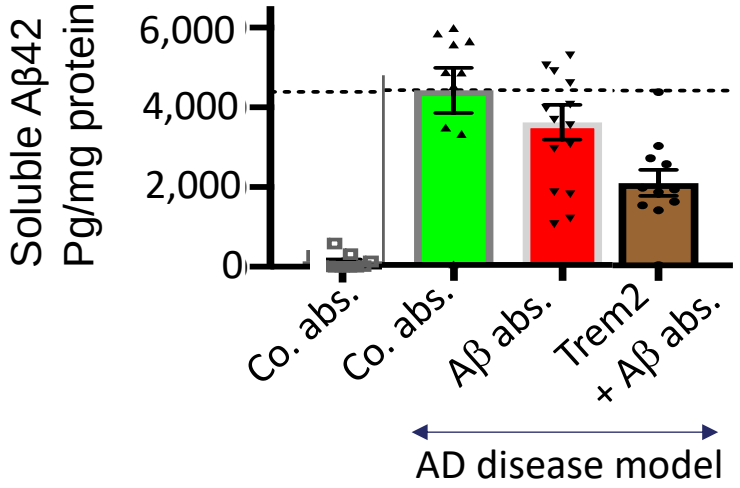
Phagocytosis of $fA\beta_{42}$ by primary microglia from wt and *TREM2* KO animals in the presence or absence of mAb11, or an isotype control antibody[1]




Aβ plaques staining from APP/PS1 mice that were treated with anti-amyloid antibodies with or without functional TREM2[1]




Aducanumab reduces soluble Aβ (red vs. green bars)
TREM2 agonist further reduces soluble Aβ (brown vs. red bars)[2]




1. Xiang X et al., *EMBO Mol Med.* 2016 Sep 1;8(9):992-1004

2. Alector data on file.

# INVOKE-2: What Are Our Goals for AL002 in the Long-Term and from the Trial?

## AL002 Hypothesis

Therapeutic restoration of microglial function by AL002 may slow Alzheimer's disease progression by:

- Enhancing beneficial effects of microglia on brain health, including clearance of misfolded proteins, such as amyloid
- Compacting and reducing the toxicity of fibrillar amyloid

| | |
|---|---|
| Maintenance of synaptic connections | Support of astrocyte and oligodendrocyte function |
| Maintenance and repair of the BBB and vasculature | Preservation of immune tolerance |

## INVOKE-2 Trial Goals

The INVOKE-2 trial aims to show evidence of treatment-related slowing of Alzheimer's disease progression across a combination of readouts:

- Clinical
- Functional
- Biomarker

## AL002 Efficacy Potential

Given the multiple mechanisms by which healthy microglia protect the brain against neurodegenerative diseases,

by the end of development,

we believe AL002 has the potential to ultimately display stronger efficacy than current therapies that target individual misfolded proteins

## AL002 Stand-Alone or Combo Therapy Potential

AL002's MOA increases TREM2 signaling, potentially leading to broad downstream effects that may enhance the beneficial functions of microglia. Therefore, we believe AL002 has the potential to act either as:

- a stand-alone therapy
- or in combination with anti-amyloid beta therapies

# INVOKE-2: Hypothesized Potential Differences from Anti-Amyloid Trials

## Biomarker Responses

Example: lowering cerebral amyloid PET signal to the 20-30 centiloid threshold for clinical efficacy may not be necessary for the MOA of AL002, which goes beyond amyloid clearance

## Optimal Disease Stage(s) for Intervention May be Broader

Given AL002's MOA increases TREM2 signaling, potentially leading to broad downstream effects on microglia, we do not expect the beneficial functions of healthy microglia to be limited to specific pathophysiological stages of disease

Thus, it may include patients with preclinical AD to advanced dementia

## Temporal Dynamics of Treatment Effects May be Broader

Some effects of improved microglia function may manifest early in treatment:

- amyloid clearance
- maintenance of synaptic function

Others may become apparent later:

- support of astrocyte and oligodendrocyte function
- repair of vasculature and BBB

This may not be fully appreciated early in treatment and may be more evident in our LTE

# AL002: Currently Partnered in an Option Agreement with AbbVie

abbvie

**AL002**

$205M upfront payment (2017 and 2018)
$20M equity investment (2018)
$17.8M milestone payment received (2023)
$12.5M received in support of enrollment (2023)
$250M if opt-in exercised (anticipated early 2025)
$225M in potential additional milestones
Global 50-50 profit share

# Latozinemab and AL101: Promising PGRN-Elevating Candidates for Neuro-degeneration

## THE HYPOTHESIS

PGRN elevation may promote neuronal survival and microglia functionality to reduce neurodegeneration

## POTENTIAL THERAPEUTIC BENEFITS

Potential for efficacy as stand-alone therapy and/or in combination with other therapies

Potential for clinical benefit in multiple neurodegenerative diseases

## LATOZINEMAB STATUS

- Achieved target enrollment in pivotal Phase 3 clinical trial in FTD-*GRN*
- Most advanced PGRN-elevating candidate in clinical development for FTD[1]
- Granted Orphan Drug Designation for FTD as well as Breakthrough Therapy and Fast Track designations for FTD-*GRN*

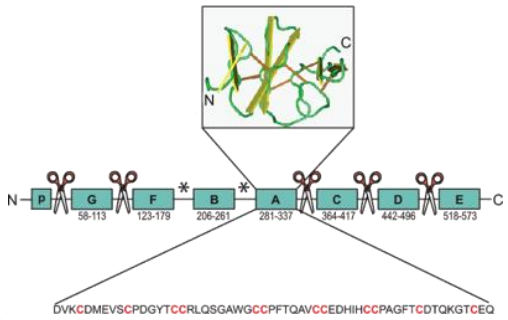
## AL101 STATUS

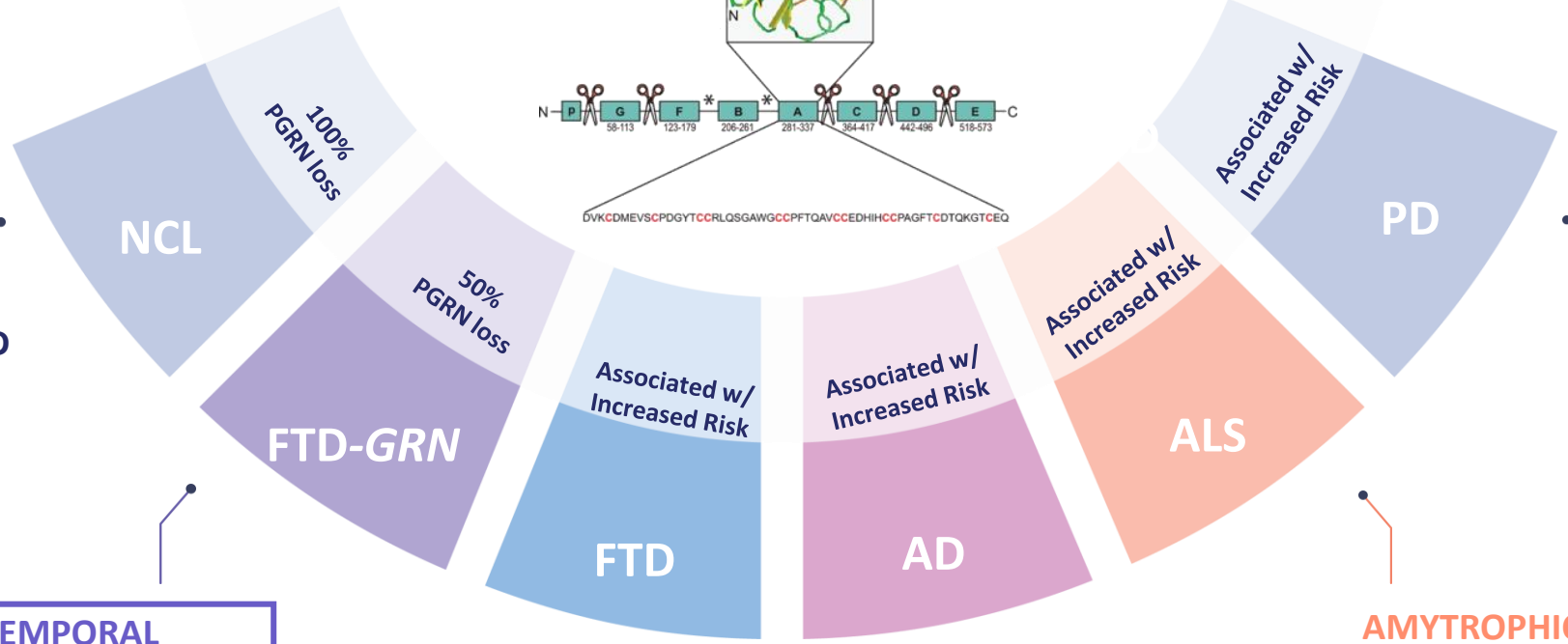
- Global Phase 2 trial in early AD is ongoing
- Most advanced, PGRN-elevating candidate in clinical development for AD[1]

1. Alector is not aware of any other PGRN-elevating candidates in a Phase 3 trial for FTD or in a Phase 2 or Phase 3 trial for AD as of November 2024.

