Alector Company Overview

August 2022

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 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.

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.

Experienced Leadership and Advisors Guide Clinical and Corporate Execution

MANAGEMENT

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CEO, Co-founder

Sara Kenkare-Mitra, PhD
President, Head of R&D

Gary Romano, MD, PhD
CMO

Peter Heutink, PhD
Incoming CSO

Marc Grasso, MD
CFO

Robert King, PhD
CDO

Kristina Vlaovic
SVP, Regulatory and Pharmacovigilance

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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: *20 issued patents, 450+ patent applications*

MULTIPLE CLINICAL TRIALS

Phase III Clinical Program for FTD-PGRN

Clinical Programs for AD, FTD-GRN, FTD-C9ORF72, ALS

Pre-Clinical Programs for AD, PD, Solid tumors

WORLD CLASS PARTNERS

$700M upfront
$1.5B+ milestone
50-50 U.S. profit share
Tiered double-digit royalties ex-U.S.

gsk

$205M upfront payment
$20M equity investment
$986M milestone payments
Global 50-50 profit share

abbvie

STRONG FINANCIALS

$809 MILLION IN CASH

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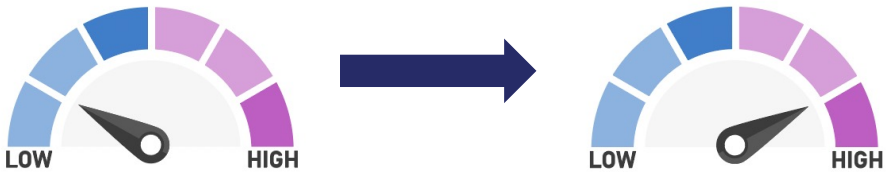
FTD = Frontotemporal dementia, PD = Parkinson's Disease, AD = Alzheimer's Disease, ALS = Amyotrophic lateral sclerosis

Immuno-Neurology: Alector's Therapeutic Strategy for Degenerative Brain Disorders

Recruiting microglia, the brain's immune system, to potentially cure neurodegeneration

