

# Alector Company Overview

February 2022

# Forward-Looking Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation 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 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 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](http://www.sec.gov).

This presentation discusses certain AL001 and other 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.

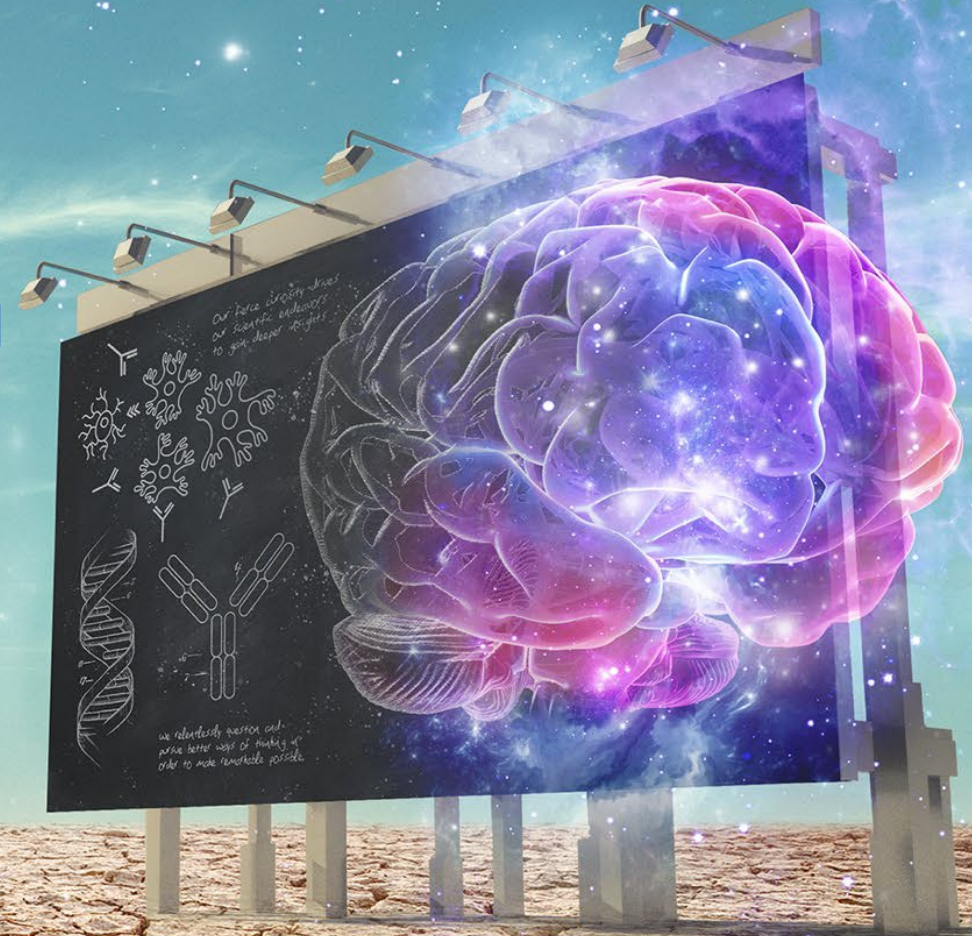
This presentation contains statistical data based on independent industry publications or other publicly available information, as well as other information based on our internal sources. We have not independently verified the accuracy or completeness of the data contained in these industry publications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



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At Alector, we envision a world where each individual retains his or her full brain function and cognitive faculties throughout life—a world where dementia and neurodegeneration are illnesses of the past.”

Arnon Rosenthal, PhD, Chief Executive Officer, Co-Founder





# Rapidly translating scientific insights into a broad portfolio of first-in-class programs

## 1 novel approach

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

## 4 candidates in clinical trials

- Clinical-stage programs targeting progranulin, TREM2 and SIGLEC3
- Potential treatments in development for FTD (Phase 3), ALS (Phase 2), Alzheimer's (Phase 2) + Parkinson's and solid tumors (upcoming)

## 3 more candidates entering the clinic

- Emerging programs in immuno-neurology and immuno-oncology readying for INDs in 2022
- ~A dozen more innate immunology research programs in early evaluation
- Continued investment in research and discovery

## 3 world class partners

- Agreements in place with GSK, Abbvie and Innovent
- Retained significant rights in the U.S.
- Well funded through major value inflection points

**MILLIONS** OF PATIENTS WAITING

# Pioneering immuno-neurology

## Human Genetics

Genetic risk factors for neurodegenerative diseases point to neuroinflammation as a causal factor



## Immunology

Our therapeutics target microglia cells, regulators of the brain's immune system



## Neuroscience

Measuring biomarkers of neurodegeneration enhance probability of success

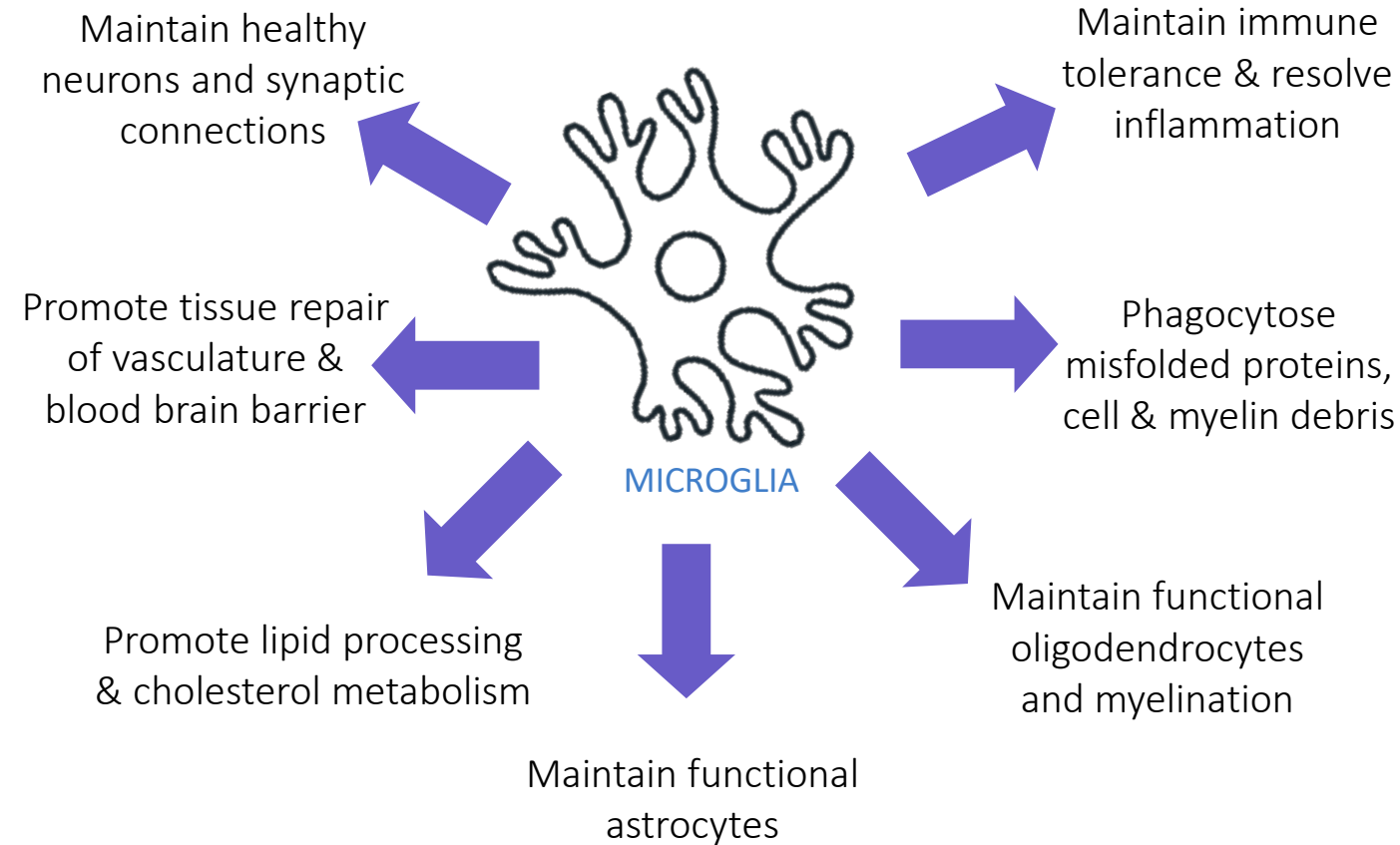


## IMMUNO-NEUROLOGY

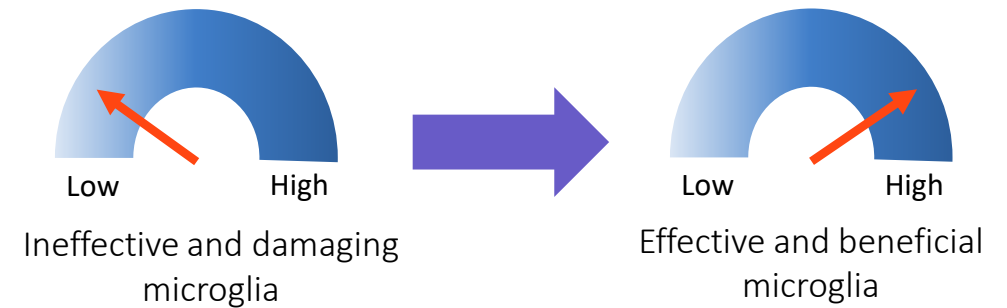
Recruiting the brain's immune system to address neurodegeneration