PGRN = progranulin protein

# *GRN* Mutations: Causal or Increase Risk for Multiple Neurodegenerative Diseases




NEURONAL CEROID LIPOFUSCINOSIS

FRONTOTEMPORAL DEMENTIA WITH *GRN* MUTATIONS

SPORADIC FRONTOTEMPORAL DEMENTIA

ALZHEIMER'S DISEASE

AMYTROPHIC LATERAL SCLEROSIS

PARKINSON'S DISEASE


Rhinn H, et al. *Trends Pharmacol Sci.* 2022;43(8):641–652.
Nalls MA, et al. *Brain Commun*. 2021;3(2):fcab095.
Sheng J, et al. *Gene*. 2014;542(2):141–145.
Kumar-Singh S. *J Mol Neurosci*. 2011;45:561–573.
Paushter DH, et al. *Acta Neuropathol.* 2018;136(1):1–17.


GRN = gene that encodes the protein progranulin

# Frontotemporal Dementia (FTD): A Rapidly Progressive Form of Dementia, with No Approved Treatment

*Tommy Nash Jr., with his daughter, Alyssa Nash. Tommy was diagnosed with FTD at 38 years old.*[1]

- **Prevalence:** Most common cause of dementia under age 60

- **Progression:**
  - Rapid progression of memory impairment, other cognitive functions
  - Life expectancy after diagnoses is 7-10 years

- **Diagnosis:**
  - Compulsive behavior, lack of restraint, apathy, anxiety, and aphasia
  - Symptoms typically begin between the ages of 45-64 years old
  - Frequently misdiagnosed as AD, depression, PD, or psychiatric condition

- **Treatment:** No approved treatments to cure or slow progression of FTD

- **Forms:**
  - Sporadic FTD occurs without a clear familial or inherited pattern
  - Genetic FTD occurs due to autosomal dominant mutations in one of three genes: *GRN*, *C9orf72* or *MAPT*

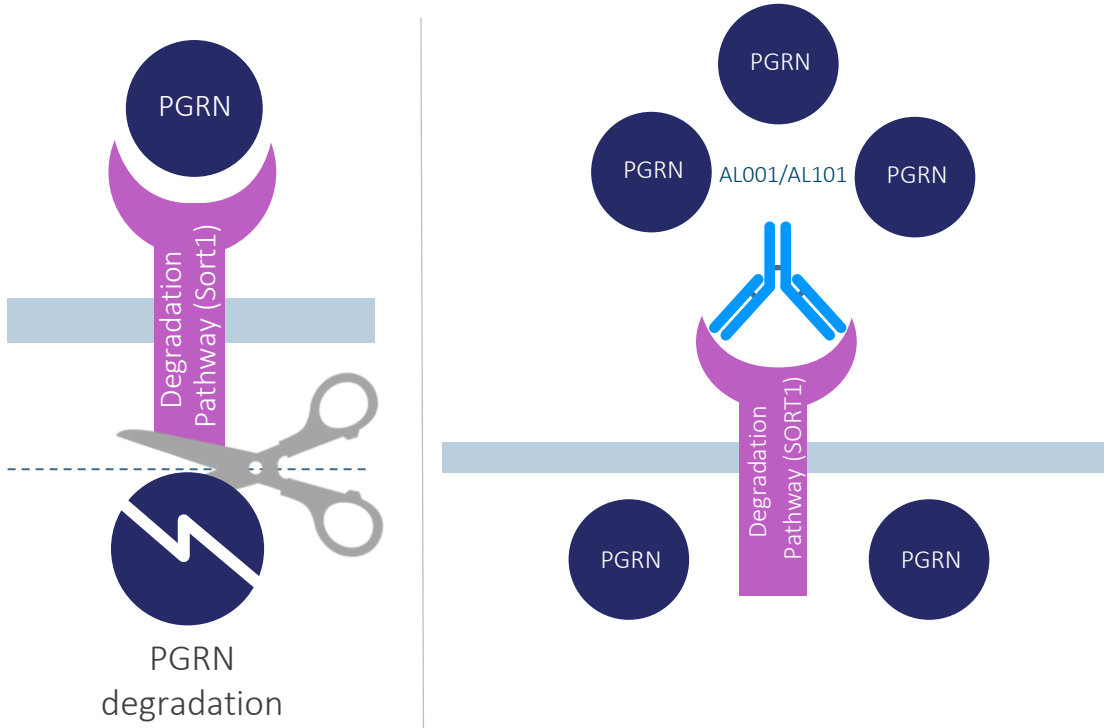

1. With permission from Tommy Nash Jr. and Alyssa Nash, May 2023
Greaves et al. *J Neurol.* 2019;266:2075-2086.
Taylor RT, et al. *Pract Neurol.* 2019:72-77.
Kansal K, et al. *Dement Geriatr Cogn Disord.* 2016;41:109-122.
Boeve BF, et al. *Brain.* 2006;129:3103-3114.
UCSF Weill Institute for Neurosciences Memory and Aging Center: Familial FTD

# Latozinemab and AL101 : Pioneering Approach to Elevating Progranulin Levels With Potential to Enhance Microglial and Neuronal Function and Treat FTD and AD

## PGRN: Genetic and Biologic Rationale

- **Genetics:** Mutations in PGRN are deleterious.
  - Homozygous (100% LOF): Neuronal ceroid lipofuscinosis with onset <25 years of age, 100% penetrance.
  - Heterozygous (50% LOF): Reduce progranulin levels to 50% of normal; Frontotemporal dementia with onset ~58 years of age, >90% penetrance.
  - Non-coding mutations (~10-20% LOF): Increase risk for ALS, FTD, AD, PD.
- **Biology:** PGRN is a critical immune regulator, neuronal survival factor and a lysosomal chaperone.