Immuno-neurology Therapeutics

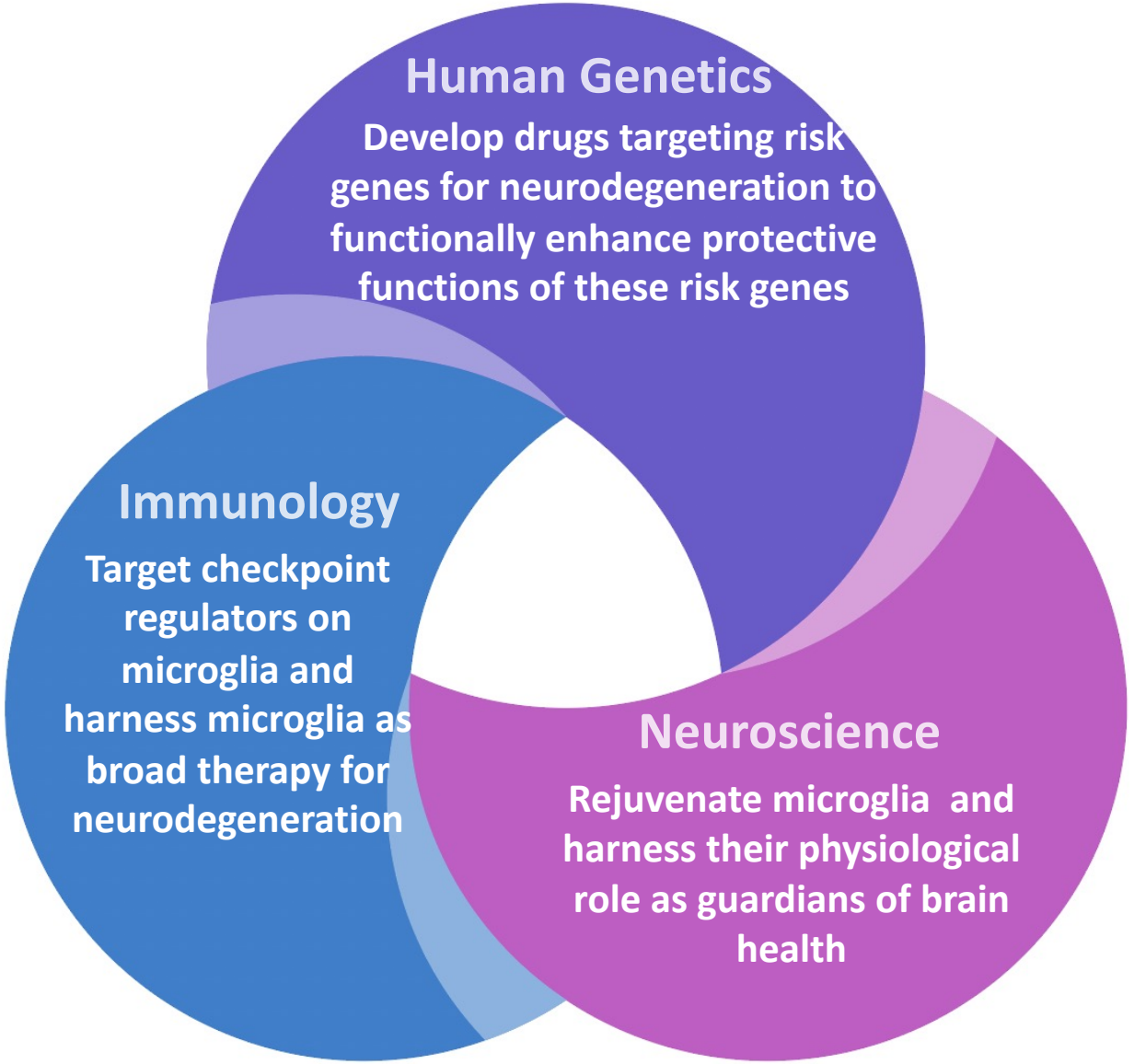


Ineffective and damaging microglia

Effective and beneficial microglia

Using the immuno-oncology concept of harnessing the immune system as a broad, effective and long-lasting therapy

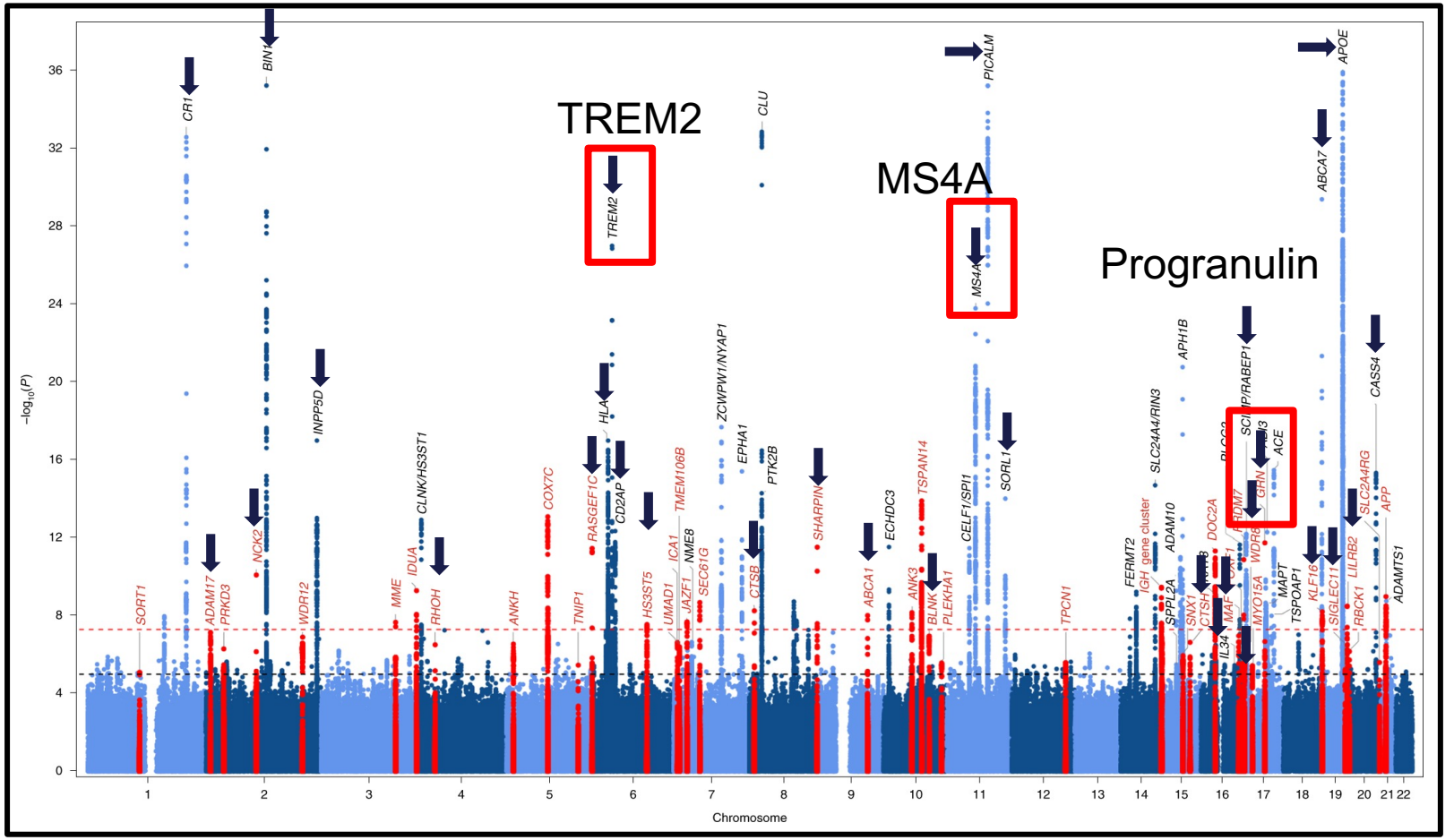
Multiple programs are in or entering the clinic for multiple neurodegenerative diseases