# Microglia are essential for maintaining a healthy brain

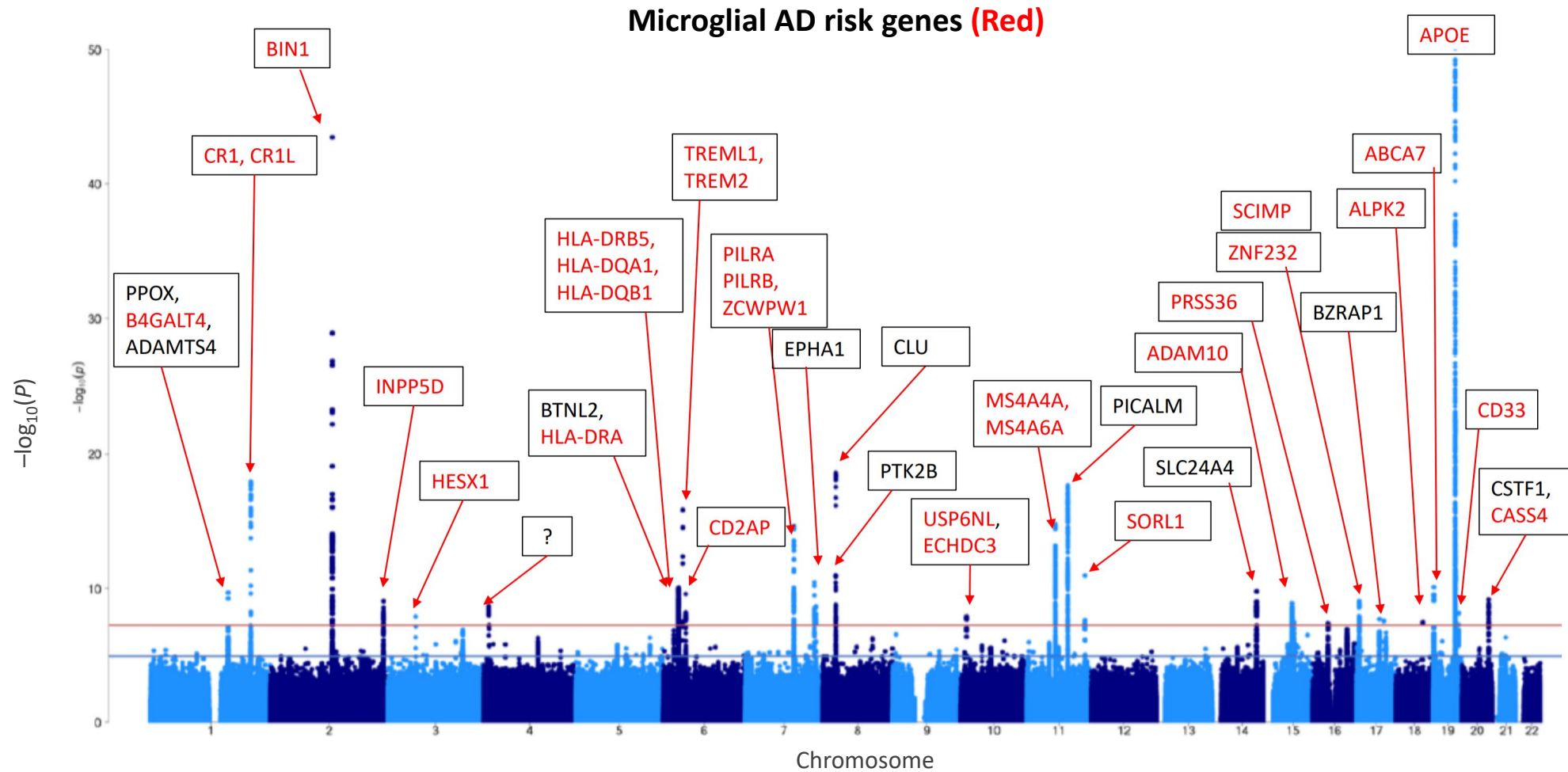
Microglia serve as the brain's garbage collector, police force and first responders






Alector's immuno-neurology therapeutics aim to harness the immune system to combat neurodegenerative diseases



# A large proportion of AD risk genes are microglial immune regulators



# Portfolio of product candidates targeting genetic causes of neurodegeneration as well as promising innate immune system targets for oncology

	TARGET	CANDIDATE	RESEARCH	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	COMMERCIAL RIGHTS
Progranulin Franchise	PGRN	AL001	FTD-GRN >					gsk 
		AL001	FTD-C9orf72 >					
		AL001	ALS- C9orf72 >					
		AL101	Healthy volunteers for AD and PD >					
Alzheimer Programs	TREM2	AL002	Alzheimer's disease >					abbvie 
	Siglec3 (CD33)	AL003	Alzheimer's disease >					
	MS4A	AL044	Alzheimer's disease >					
		AL044	Orphan neuro indication >					
Oncology Programs	SIRP-alpha	AL008	Solid tumors >					Innovent (China) 
	Multi-Siglec	AL009	Solid tumors >					

Target indications include AD, PD, FTD, MS & cancer

12+ programs



IP portfolio contains 50+ patent application families, which includes 20 issued patents and >380 pending patent applications directed to more than 20 targets and/or technologies



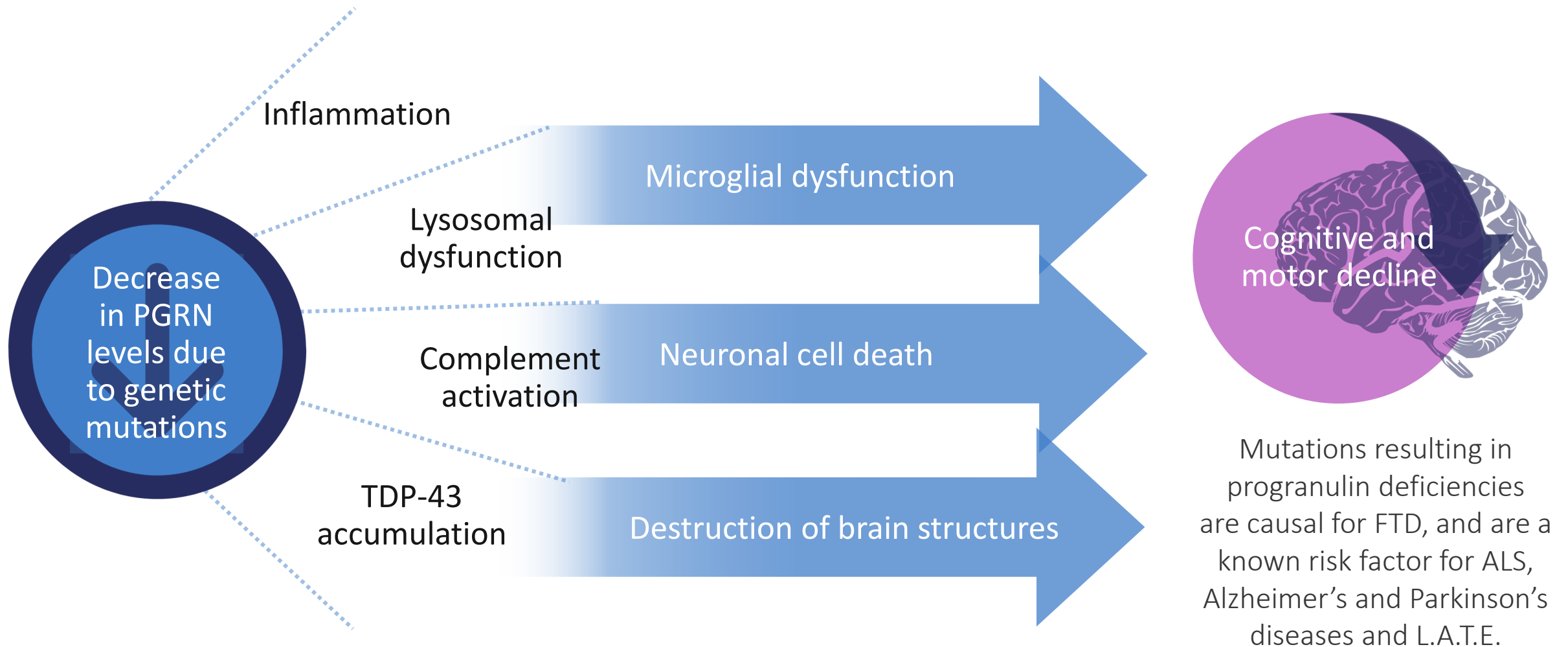
AD = Alzheimer's disease  
 PD = Parkinson's disease  
 FTD = Frontotemporal dementia  
 ALS = Amyotrophic lateral sclerosis  
 MS = Multiple sclerosis



# Progranulin franchise programs AL001 and AL101

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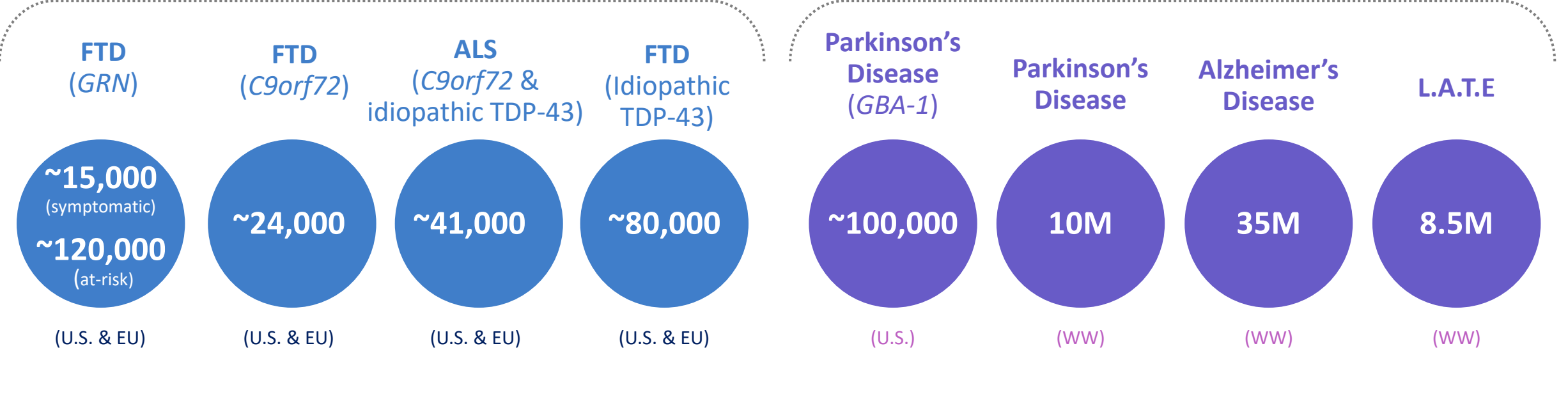
# The role of progranulin in neurodegeneration



# Broad therapeutic potential grounded in genetic evidence and animal models

## AL001

## AL101



Causal

GENETIC EVIDENCE

Known risk factor/Positive correlation

# AL001 and AL101: Targeting progranulin to restore function of microglia

## MECHANISM

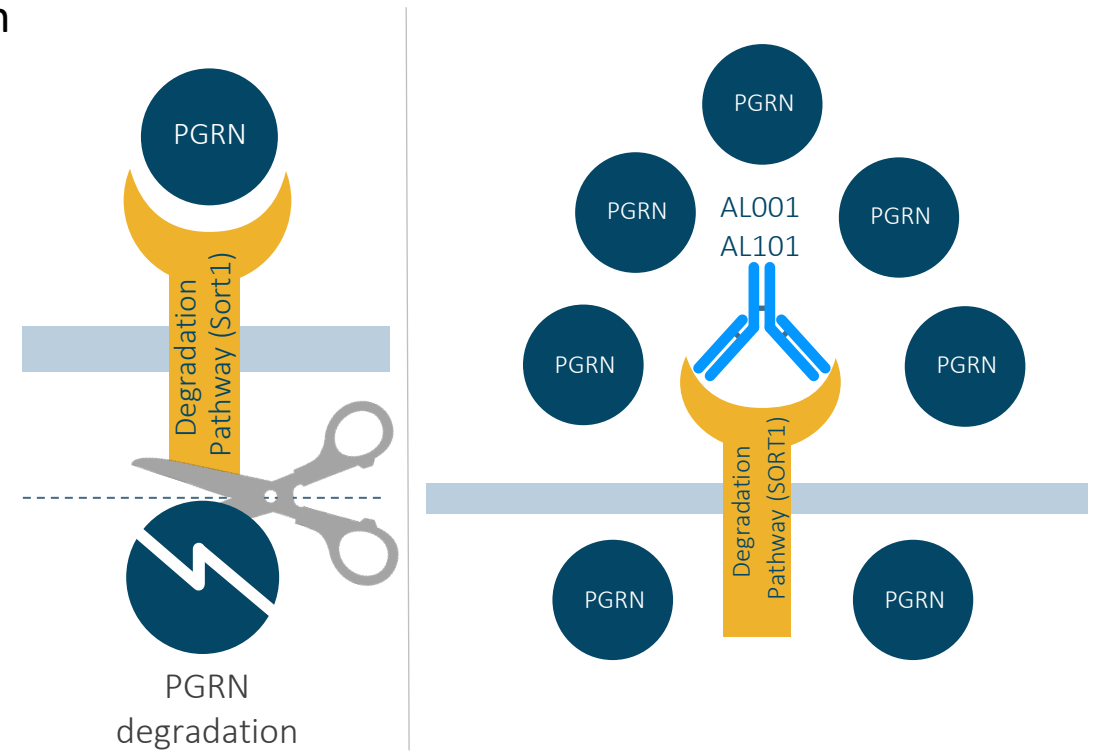
- Increases the half-life of PGRN by blocking Sortilin, a degradation receptor, in order to restore PGRN to normal levels