## Latozinemab and AL101: PGRN Elevating Program

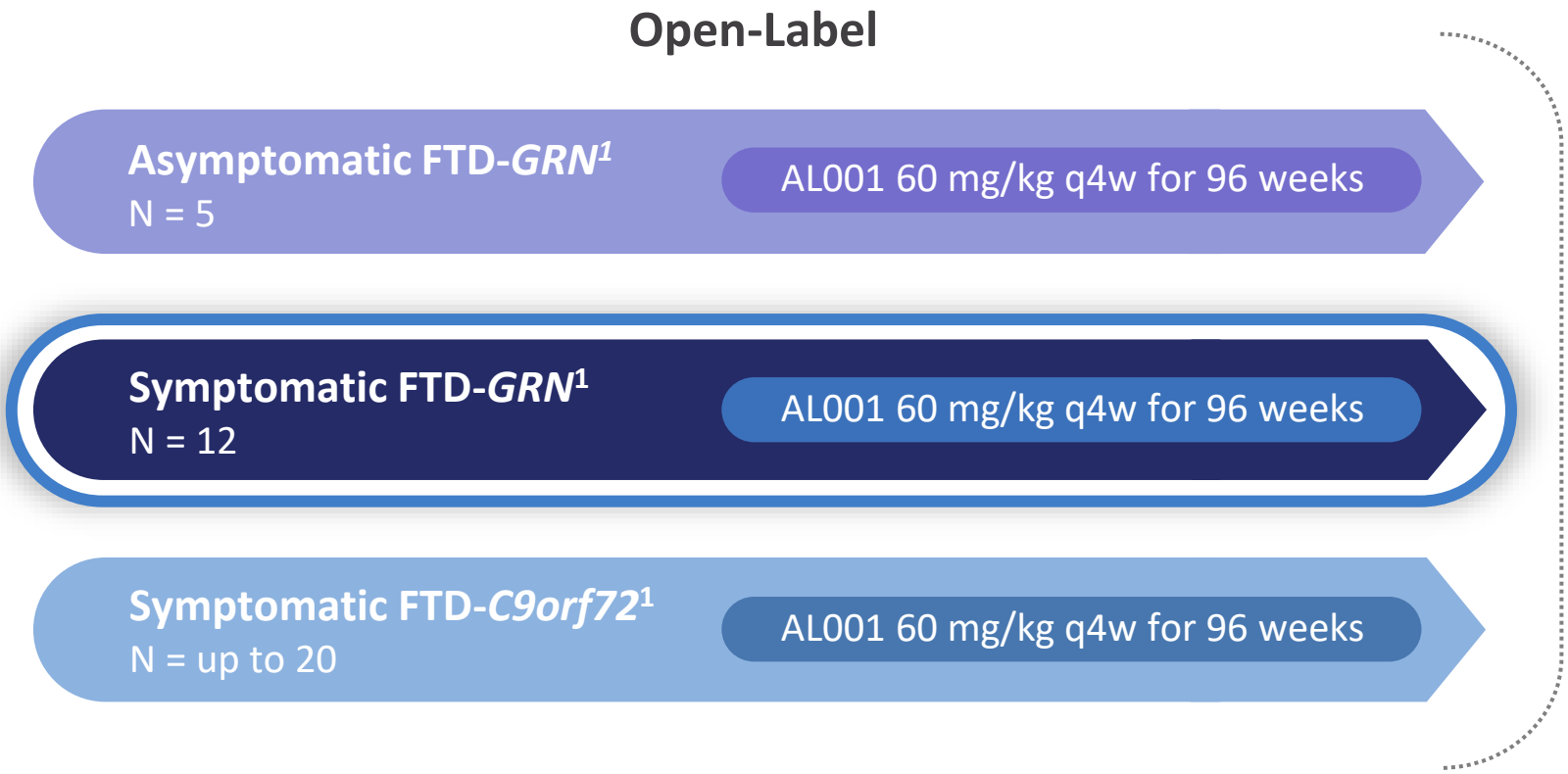



Latozinemab (AL001) and AL101 elevate PGRN levels by blocking sortilin (SORT1), a degradation receptor for PGRN

Source: Alz Res Therapy 4, 4 (2012); Sci Transl Med. 2017 Apr 12;9(385); Dement Geriatr Cogn Disord Extra 2016;6:330-34.; Eur J Neurol. 2013 Dec;20(12):1571-3; Gene. 2014 Jun 1;542(2):141-5.

PGRN = progranulin protein
LOF = loss of function
FTD = frontotemporal dementia
ALS = amyotrophic lateral sclerosis
AD = Alzheimer's disease
PD = Parkinson's disease

# INFRONT-2: Phase 2 Trial in FTD




**PRIMARY ENDPOINT**

Safety and Tolerability

**SECONDARY ENDPOINT**

PK, PD

**EXPLORATORY ENDPOINTS**

CSF and Plasma Biomarkers (Lysosomal, inflammation, neurodegeneration)

Volumetric MRI (vMRI)

Clinical Outcome Assessment (CDR® plus NACC FTLD-SB[2])

1. Asymptomatic and symptomatic FTD-GRN enrollment closed; FTD-C9orf72 cohort currently enrolling
2. 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)

AL001 = latozinemab
FTD = frontotemporal dementia
GRN = granulin gene
C9orf72 = chromosome 9 open reading frame 72 gene
PK = pharmacokinetic, PD = pharmacodynamic
CSF = cerebrospinal fluid

# INFRONT-2: Clinical Outcome Assessments Supported by Biomarkers in FTD-*GRN*

Key biomarkers and clinical outcome assessments reflect underlying disease activity in FTD-*GRN* patients

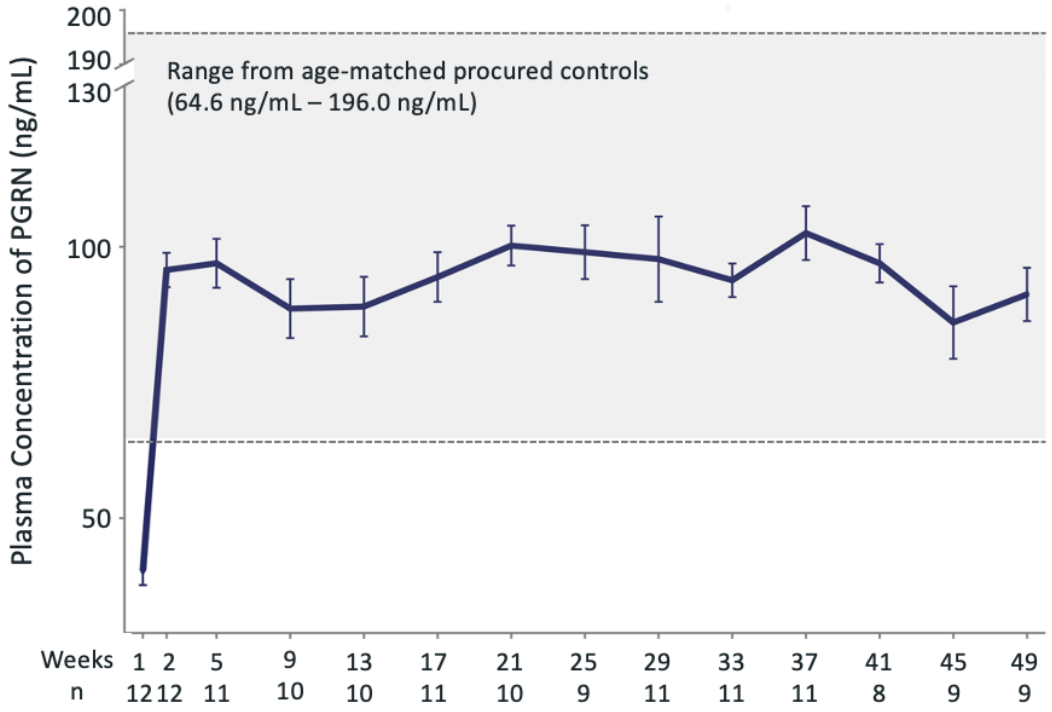
| TARGET ENGAGEMENT | BIOMARKERS OF DISEASE ACTIVITY | | | | CLINICAL BENEFIT |
|---|---|---|---|---|---|
| PGRN (Plasma and CSF) | Lysosomal Dysfunction | Inflammation | Brain Health | Brain Atrophy | Clinical Outcome Assessments |
| **PGRN**<br><br>CSF and plasma PGRN levels | **e.g. CTSD, LAMP1**<br><br>Dysfunctional lysosomes are hallmarks of FTD-*GRN* | **e.g. C1QB**<br><br>Elevation of complement proteins occurs in FTD-*GRN* | **GFAP**<br><br>Elevation of GFAP is a hallmark of FTD-*GRN* correlates with cognitive decline | **MRI**<br><br>Accelerated brain tissue loss is a hallmark of FTD-*GRN* and correlates with cognitive decline | **CDR® plus NACC FTLD-SB**<br><br>FDA approvable endpoint for measuring clinical decline in FTD |

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

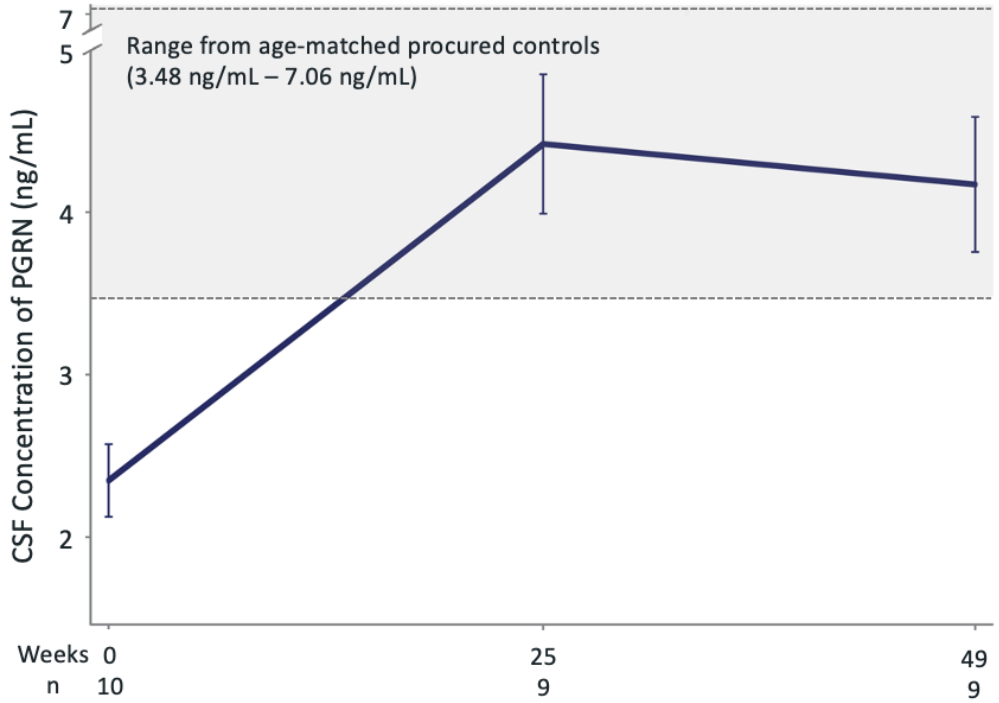
# INFRONT-2: Latozinemab Restores PGRN in Plasma and CSF to Levels Seen in Healthy Volunteer Age-Matched Controls