Immuno-neurology: targeting the brain immune system as a novel therapeutic strategy for dementia and neurodegeneration

Genetic Rationale for Immuno-Neurology

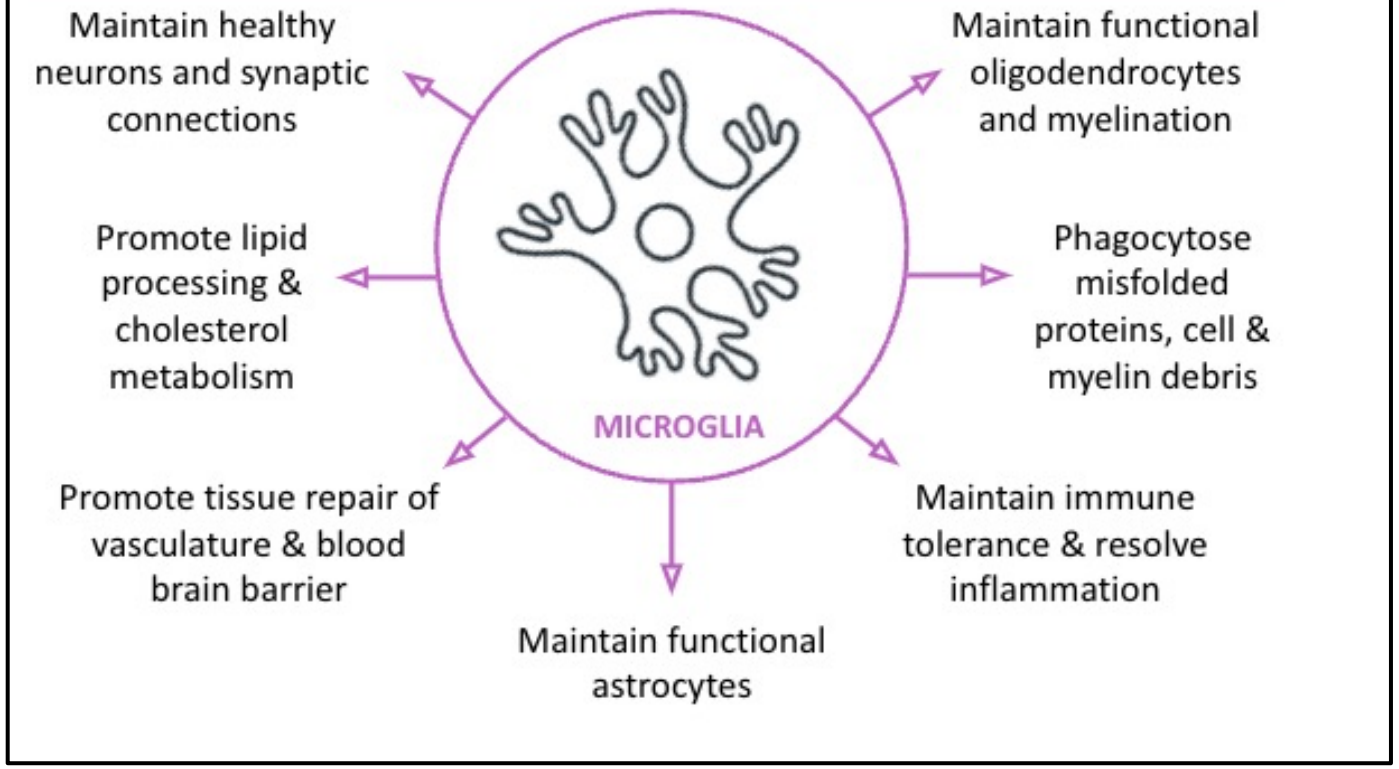
Many AD risk genes are regulators of the microglia brain immune cells
(Arrows in black) Alector's programs are boxed



Bellenguez C et al. *Nat Genet.* 2022; 54(4): 412–36.