## AL001 STATUS

- Orphan Drug and Fast Track Designation
- Phase 1 studies in healthy volunteers complete
- Ongoing Phase 2 study in FTD-GRN and FTD-C9orf72
- Ongoing Phase 2 study in ALS-C9orf72
- Pivotal Phase 3 study in FTD-GRN actively enrolling

## AL101 STATUS

- Ongoing Phase 1 study in healthy volunteers

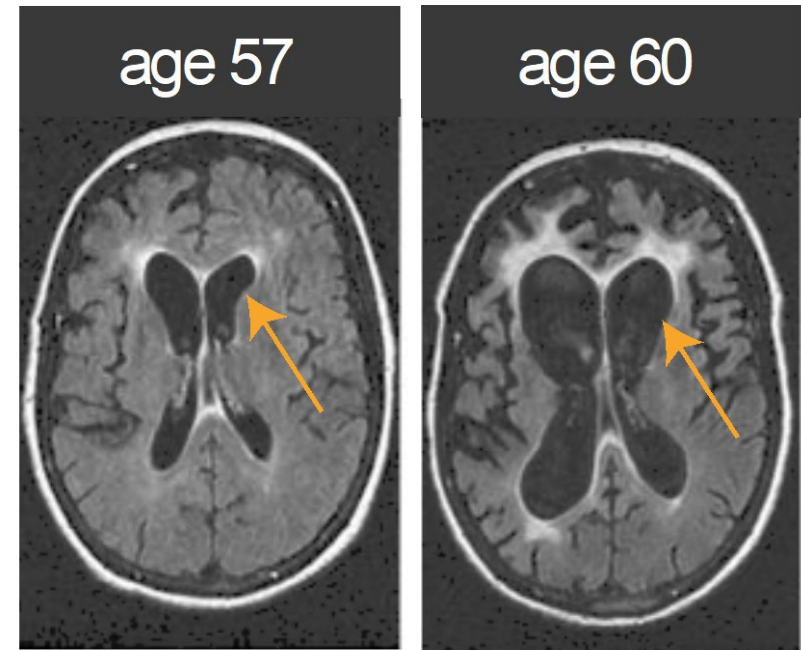




# Frontotemporal dementia: A rapidly progressive form of dementia with no current treatment

- Most common form of dementia under the age of 60
- Patients present with compulsive behavior, lack of restraint, apathy, anxiety, and aphasia
- Life expectancy after diagnosis is 7 - 10 years
- 15,000 symptomatic + ~120,000 at-risk people with progranulin mutations (FTD-GRN) in the U.S. and E.U.
  - FTD-GRN caused by coding mutations in progranulin
  - Lead to a complete loss of function in the mutated gene

**MRI of frontal and temporal atrophy in FTD**



# INFRONT-2: Phase 2 in frontotemporal dementia populations

## Open-Label, Single Arm

Asymptomatic FTD-GRN<sup>1</sup>  
N = 5

AL001 60 mg/kg q4w for 96 weeks

Symptomatic FTD-GRN<sup>1</sup>  
N = 12

AL001 60 mg/kg q4w for 96 weeks

Symptomatic FTD-C9orf72<sup>1</sup>  
N = up to 20

AL001 60 mg/kg q4w for 96 weeks

### PRIMARY ENDPOINT

- Safety and tolerability

### SECONDARY ENDPOINTS

- PK, PD

### EXPLORATORY ENDPOINTS

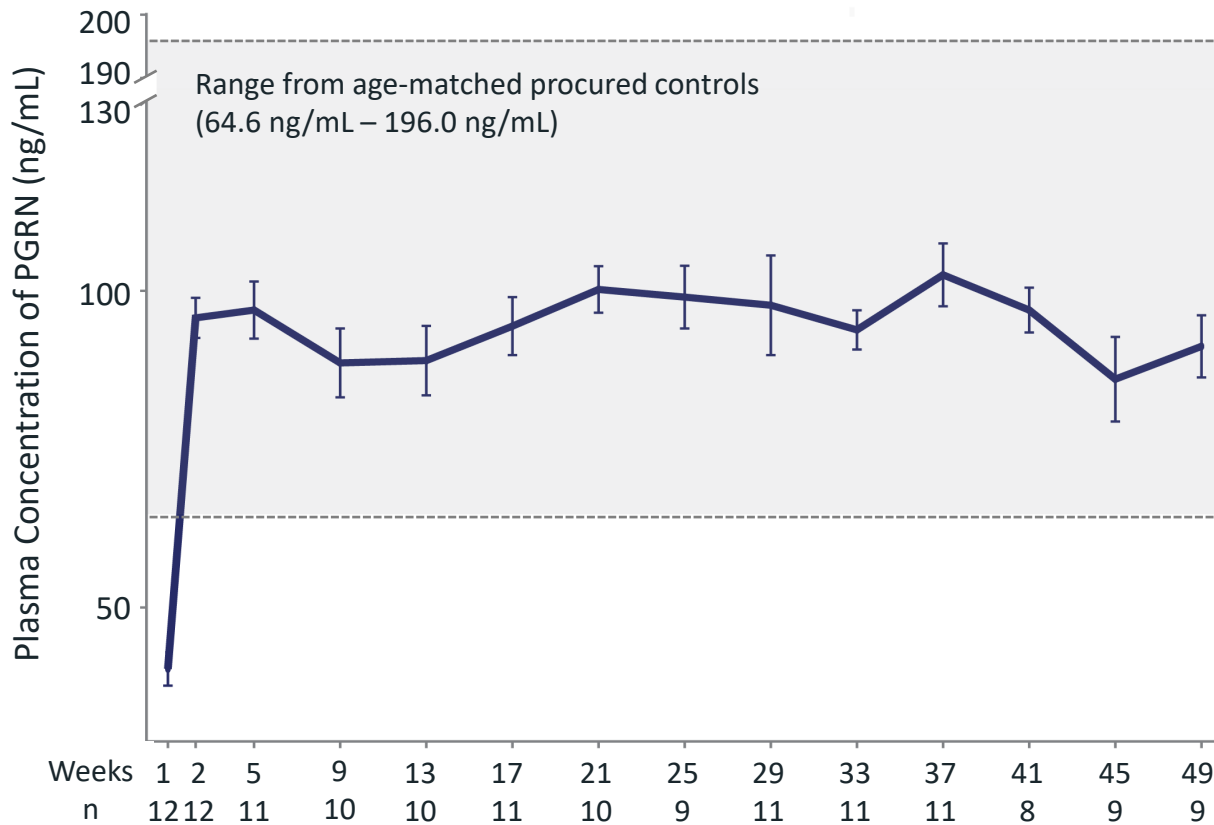
- CSF and plasma biomarkers
- Clinical Outcome Assessment (CDR<sup>®</sup> plus NACC FTLD-SB<sup>2</sup>)
- Volumetric MRI (vMRI)

Twelve-month biomarker and clinical data presented at 2021 AAIC and CTAD conferences  
from the symptomatic FTD-GRN cohort

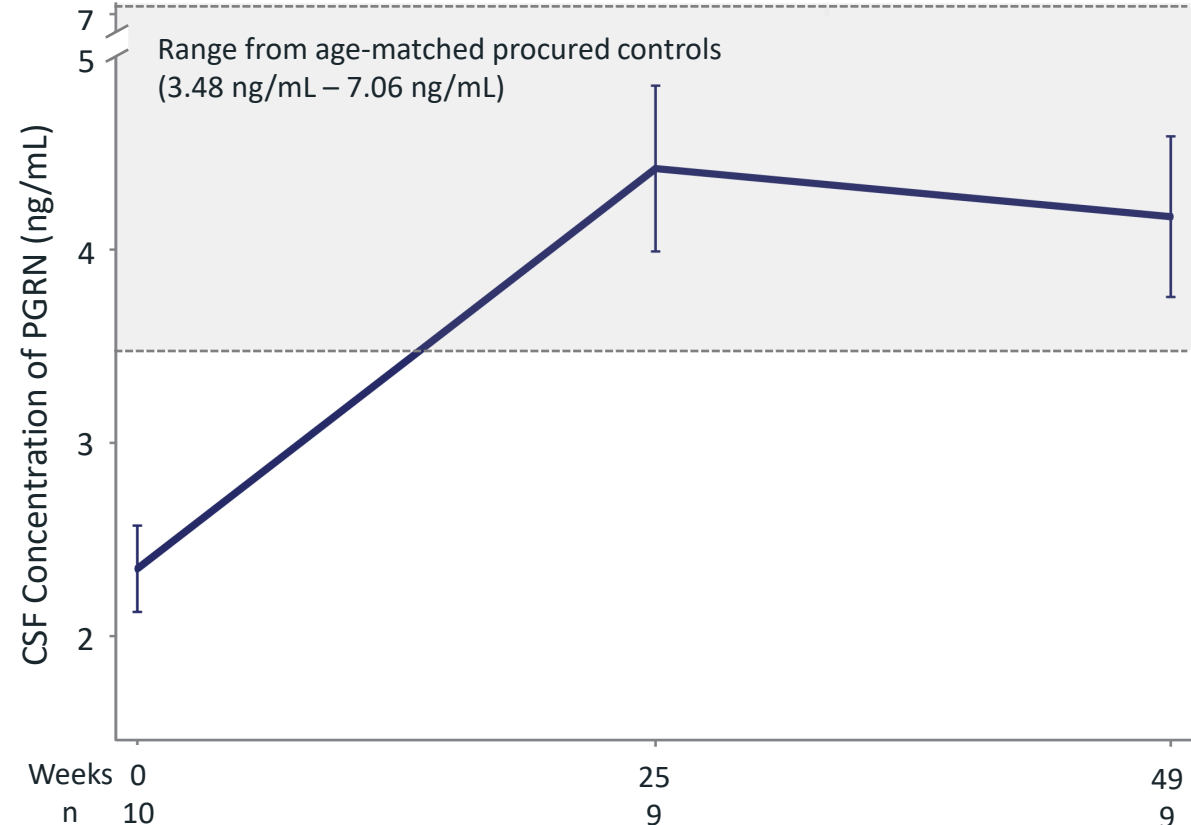
# INFRONT-2: AL001 restores PGRN in plasma and CSF to normal levels