## ACHIEVED PGRN RESTORATION IN FTD-*GRN* PARTICIPANTS

### PGRN Plasma Concentration




### PGRN CSF Concentration

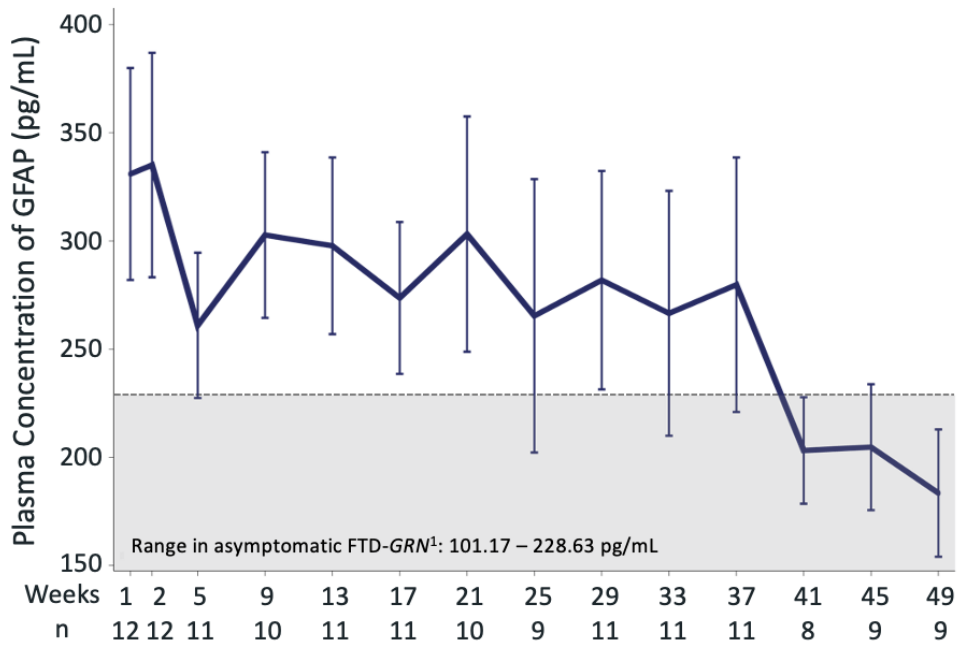



Data cut-off June 15, 2021
Mean +/- SEM
Source: AAIC 2021.

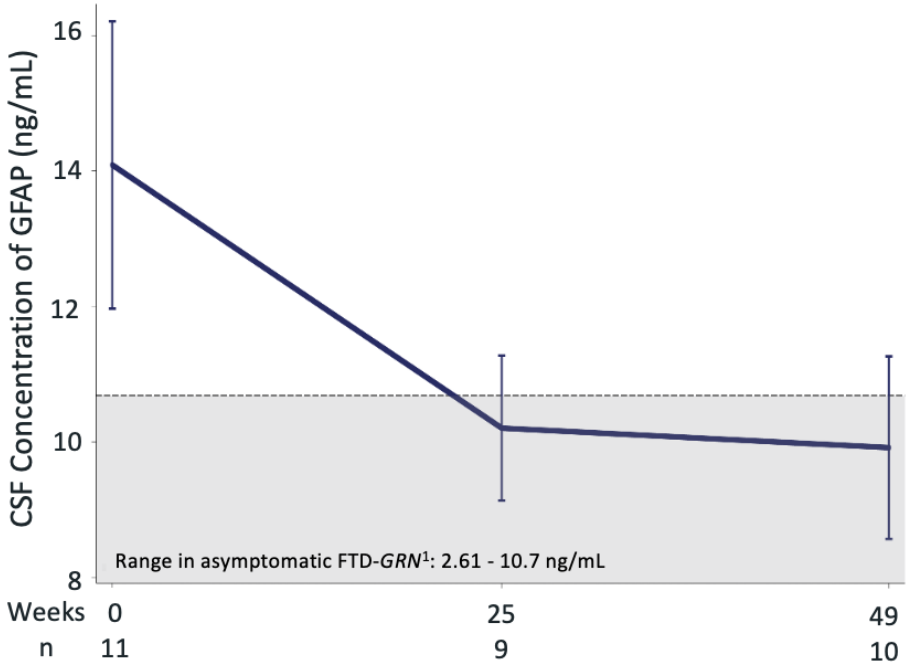
# INFRONT-2: Latozinemab Treatment Decreases Glial Fibrillary Acidic Protein (GFAP) Levels Towards Range Seen in Asymptomatic Carriers of FTD-*GRN* Mutation

## BIOMARKERS OF DISEASE ACTIVITY – ASTROGLIOSIS

### GFAP Plasma Concentration




### GFAP CSF Concentration




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.

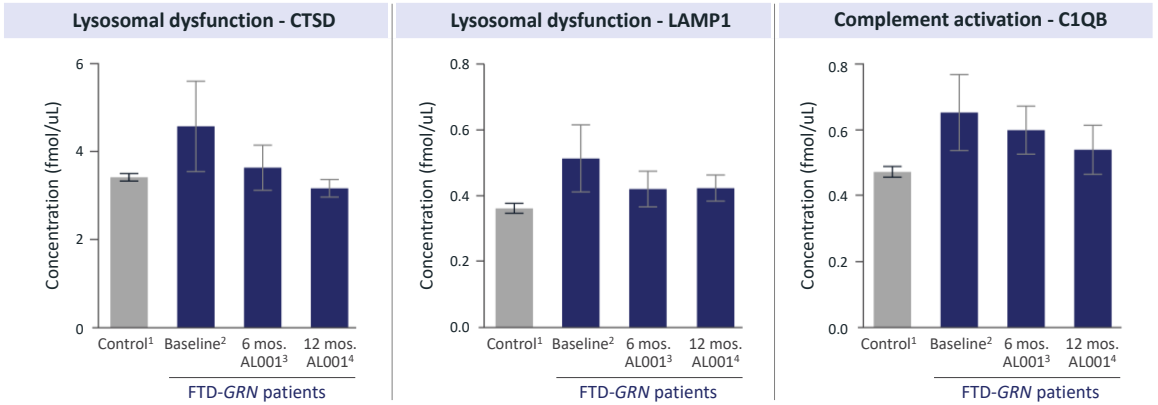
# INFRONT-2: Encouraging Trends Across Biomarkers Of Disease Activity