## TARGET ENGAGEMENT

### PGRN plasma concentration



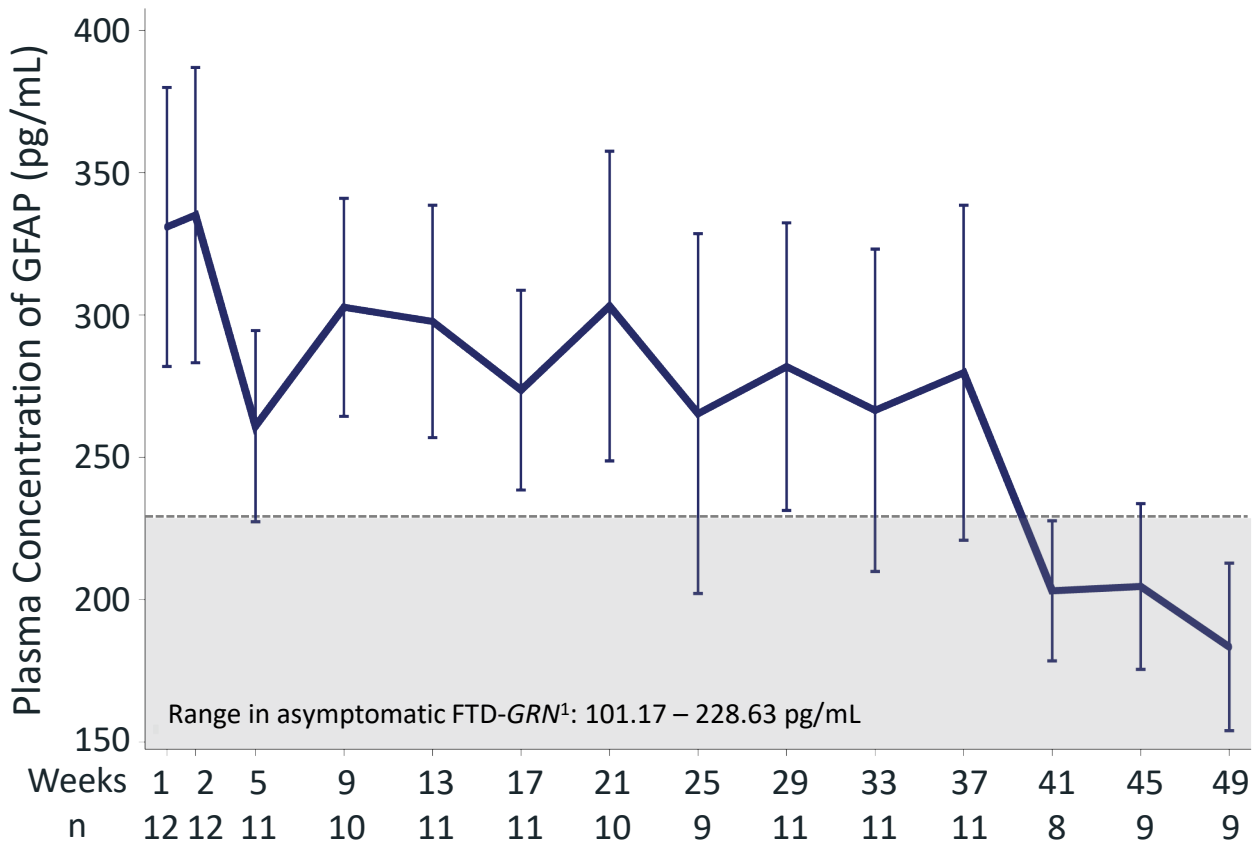
### PGRN CSF concentration



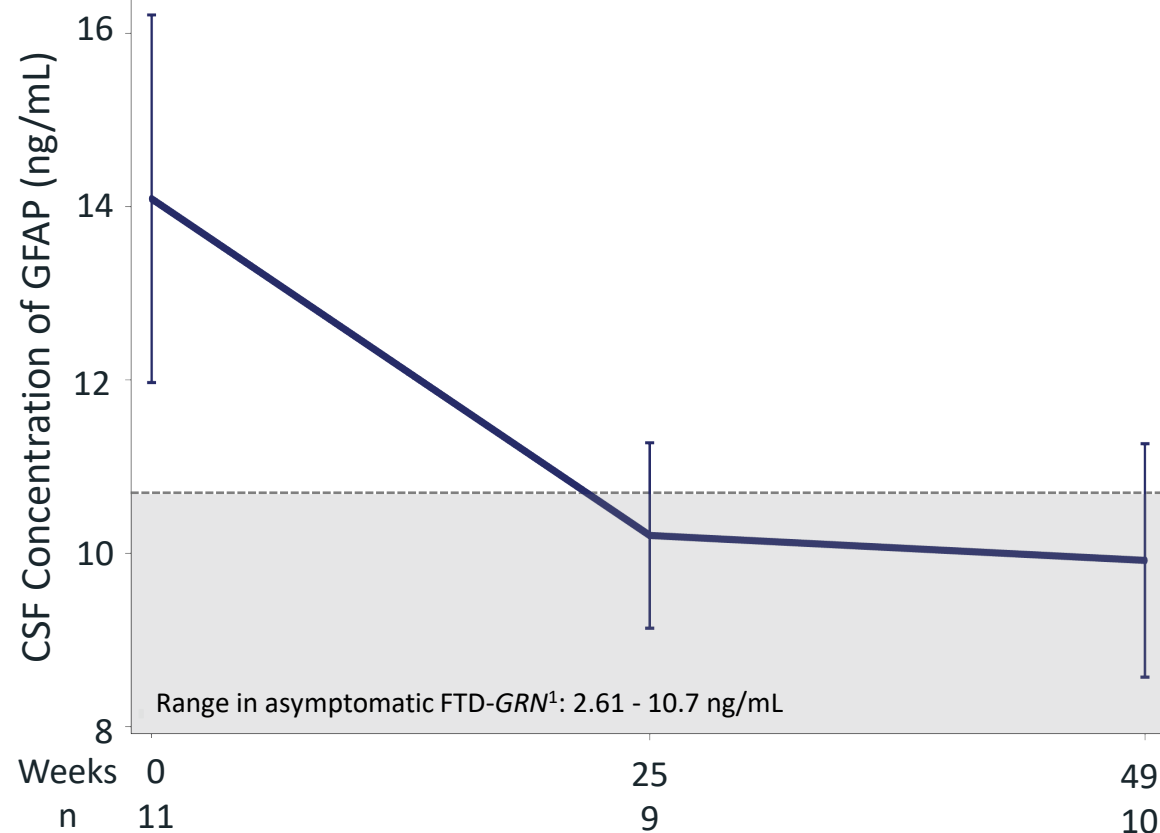
# INFRONT-2: AL001 treatment decreases glial fibrillary acidic protein (GFAP) levels towards normal levels

## BIOMARKERS OF DISEASE ACTIVITY – ASTROGLIOSIS

### GFAP Plasma Concentration



### GFAP CSF Concentration



Data cut-off June 15, 2021

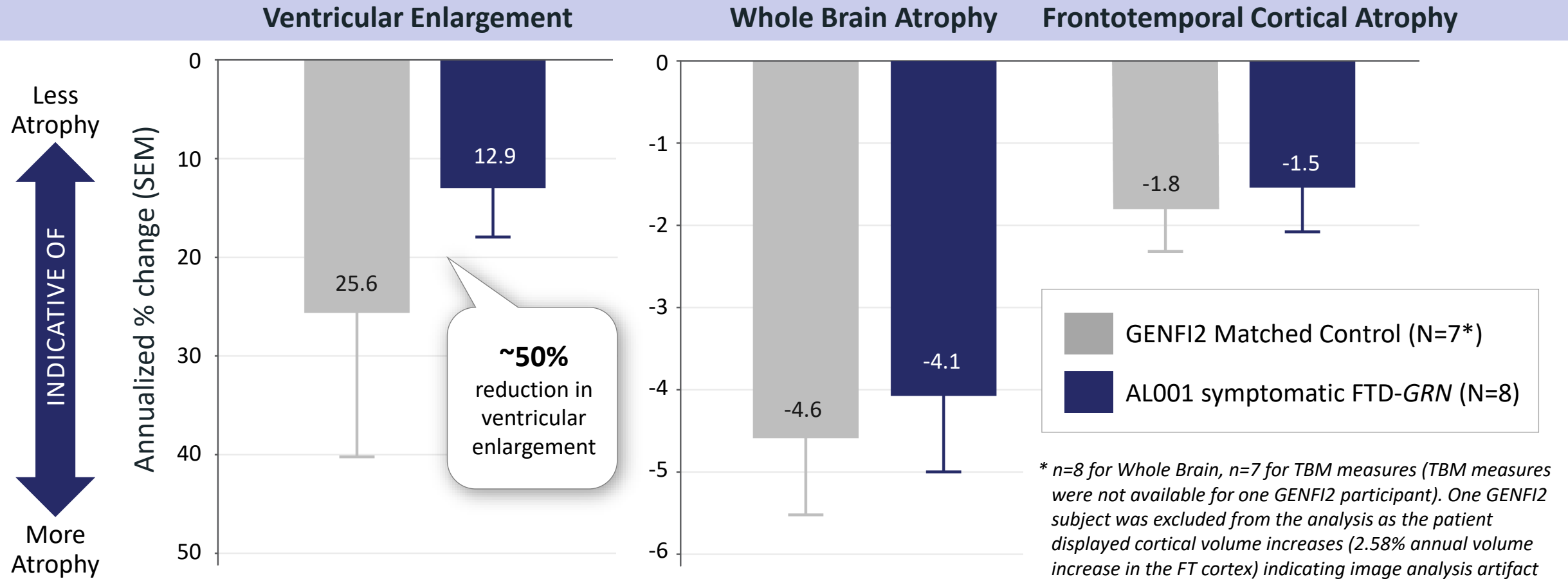
Mean +/- SEM

1. Range is of baseline GFAP levels in asymptomatic FTD-GRN patients enrolled in INFRONT-2



# INFRONT-2 vMRI data suggest slowing of ventricular enlargement and brain atrophy in AL001-treated patients vs. historic matched control