## SYMPTOMATIC FTD-*GRN* PARTICIPANTS AT 12 MONTHS IN OPEN LABEL TRIAL

## LYSOSOMAL AND INFLAMATORY BIOMARKERS

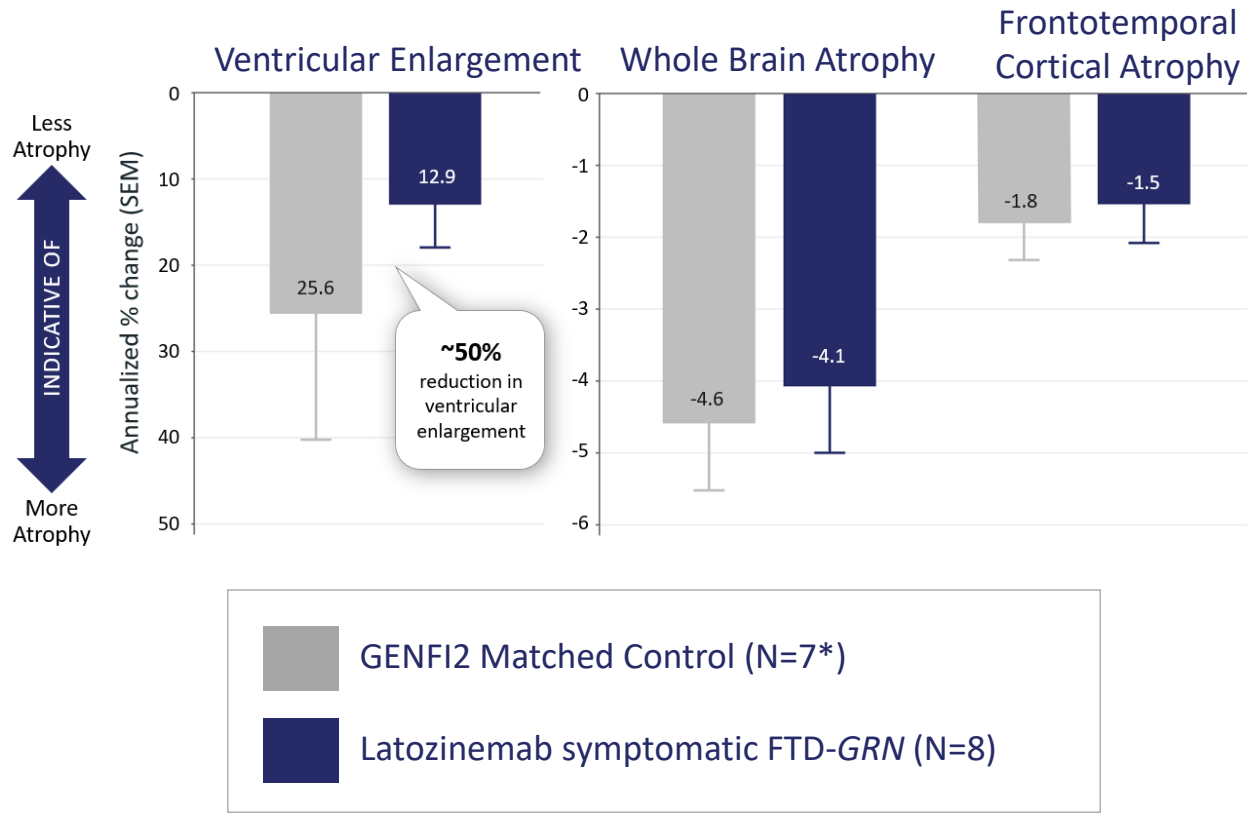
## BRAIN VOLUME CHANGES BIOMARKERS

### Normalization of lysosomal and inflammatory biomarkers




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

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



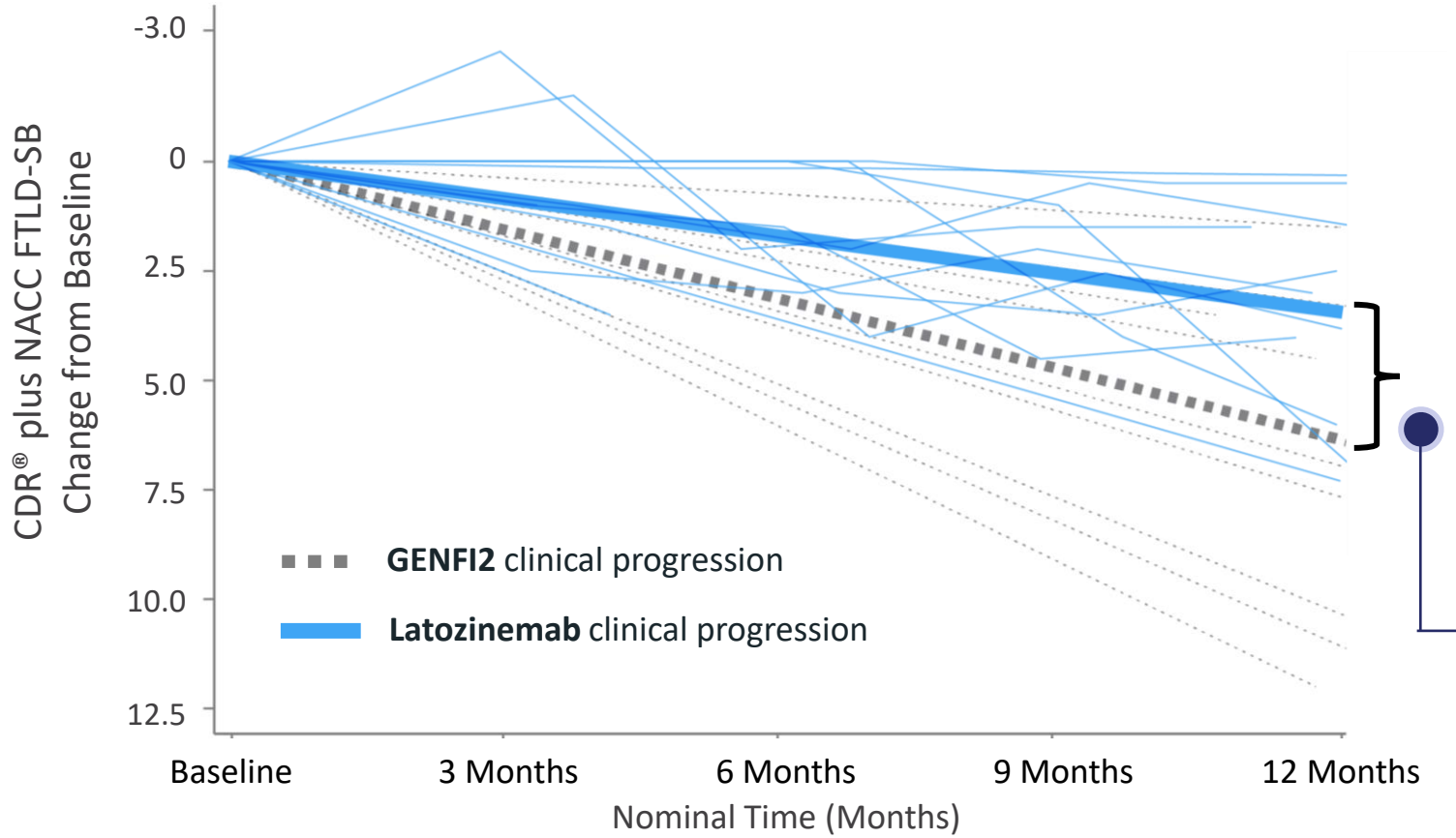

** n=8 for Whole Brain, n=7 for TBM measures (TBM measures were not available for one GENFI2 participant). One GENFI2 subject was excluded from the analysis as the patient displayed cortical volume increases (2.58% annual volume increase in the FT cortex) indicating image analysis artifact*

TBM = Tensor-based Morphometry (TBM) used for frontotemporal cortex and ventricles
Source: AAIC 2021

# INFRONT-2: Preliminary Data Suggests Latozinemab May Slow Disease Progression in FTD-*GRN* Participants Compared to Matched Historical Controls

## CLINICAL MEASURE

### CDR® plus NACC FTLD-SB




| Parameter | Estimate[1] | 95% CI |
|---|---|---|
| Annual Change in **GENFI2** (n=10) | 6.4 | [4.35,8.42] |
| Annual Change in **Latozinemab** (n=12) | 3.3 | [1.38,5.28] |
| **Difference in Annual Change (GENFI2 – Latozinemab)** | **3.1** | **[0.24,5.88]** |

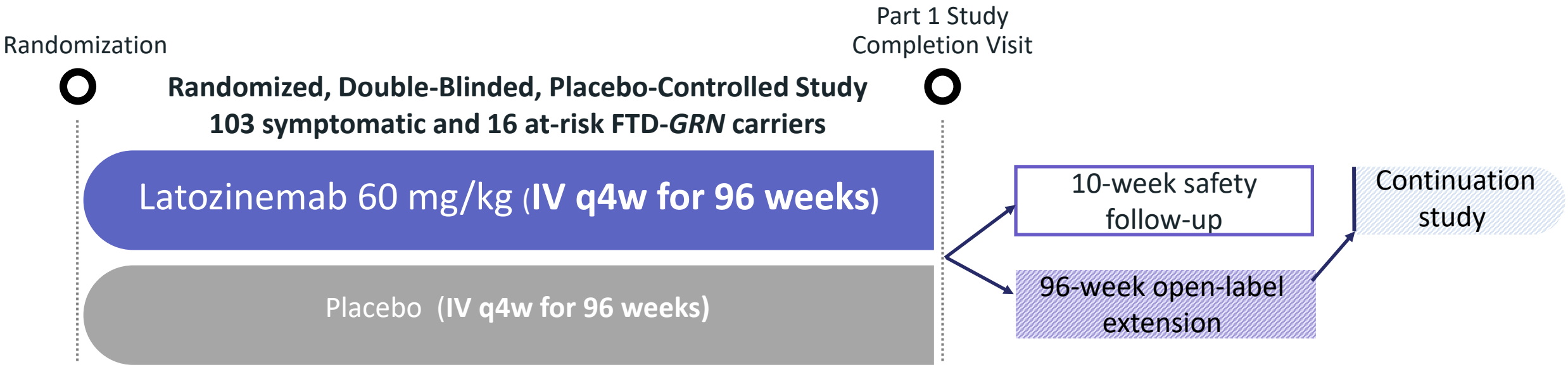
**Estimated to slow annual disease progression by ~48% (3.1 point change)**

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

# INFRONT-3: Ongoing Pivotal Phase 3 Study with Latozinemab

## ACHIEVED TARGET ENROLLMENT IN Q4 2023




| PRIMARY ENDPOINT | SECONDARY CLINICAL OUTCOMES ASSESSMENTS: | EXPLORATORY ENDPOINTS |
|---|---|---|
| CDR® plus NACC FTLD-SB | CGI-S, CGI-I, FRS, RBANS | vMRI, Plasma Biomarkers |

"At risk" = GRN carriers who are pre-symptomatic and meet a pre-specified NfL threshold for enrollment in the Phase 3 trial;
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

# INFRONT-3 Baseline Characteristics: Data Suggest a Representative Study Population for Testing Effects of Latozinemab in FTD-*GRN* Compared Against Registry Data

## INFRONT-3 Baseline Age

| | At-Risk (n=16) | Symptomatic (n=103) | Total (N=119) |
|---|---|---|---|
| **Age, mean (min, max), years** | 59.2 (37, 79) | 62.5 (48, 85) | 62.1 (37, 85) |

## INFRONT-3 Baseline Clinical Characteristics[a]

| | At-Risk (n=16) | Symptomatic (n=103) | Total (N=119) |
|---|---|---|---|
| **CDR® plus NACC FTLD-GS, n (%)** | | | |
| 0 | 15 (93.8) | 0 | 15 (12.6) |
| 0.5 | 1 (6.3) | 23 (22.3) | 24 (20.2) |
| 1 | 0 | 49 (47.6) | 49 (41.2) |
| 2 | 0 | 31 (30.1) | 31 (26.1) |
| **CDR® plus NACC FTLD-SB, n** | 16 | 103 | 119 |
| Mean (SD) | 0.0 (0.1) | 6.9 (4.1) | 6.0 (4.4) |
| **NfL concentration (pg/mL), n** | 12 | 87 | 99 |
| Mean (SD) | 16.0 (9.7) | 73.0 (41.5) | 66.1 (43.3) |
| Median (min, max) | 14.4 (7.8, 42.9) | 66.9 (6.5, 190.0) | 61.7 (6.5, 190.0) |

**Symptomatic FTD-*GRN* participants from ALLFTD and GENFI Registry Studies (n=84):[1]**

**Mean age of 63.7 years (SD: 8.8)**

**Mean CDR® plus NACC FTLD-SB score of 9.19 (SD: 6.53)**

**Mean plasma NfL (natural log) of 4.04 (geometric mean: 56.8 pg/mL)**

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a. As of July 2024.

1. Staffaroni AM, et al. *Nat Med*. 2022;28:2194-2206.

CDR® plus NACC FTLD-GS, Clinical Dementia Rating scale plus National Alzheimer's Disease Coordinating Center Frontotemporal Lobar Degeneration Global Score; CDR® plus NACC FTLD-SB, Clinical Dementia Rating scale plus National Alzheimer's Disease Coordinating Center Frontotemporal Lobar Degeneration Sum of Boxes; NfL, neurofilament light chain; SD, standard deviation

# AL101/GSK4527226: Developed to Align with Needs of Larger Indications (AD)

## PGRN: Genetic and Biologic Rationale for AD

- **Genetics:** PGRN deficiency is a risk for AD.
- **Biology:** Modulation of PGRN in AD disease models.
  - PGRN ablation exacerbates AD in disease models.
  - PGRN overexpression is protective in AD disease models.

## AL101 AD Program

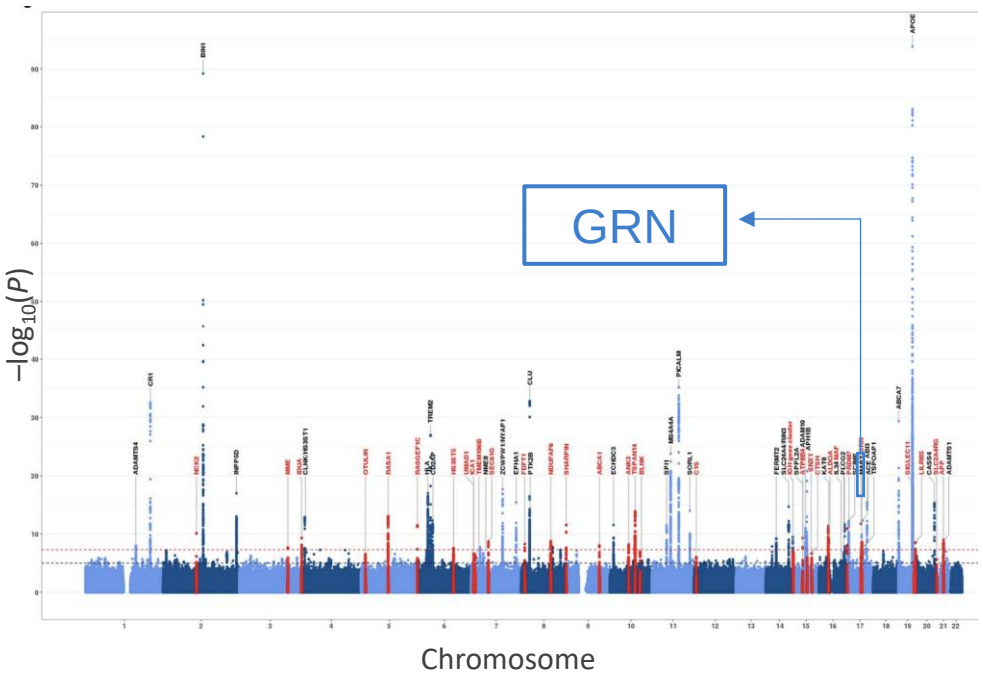
- **Phase 1:** Completed in healthy volunteers.
- **Phase 2:** Received IND clearance from FDA in AD.
- **Phase 2:** Enrollment is ongoing, with dosing initiated in February 2024.

Mendsaikhan, A., et al. Characterization of lysosomal proteins Progranulin and Prosaposin and their interactions in Alzheimer's disease and aged brains: increased levels correlate with neuropathology. *acta neuropathol commun 7, 215 (2019). The breakdown of clinical diagnoses among ARTFL FTD mutations carriers. [Courtesy of Adam Boxer.]* https://www.alzforum.org/print-series/1093496; Bellenguez C, Küçükali F, Jansen I, et al. New insights on the genetic etiology of Alzheimer's and related dementia. medRxiv; 2020.

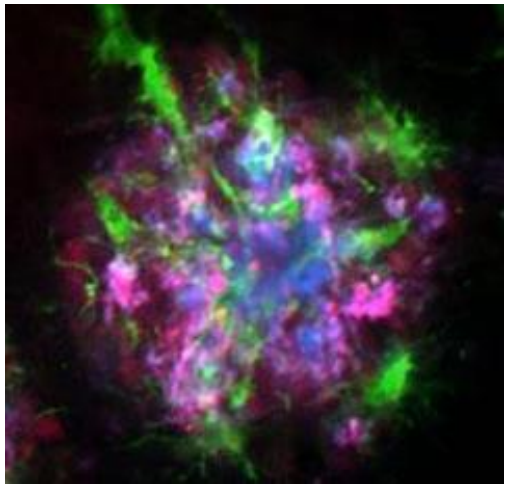
PGRN = progranulin protein
LOF = loss of function
AD = Alzheimer's disease

# Rationale for PGRN-Elevating Drugs in Alzheimer's Disease

## PGRN is a Risk Gene for AD

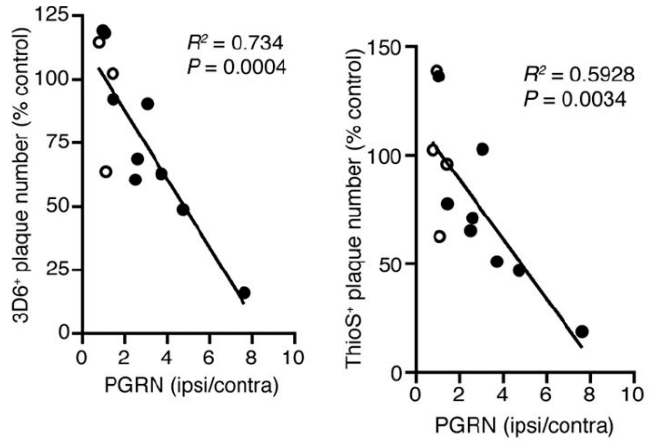



## PGRN is Embedded in Aβ Plaques



Microglia (green) surround amyloid plaques (blue), which also contain high levels of PGRN (purple)