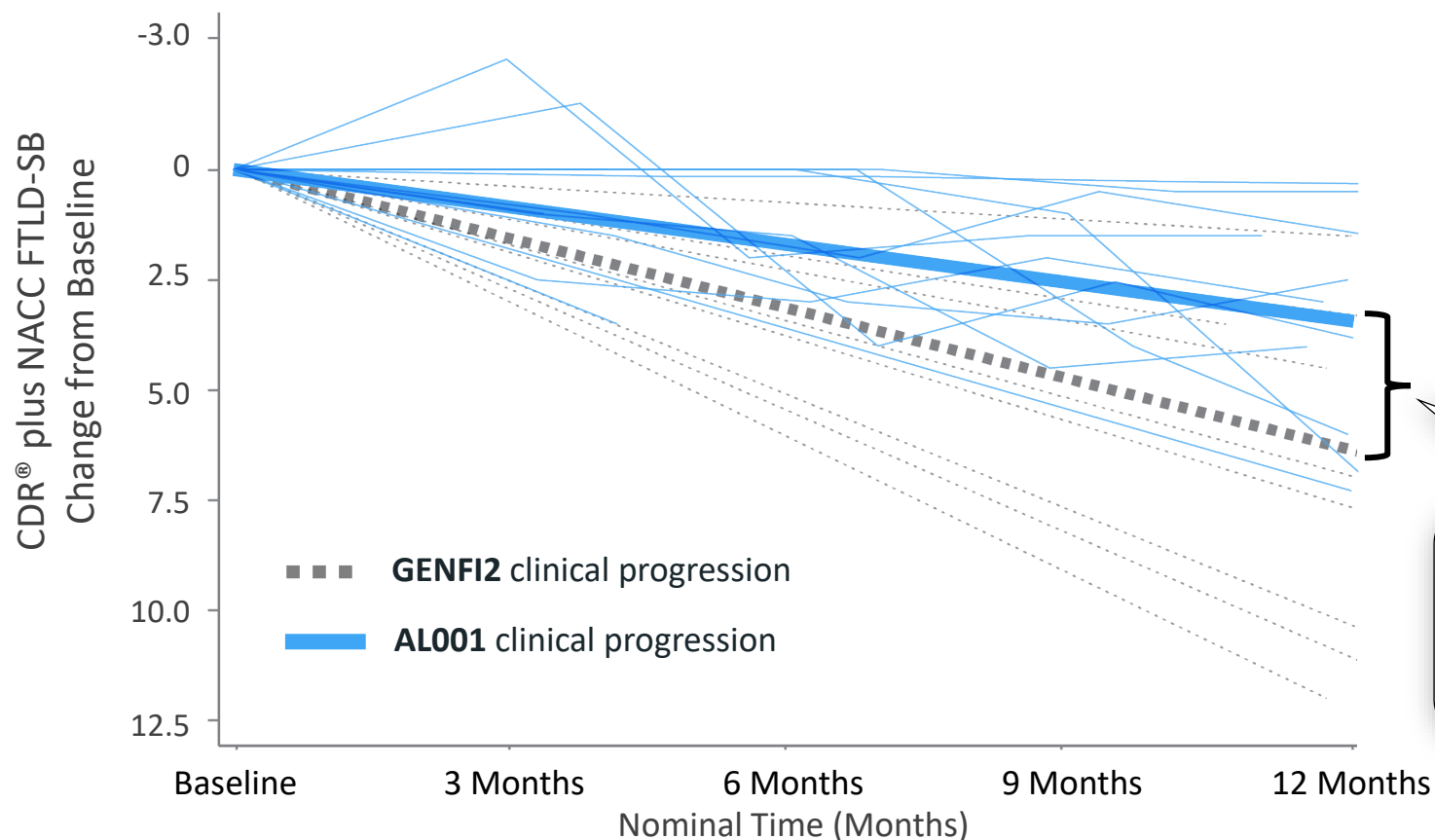
## BIOMARKERS OF DISEASE ACTIVITY – BRAIN VOLUME CHANGES



# INFRONT-2: AL001 showed a slowing of clinical progression in AL001-treated patients relative to matched GENFI2 controls

## CLINICAL BENEFIT

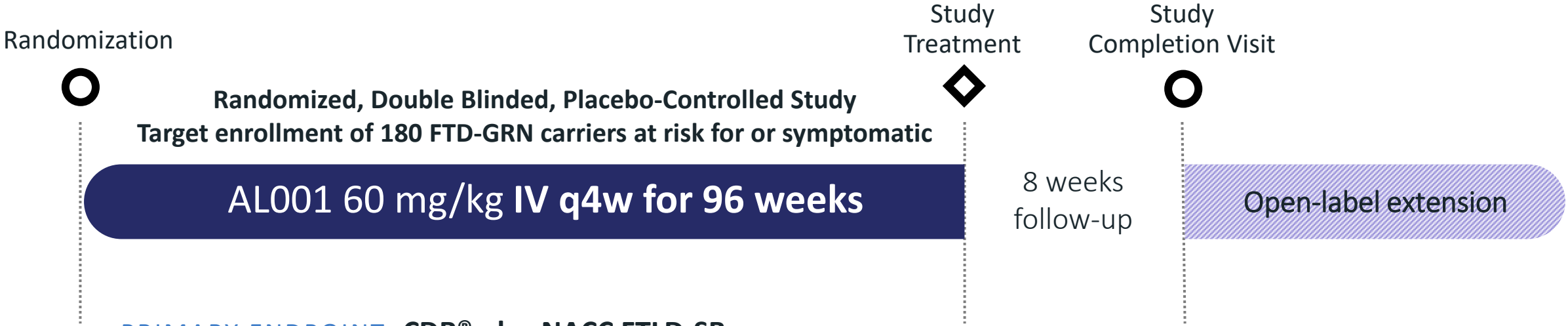
### CDR® plus NACC FTLD-SB



Parameter	Estimate <sup>1</sup>	95% CI
Annual Change in <b>GENFI2</b> (n=10)	6.4	[4.35,8.42]
Annual Change in <b>AL001</b> (n=12)	3.3	[1.38,5.28]
<b>Difference in Annual Change (GENFI2 – AL001)</b>	<b>3.1</b>	<b>[0.24,5.88]</b>

**~48%**  
slowing of clinical progression  
(3.1 point change)

# Enrollment ongoing for pivotal INFRONT-3 Phase 3 study of AL001



PRIMARY ENDPOINT: **CDR<sup>®</sup> plus NACC FTLD-SB**

SECONDARY CLINICAL OUTCOME ASSESSMENTS: **CGI-S, CGI-I, FRS, RBANS**

EXPLORATORY ENDPOINTS: **vMRI, CSF and plasma biomarkers**

Study taking place at approximately 45 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<sup>®</sup> plus NACC FT1. LD-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

# Rationale for exploring the potential impact of AL001 in FTD-*C9orf72*

## Genetics

Progranulin polymorphisms:

- Exacerbate *C9orf72* FTD and ALS<sup>1</sup>
- Associated with accelerated disease progression and earlier age of onset in ALS<sup>2</sup>

## Mechanistic

*C9orf72* repeats cause<sup>3</sup>:

- TDP-43 aggregation
- Microglia pathology

## Therapeutic

PGRN counteracts:

- TDP-43 pathology<sup>4</sup>
- Microglia pathology
- Lysosomal pathology that typify ALS and FTD

Upcoming presentation of 12-month data in up to 10 FTD-*C9orf72* participants will provide the first look at the therapeutic potential of elevating progranulin levels above normal

**AD/PD™ 2022**  
ADVANCES IN SCIENCE & THERAPY

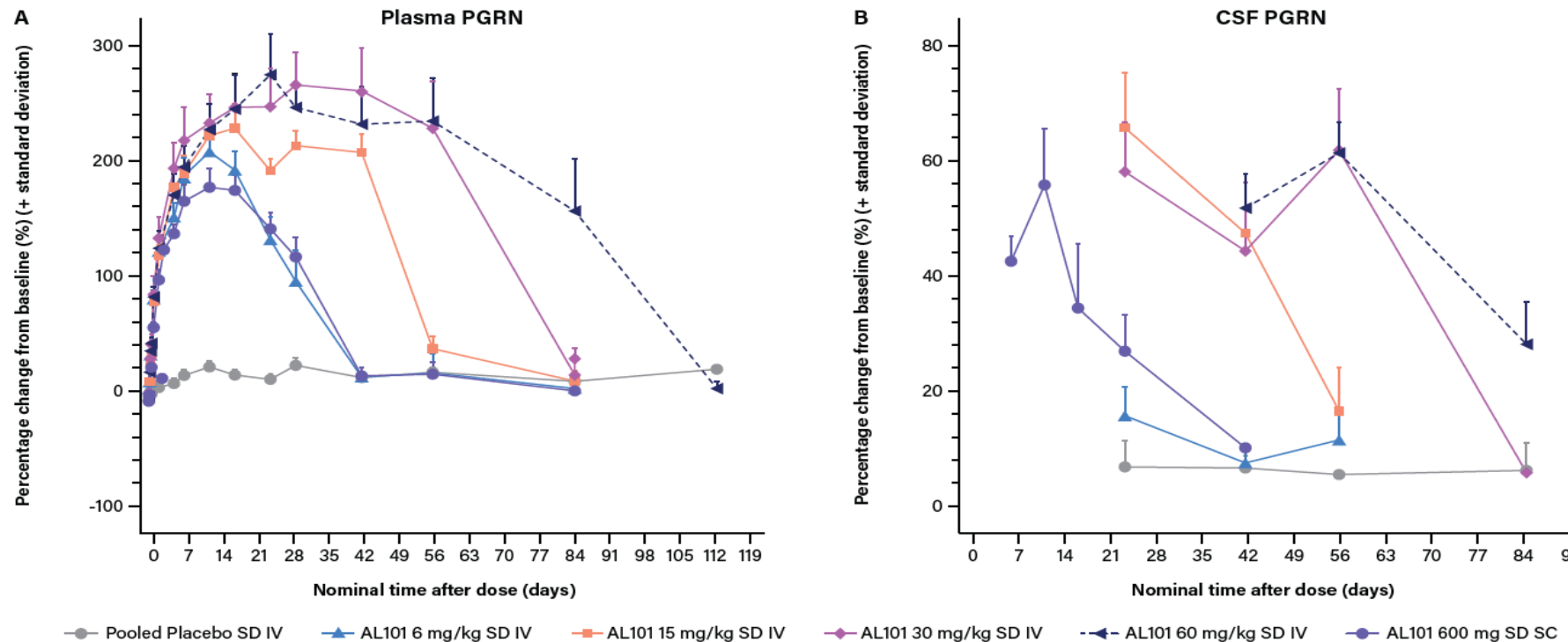
**March 15-20, 2022**



# AL101 elevated progranulin levels in periphery and CSF in Phase 1

Generally well tolerated in healthy volunteers; initial Phase 1 data suggest less frequent dosing may be possible

**Mean Percentage Change from Baseline in Plasma (A) and CSF (B) Concentrations of Progranulin as a Function of Time After Single Administration of AL101**



Phase 1 ongoing with additional cohorts being enrolled to evaluate subcutaneous dosing

# Clinical-stage Alzheimer's disease candidates: AL002 and AL003

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# AL002: Designed to activate TREM2 in order to enhance microglia function

## RATIONALE

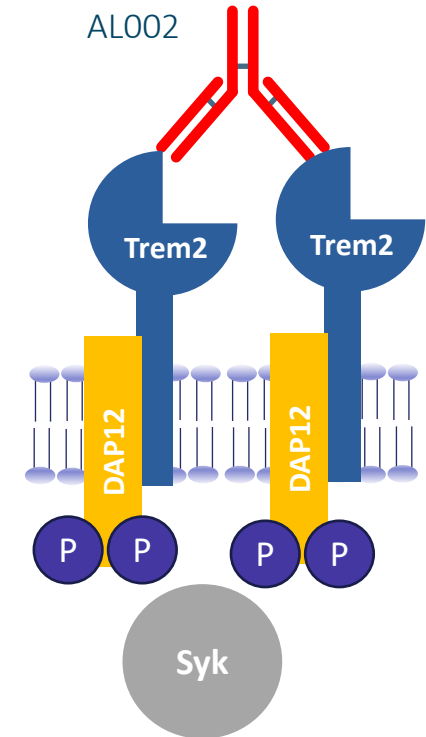
- TREM2 signaling controls critical microglial activity
- TREM2 is a prominent risk gene for Alzheimer's disease
  - Homozygous mutations cause dementia (NHD, FTD)
  - Heterozygous mutations increase risk for Alzheimer's disease by 3x
  - Ligands include APOE, an Alzheimer's risk gene

## MECHANISM

- Activates TREM2 signaling to improve functionality of microglia to clear pathology and protect neurons