## PGRN is Protective in AD Model

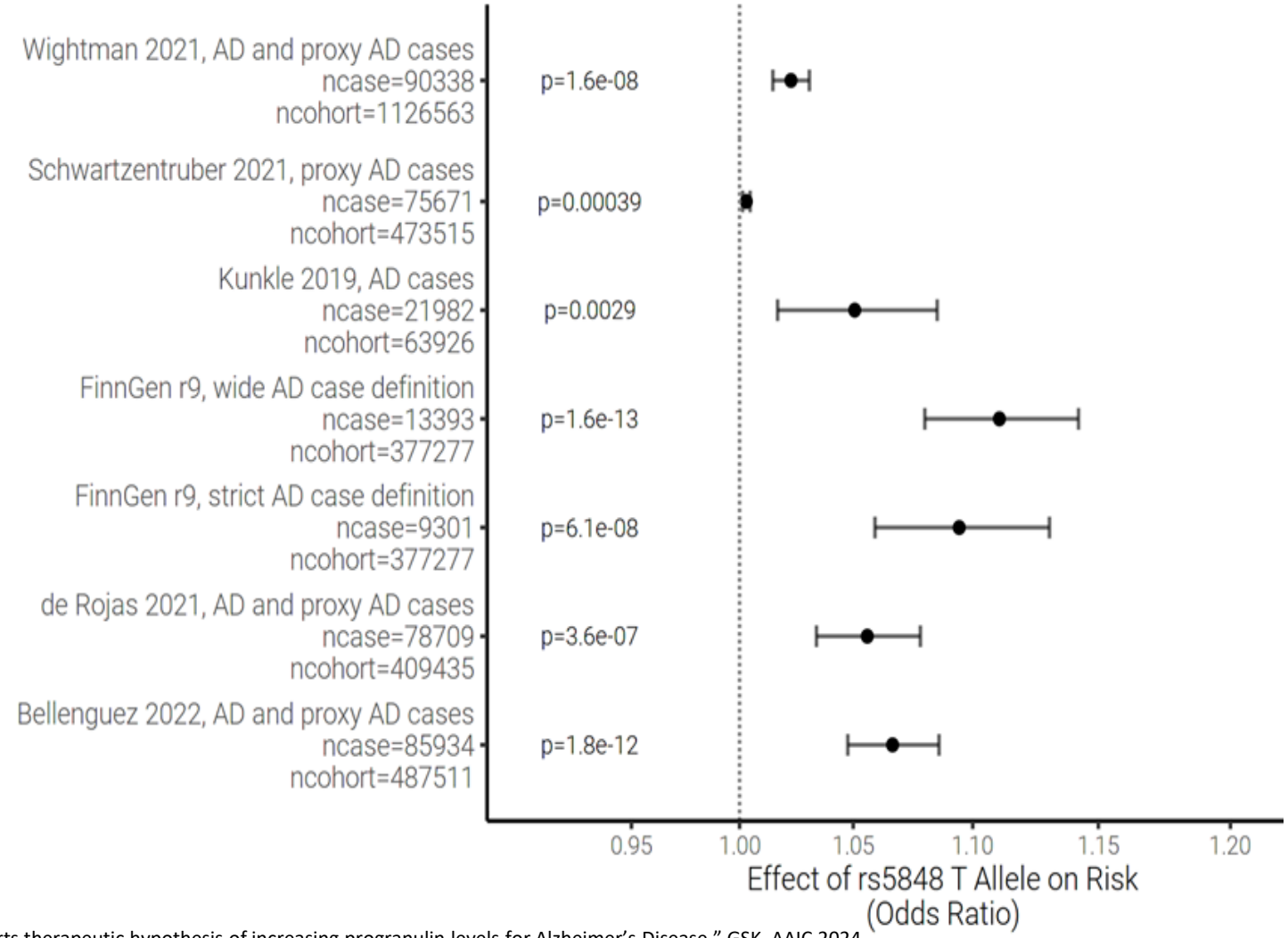



PGRN overexpression decreases Aβ plaque load in the dentate gyrus of AD mice

*Source(s): https://doi.org/10.1101/2020.10.01.20200659 (Left); ARTFL Diagnoses. The breakdown of clinical diagnoses among ARTFL FTD mutations carriers. [Courtesy of Adam Boxer.] https://www.alzforum.org/print-series/1093496 (Right); Source: doi: https://doi.org/10.1101/2020.10.01.20200659; Acta Neuropathologica Communications* **volume 7**, Article number: 215 (2019); *Nat Med*. 2014; *Nat Med. 2014 Oct; 20(10): 1157–1164.*

# Genetic Evidence Supports Increasing PGRN Levels in AD

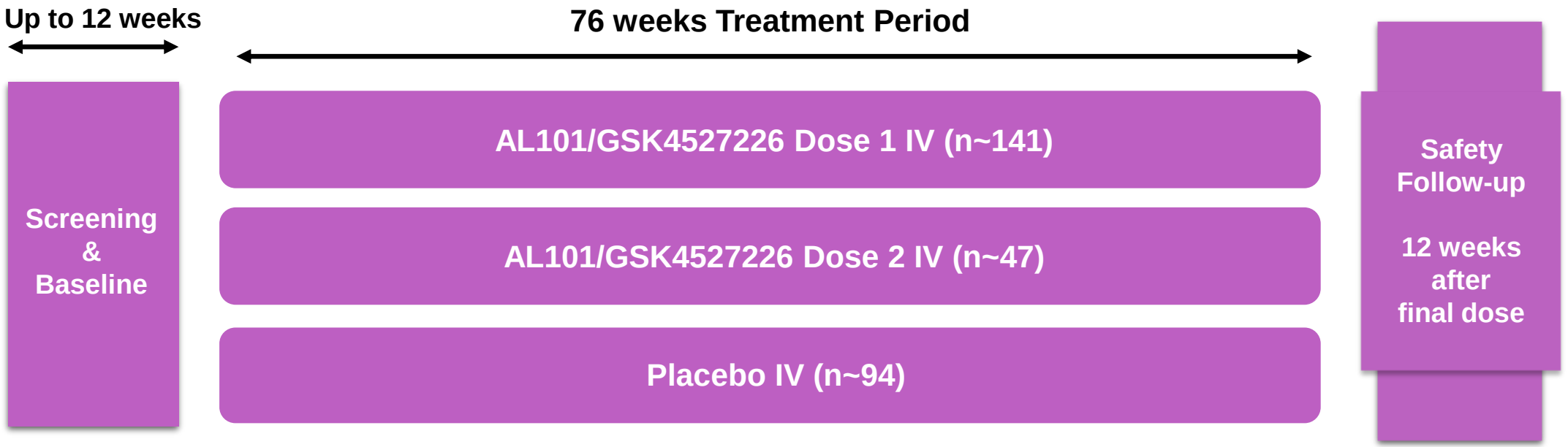
Common *GRN* variant rs5848 T allele is associated with (A) AD risk and (B) decreased PGRN levels in CSF and plasma




"Genetic evidence supports therapeutic hypothesis of increasing progranulin levels for Alzheimer's Disease," GSK, AAIC 2024.

# AL101/GSK4527226 PROGRESS-AD Study Design

PHASE 2, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO EVALUATE THE EFFICACY AND SAFETY OF AL101/GSK4527226 IN PATIENTS WITH EARLY ALZHEIMER'S DISEASE




**Key inclusion criteria**
- Age 50-85 years, inclusive
- Diagnosis of MCI due to AD up to mild AD dementia
- Amyloid positivity (by PET or CSF)

**Primary endpoint**
Change from Baseline in CDR-SB across Weeks 52, 64 and 76.

**Key secondary endpoints**
Change from Baseline across Weeks 52, 64 and 76 for iADRS, ADAS-Cog14, ADCS-iADL, ADCS-ADL-MCI, ADCOMS

**Biomarkers:** Amyloid PET, Tau PET, CSF and Plasma

# Latozinemab and AL101: Currently Partnered in a Collaboration Agreement with GSK


## Latozinemab and AL101

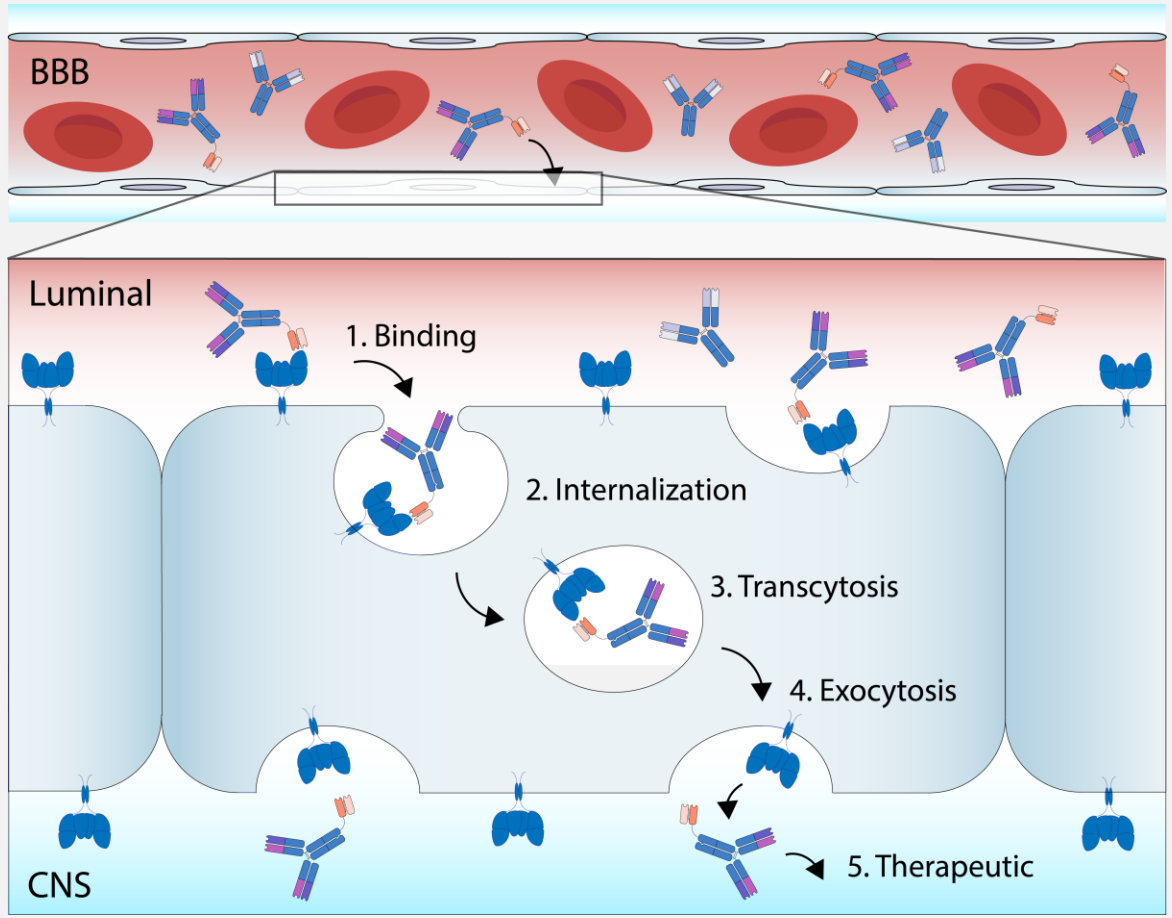
$700M upfront (2021 and 2022)
$1.5B+ in potential milestone payments
U.S. 50-50 profit share and co-commercialization
Tiered double-digit royalties ex-U.S.
$160 million for first commercial sale in the U.S.
$90 million for first commercial sale in at least two of the following countries: France, Germany, Italy, Spain, or the UK

# Alector Brain Carrier (ABC) is Designed for Effective Brain Delivery

## Alector Brain Carrier (ABC)

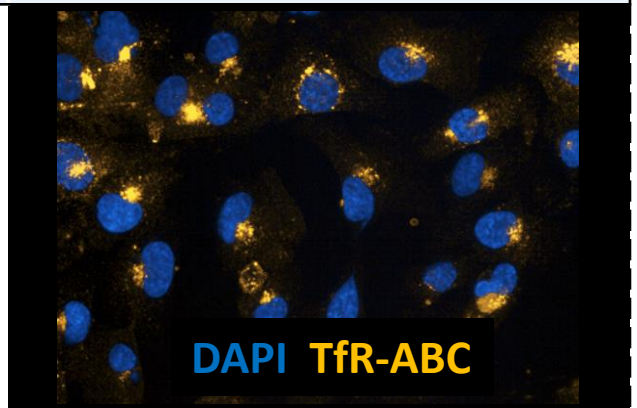
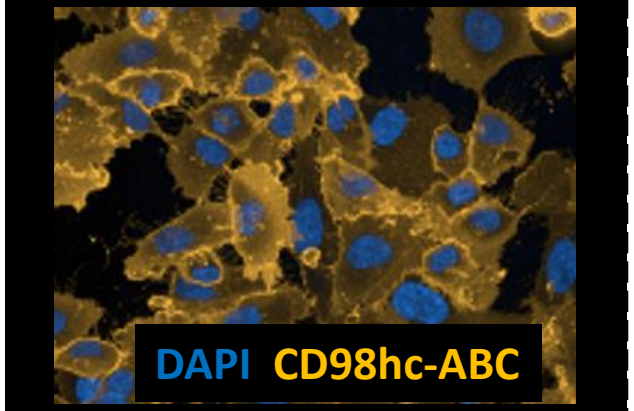
- BBB technology that enables **precise** and **non-invasive peripheral delivery** of therapeutics to the brain
- **Versatile** and **tunable** design seeks to optimize **efficacy** and **safety**
- Validated for brain uptake with **multiple therapeutic cargos**
- Enables the potential to **widen the therapeutic window** while **lowering the costs of goods** and facilitating **convenient delivery** options

## Receptor-Mediated Transcytosis




alector™ Alector Brain Carrier is herein abbreviated as ABC

# TfR and CD98hc Offer Distinct Advantages for Cargo Selection

| Target | Receptor Function | CNS Cell Expression | BBB Expression Level | Localization | Trafficking of ABC in Brain Endothelial Cell Line |
|---|---|---|---|---|---|
| Transferrin Receptor (TfR) | Iron transport receptor | Neuronal, microglia | High | Punctate, endolysosomal |   |
| CD98hc/ Slc3a2 | Amino acid transport complex | Broad | High | Broad, cell surface |   |

***Therapeutic cargo will also impact target cell localization and trafficking***

*hCMEC/D3 cells; 2h incubation, huIgG detection; 40x*

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Alector data on file

# Enhanced Long-Term Future with Alector Brain Carrier (ABC) Platform

| | 2024 | | | | 2025 | | | | 2026 | | | | 2027 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Anticipated | Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 |
| Clinical Readouts | | | | ▲ AL002 AD Phase 2 | | | | | Latozinemab FTD-*GRN* Phase 3 | | | | AL101 AD Phase 2 | | | |

***Expanding our ability to deliver first and best-in-class therapies for degenerative brain disorders***

ABC: An Integral Part of Alector Drug Discovery Platform

- **Novel Targets**
  Brain Penetrant Proteins, Enzymes & Antibodies
- **Validated targets**
  Best-in -Class Brain-Penetrant Proteins, Enzymes & Antibodies
- **2nd Gen Targets**
  Brain-Penetrant Proteins, Enzymes & Antibodies
- **Non-Protein drugs**
  Best-in-Class Brain Penetrant

→

- Years in the making
- May enable targeting diseases that require protein replacement
- May enable lower dosing, better brain distribution & subQ delivery
- May enable development of 2nd gen. drugs for clinical programs
- May enable development of best-in-class drugs for validated targets
- May enable brain delivery of non-protein drug modalities

***Expanded Partnering Opportunities***

Partnerships →
- Proteins
- Enzymes
- Antibodies
- Nucleic Acids

**Partnering Opportunities with Drug Modalities Experts**

# Alector Value Proposition: Aims to Deliver Innovation to Make Brain Disorders History

## Accomplishments to date

***Pioneering firsts for patients***

- **Latozinemab (AL001) first anti-SORT1** molecule in FTD-*GRN*[1]
- **Achieved target enrollment** in latozinemab FTD-*GRN* pivotal P3
- **AL002 first TREM2** molecule in AD[1]
- **Completed enrollment** in AL002 AD P2
- **Enrollment ongoing** in AL101 AD Ph 2
- **Pipeline of first-in-class** approaches for brain disorders[1]

## Goals for Next 3 years

***Aim to deliver firsts for patients***

- **Deliver data** for AL002 AD P2 and latozinemab FTD-*GRN* pivotal P3
- **Complete enrollment** of AL101 AD P2
- **Deliver blood brain barrier** platform technology to enhance our novel programs
- **Deliver 2-3 first-in-class leads** for IND enabling studies for neurodegenerative diseases

## Goals for 3+ years

***Aim to make brain disorders history***

- Obtain **regulatory approval** and **commercialize** latozinemab in FTD-*GRN**
- **Deliver data** for AL101 AD P2
- **Launch our initial first-in-class AD programs** with partners globally**
- **Continue to advance our pioneering science** from research to the clinic with multiple INDs for novel programs

$457.2 MILLION[2] IN CASH PROVIDES RUNWAY THROUGH 2026

1. Alector is not aware of any other TREM2-activating candidates in a Phase 2 or a Phase 3 trial for AD, PGRN-elevating candidates in a Phase 3 trial for FTD, or PGRN-elevating candidates in a Phase 2 or Phase 3 trial for AD as of November 2024.
2. Cash, cash equivalents, and marketable securities as of September 30, 2024, were $457.2 million.

AL001 (latozinemab), AL101 and AL002 are investigational therapies.

AD = Alzheimer's disease
FTD = Frontotemporal dementia
GRN = granulin gene
*Assuming positive Phase 3 data
**Assuming regulatory approval

# Thank You