## STATUS

- Phase 1 study complete
- INVOKE-2 Phase 2 clinical trial on-going

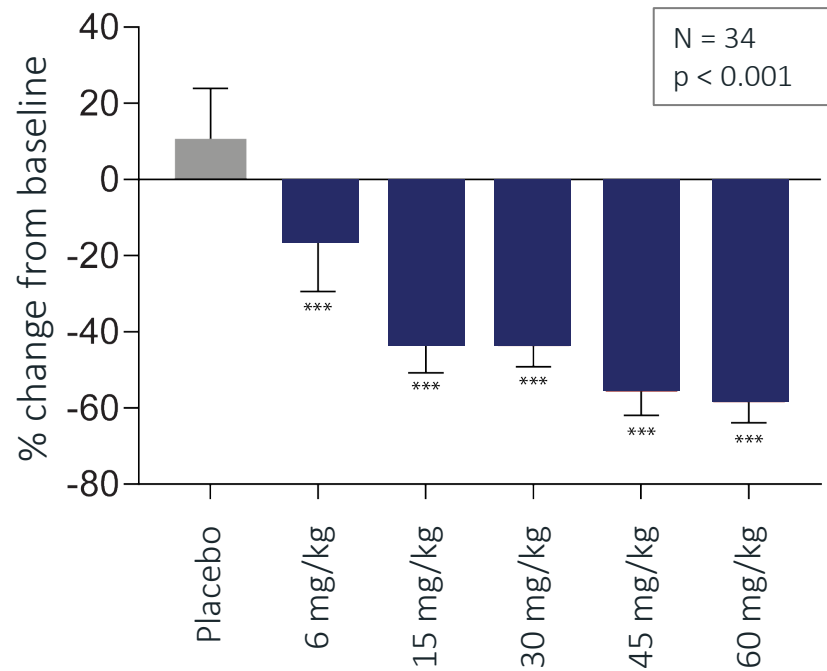


**Intended to improve survival,  
proliferation, function  
of microglia**

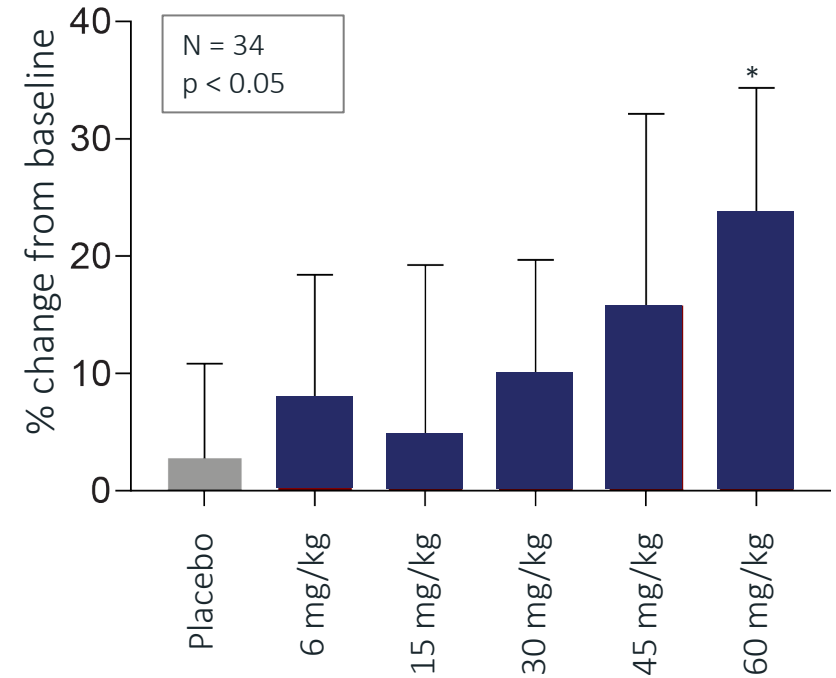
# AL002 target and microglia engagement achieved in Phase 1

Generally well tolerated in healthy volunteers

### Dose-dependent reduction in soluble TREM2

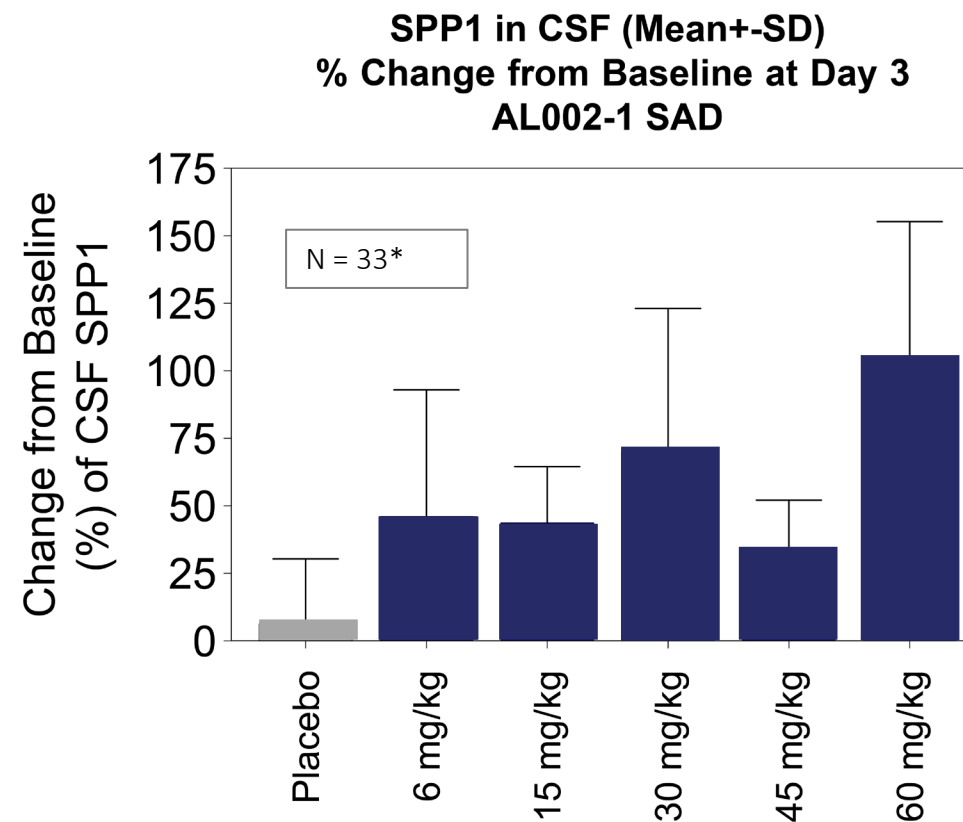
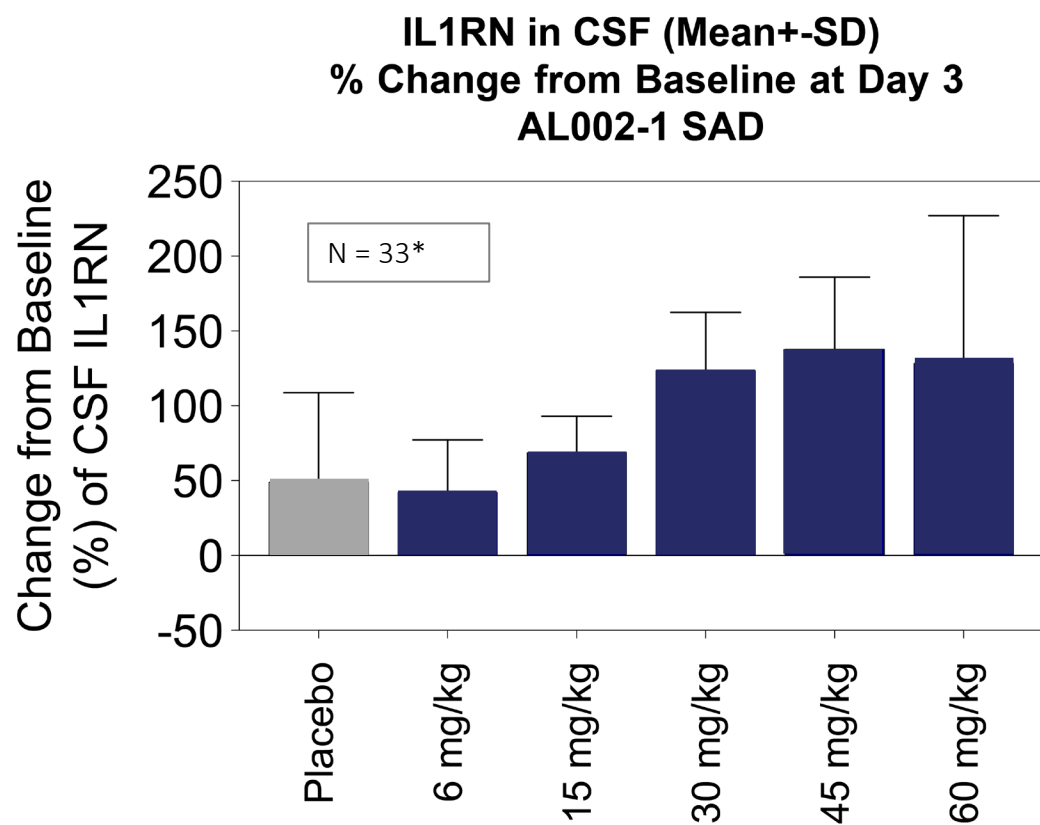


### Dose-dependent elevation in sCSF-1R, associated with microglia activation

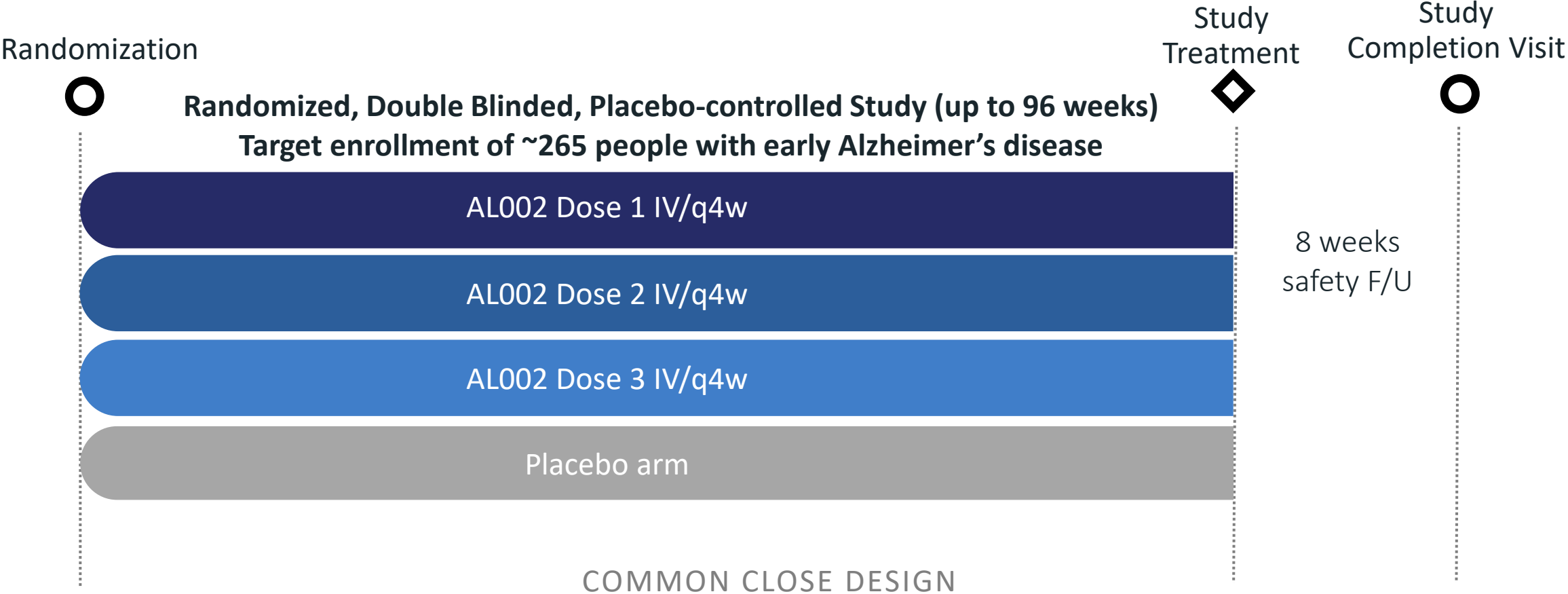




AL002 treatment in Phase 1 also caused an increase in CSF levels of IL1RN and SPP1, indicating further evidence of microglial activation



# INVOKE-2 Phase 2 AL002 study in individuals with early Alzheimer's disease



PRIMARY ENDPOINT: **CDR-SB**

SECONDARY CLINICAL OUTCOME ASSESSMENTS: **RBANS, ADAS-Cog13, ADCS-ADL-MCI**

EXPLORATORY ENDPOINTS: **vMRI, CSF and plasma biomarkers, PET scans**

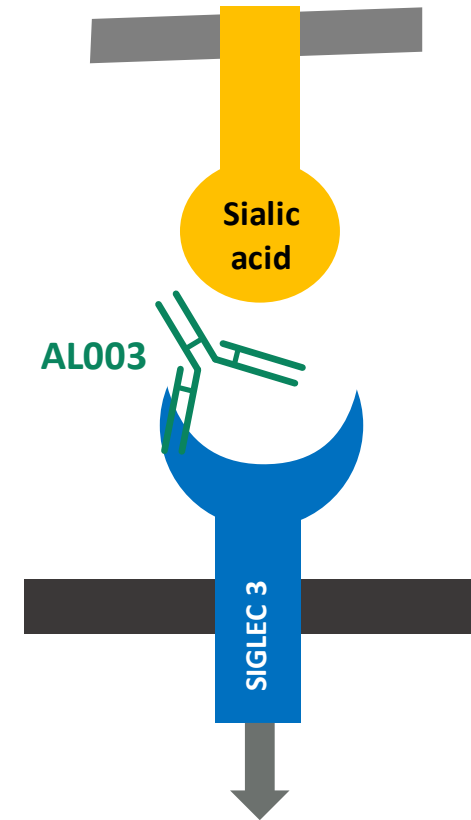
# AL003: Increase activity of microglia by blocking Siglec3

## MECHANISM

- AL003 blocks Siglec3 (CD33), an inhibitory receptor expressed on the microglia to allow immune system to work at full capacity

## STATUS

- Phase 1 study in healthy volunteers and Alzheimer's disease participants complete
- Safety profile supports Phase 2 development

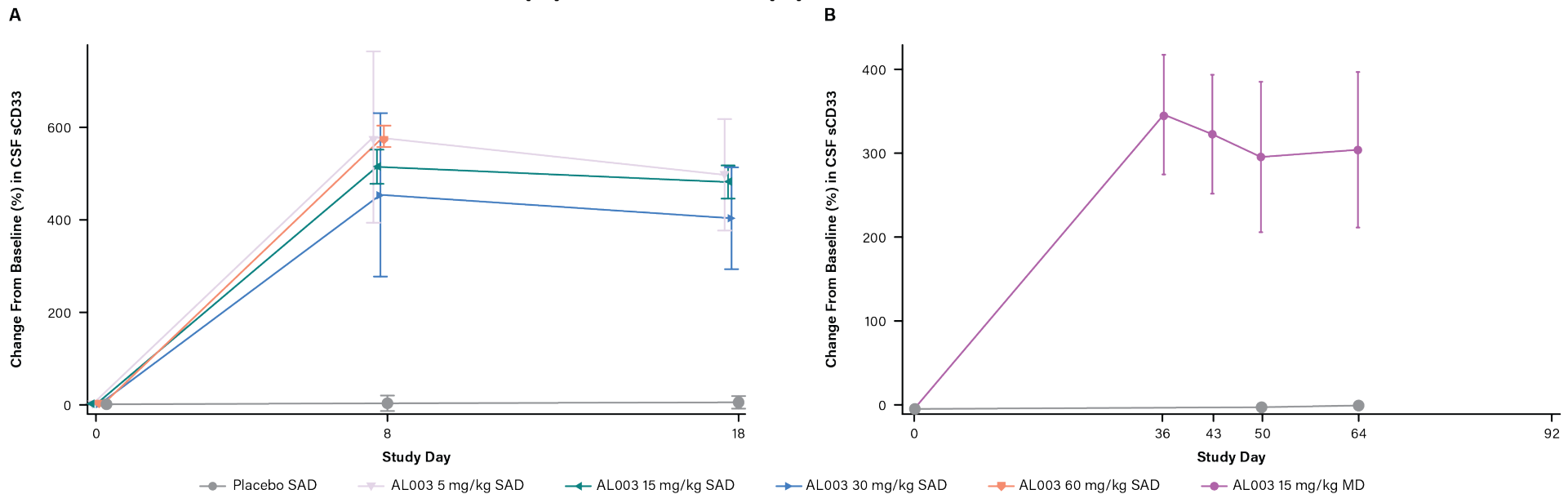


**Intended to increase function  
by releasing inhibition on  
microglia**

# INTERCEPT-1: Phase 1 study of AL003

- Manageable safety profile observed in healthy volunteers (N= 29) and patients with Alzheimer’s disease (N=10) up to and including doses of 15 mg/kg
- Target engagement demonstrated in both blood and CNS compartments across the tolerated dose range

**Mean (SD) Percentage Change From Baseline in CSF Concentration of sCD33 for (A) SAD HVs and (B) MD Patients with AD**



Safety profile and evidence of CD33 target engagement support further clinical development

Preclinical Alzheimer's disease program:

AL044

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# MS4A: A predictive risk gene for Alzheimer's disease

- MS4A are multi-transmembrane proteins expressed on microglia and macrophages that regulate their function
- MS4A controls levels of soluble TREM2 in the CNS
- MS4A impacts both disease initiation and disease progression

The MS4A **protective allele** is associated with increased TREM2 protein levels in the CSF

MS4A **risk variants** increase risks for Alzheimer's disease, younger age of onset, faster rates of disease progression and decreased survival

## Effects of MS4A variants on Alzheimer's disease

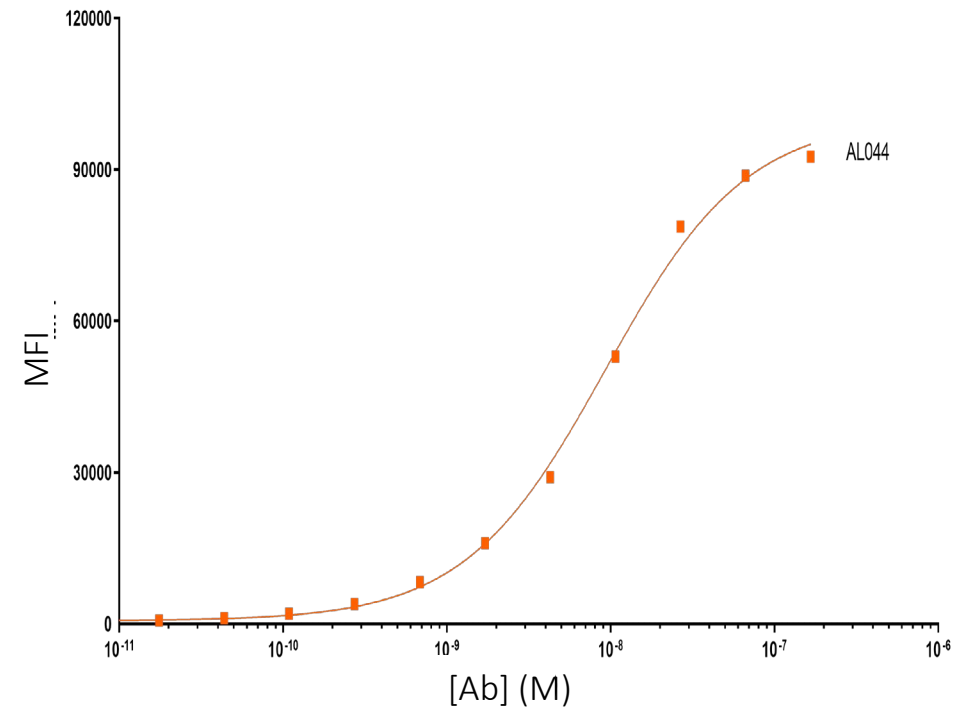
MS4A Protective allele		MS4A Risk allele
↓	Alzheimer's risk (~10%)	↑
↑	Age of onset	↓
↑	Survival	↓
↑	sTREM2 in CSF (~ 20%)	↓

# AL044: Activating the microglia to protect against Alzheimer's disease

- AL044 is designed to functionally convert the risk variants of MS4A to the protective variant
- In preclinical studies, AL044:
  - Mimics and exceeds the beneficial activities of the protective MS4A variant
  - Increases soluble TREM2 *in vitro* and *in vivo*
  - Induces microglia survival, proliferation and functionality

Advancing into Phase 1 clinical trial in 2022

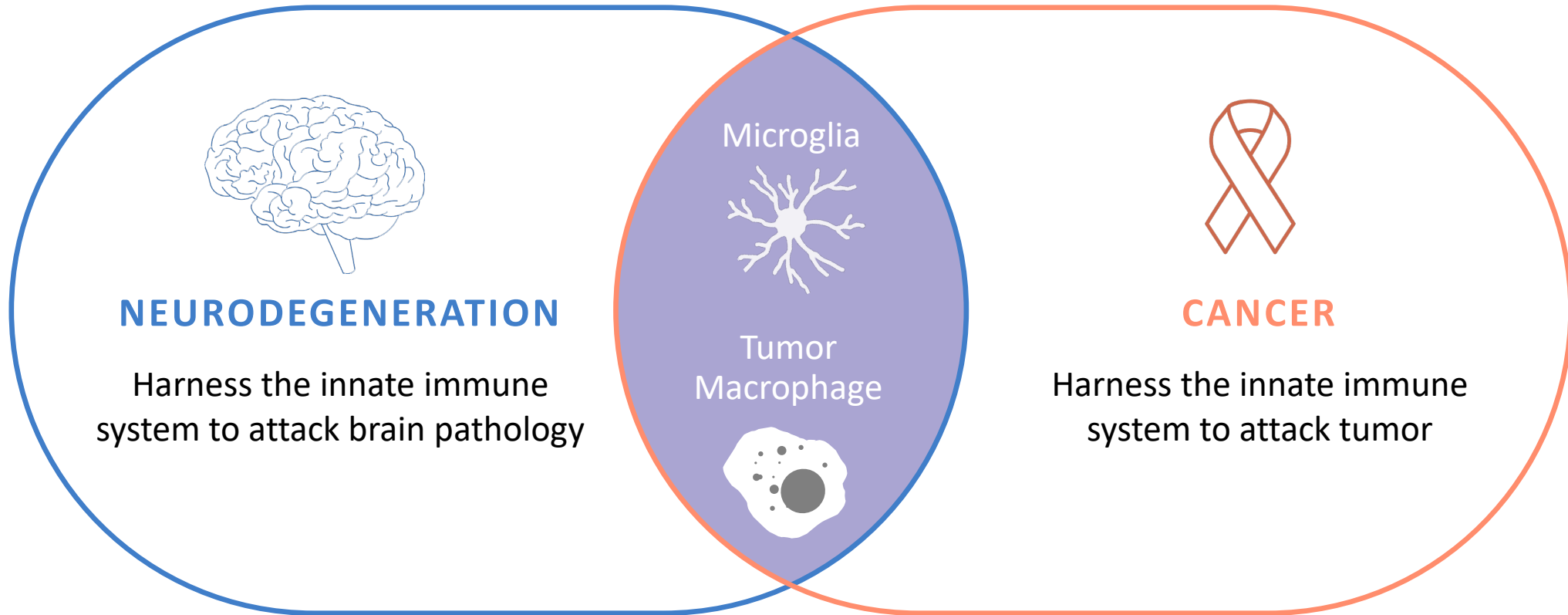
High affinity binding of AL044 to cells expressing MS4A



# Alector Oncology Overview

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# Neurodegeneration and cancer converge at the innate immune system



# AL008: Potential best-in-class dual function SIRP $\alpha$ -CD47 pathway activator

## TARGET

SIRP $\alpha$  - CD47 pathway

## SCIENTIFIC RATIONALE

Tumors leverage pathway to hide from immune system

## STATUS

FiH expected in 2022 in China

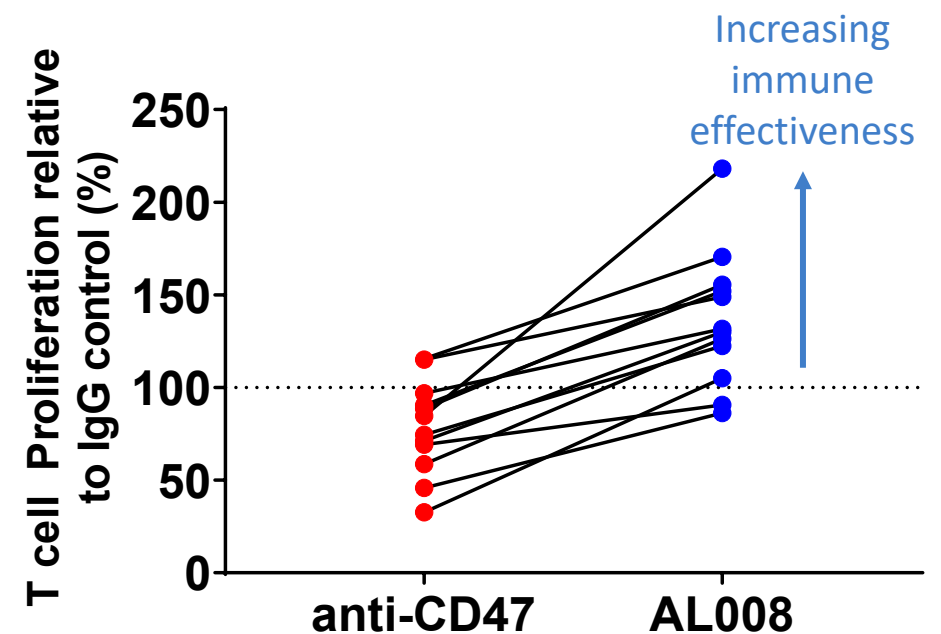
## PRODUCT CANDIDATE

- Selectively binds to multiple SIRP $\alpha$  variants
- Does not inhibit T-cell activator SIRP $\gamma$

## PRECLINICAL ACTIVITY

- Promotes T-cell proliferation more effectively than anti-CD47
- Demonstrates robust anti-tumor activity in multiple models (single agent and with checkpoint inhibitors)
- No decrease in red blood cells or platelets

## Anti-CD47 reduced T-cell activation



# AL009: Marshalling the innate immune system to combat tumor growth

## TARGET

Siglec-Sialic acid innate checkpoint pathway

## SCIENTIFIC RATIONALE

Human genetics and tumor model data show Siglecs drive immune suppression

## STATUS

FiH expected in 2022

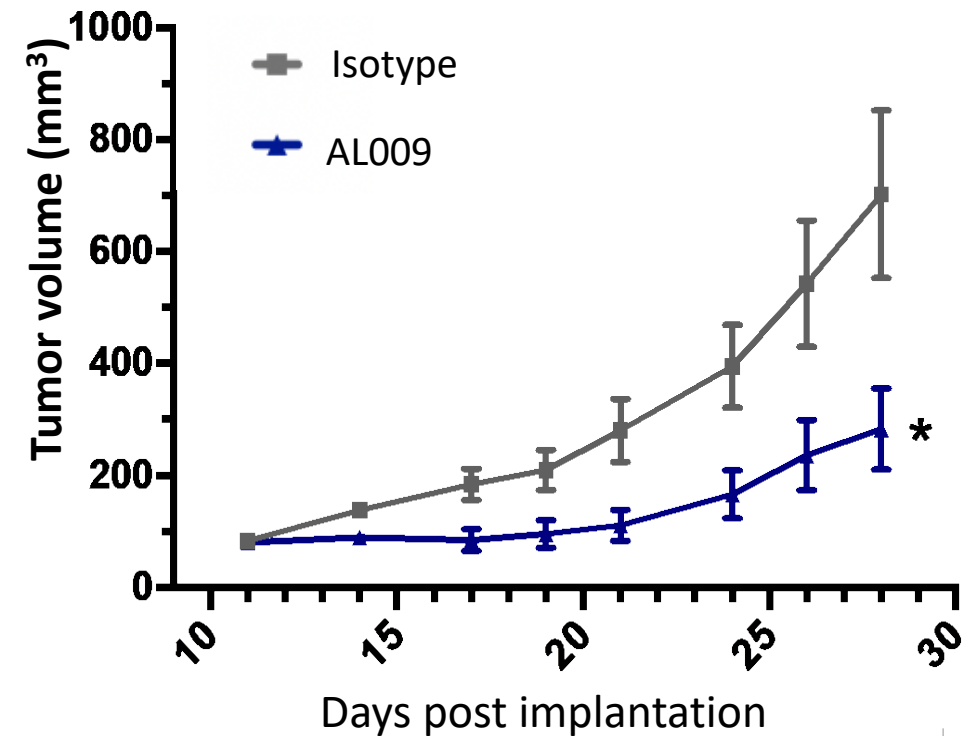
## PRODUCT CANDIDATE

- Engineered Fc fusion protein
- Blocks multiple Siglecs to activate innate and adaptive immunity
- Engages activating Fcγ receptors

## PRECLINICAL ACTIVITY

- Repolarizes suppressive macrophages, activates T cells and enhances ADCC/ADCP function
- Demonstrates robust anti-tumor activity in multiple models (single agent and combined with checkpoint inhibitors)

## Monotherapy activity in breast cancer model








# Summary

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# Partnerships further our reach while preserving control and Alector upside

	KEY TERMS	FINANCIALS	DEAL RATIONALE
 <p><b>July 2021</b></p>	<p><b>Progranulin franchise programs</b></p> <ul style="list-style-type: none"> <li>AL001 and AL101</li> <li>Global co-development</li> <li>Co-commercialization in U.S.</li> <li>Exclusive license to GSK ex- U.S.</li> </ul>	<ul style="list-style-type: none"> <li>\$700M upfront payment</li> <li>\$1.5B+ in milestone payments</li> <li>50-50 U.S. profit share</li> <li>40-60 development cost share Phase 3 and beyond</li> <li>Tiered double-digit royalties ex-U.S.</li> </ul>	<ul style="list-style-type: none"> <li>Enables broader and faster development of AL001 and AL101 in FTD, ALS, Parkinson’s and Alzheimer’s disease; split of roles cater to strengths of each company</li> </ul>
 <p><b>March 2020</b></p>	<p><b>CD47-SIRP-alpha program</b></p> <ul style="list-style-type: none"> <li>Regional licensing agreement</li> <li>Innovent to develop and commercialize AL008 in China</li> <li>Alector retains rights for rest of the world</li> </ul>	<ul style="list-style-type: none"> <li>Undisclosed</li> </ul>	<ul style="list-style-type: none"> <li>Advances AL008 into the clinic in solid tumors to generate early PoC data at no cost to Alector</li> </ul>
 <p><b>October 2017</b></p>	<p><b>TREM2 and SIGLEC3 programs</b></p> <ul style="list-style-type: none"> <li>AL002 and AL003</li> <li>Abbvie will lead development and commercialization activities following (post Phase 2) opt-in</li> </ul>	<ul style="list-style-type: none"> <li>\$205M upfront payment</li> <li>\$20M equity investment</li> <li>\$986M milestone payments</li> <li>Global 50-50 profit share</li> </ul>	<ul style="list-style-type: none"> <li>Supported growth of Alector’s global clinical development infrastructure in Alzheimer’s disease</li> <li>Alector maintains significant stake while gaining access to pharma capabilities to support broad indications</li> </ul>

# Experienced leadership and advisors guide clinical and corporate execution

## MANAGEMENT

**Arnon Rosenthal, PhD**  
CEO, Co-founder



**Sara Kenkare-Mitra, Ph.D.**  
President, Head of R&D



**Sam Jackson, MD**  
Interim CMO



**Marc Grasso, MD**  
CFO



**Robert King, PhD**  
CDO



**Brain Sander, PhD**  
General Counsel



**Kristina Vlaovic**  
SVP, Regulatory and Pharmacovigilance



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# OVER \$900 MILLION IN CASH

# Steady progress in advancing our mission

Expect to have 7 programs in the clinic by year-end 2022

## Key 2022 milestones

- 1H: 12-month AL001 in FTD-*C9orf72* to be presented Q1 at ADPD
- 1H: Initiate Phase 1 clinical study of AL008 in China with Innovent in patients with advanced solid tumors
- 2H: Initiate Phase 1 clinical study of AL009 in patients with advanced solid tumors
- 2H: Initiate AL044 Phase 1 clinical study in healthy volunteers
- 2H: Complete Phase 1 clinical study of AL101

### 2013 - 15

- Alector founded
- Immuno-neurology research focus established
- Initial programs underway

### 2016-18

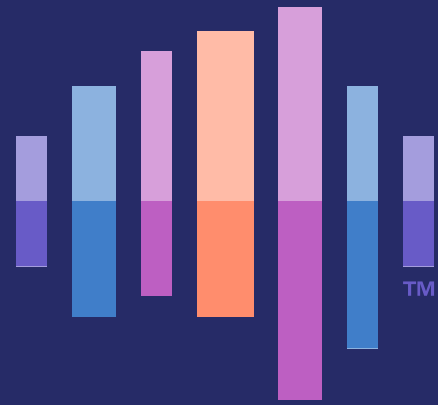
- AL001 and AL002 enter the clinic
- Partnership with Abbvie formed to co-develop AL002 and AL003 for the treatment of Alzheimer's
- Received orphan drug designation for AL001 in FTD

### 2019-2021

- Advanced AL001 into Ph 2 in FTD and ALS; and initiated Ph 3 FTD-*GRN*
- Ph 2 data for AL001 in FTD-*GRN* presented
- AL101 and AL003 enter clinic
- Entered into co-development and co-commercialization partnership with GSK for AL001 and AL101

### A bright future on the horizon

- Pivotal and proof-of-concept data read-outs for current pipeline
- Steady stream of immuno-neurology and immuno-oncology INDs and Phase 1s based on innate immunology expertise
- Establishment of U.S. commercial capabilities



Thank you