Biological Rationale for Immuno-Neurology: The Microglia Brain Immune System is Essential for Brain Function and Health

Microglia are required for maintaining a healthy functional brain throughout life



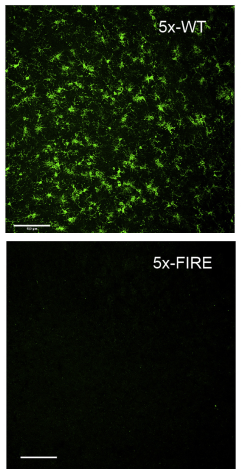
Targeting microglia immune checkpoints and harnessing microglia to cure neurodegeneration

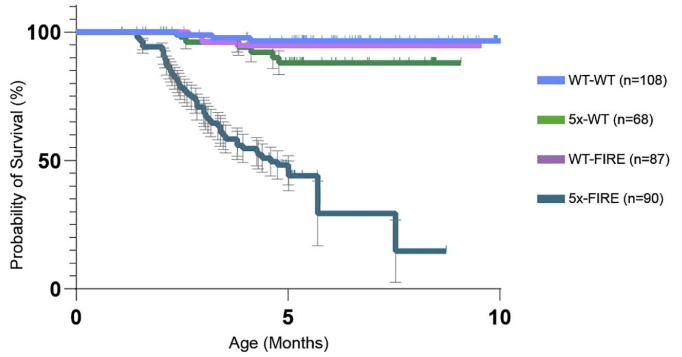
Annotated from Nature Genetics 2019 Mar;51(3):404-413.

Microglia Are Essential for Brain Health in Mouse Models

- "Microglia jointly degrade fibrillar alpha-synuclein cargo by distribution through tunneling nanotubes"[1]
- "Negative feedback control of neuronal activity by microglia"[2]
- Absence of microglia in AD mice lead to cerebral amyloid angiopathy, hemorrhages, calcification, and lethality [3]
- Transplantation of microglia reverses these pathological changes [3]

Short survival without microglia (5x-FIRE)[3]





[1]Scheiblich H et al. *Cell* 2021;184(20):5089-106.e21. [2]Badimon A et al. *Nature* 2020;586(7829):417-23. [3]Shabestari SK et al. *Cell Rep.* 2022;39(11):110961.

Microglia Are Essential for Brain Health in Humans

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

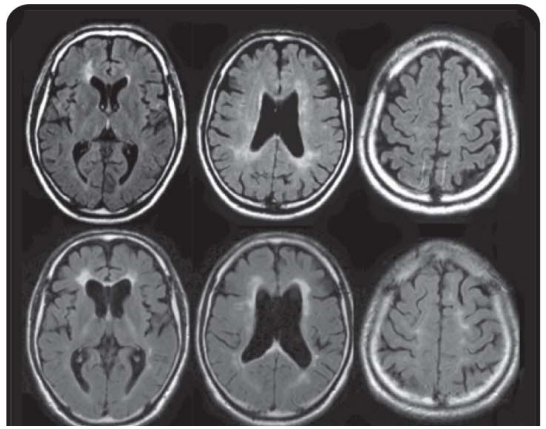
Patients experience range of psychiatric, neurocognitive, and motor symptoms; Average age of onset is ~43

Rapid brain tissue loss

Patient VI
(c.2442+1G>T)

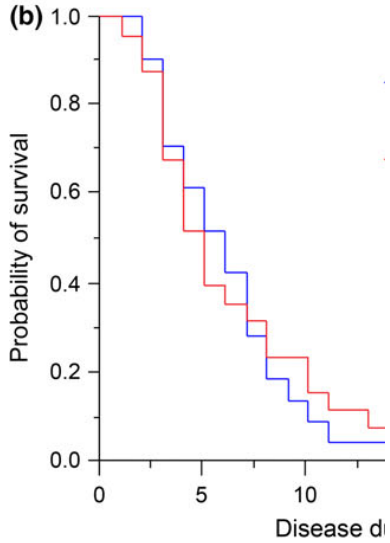
48 yo
5 Years before onset

54 yo
1 Year after onset

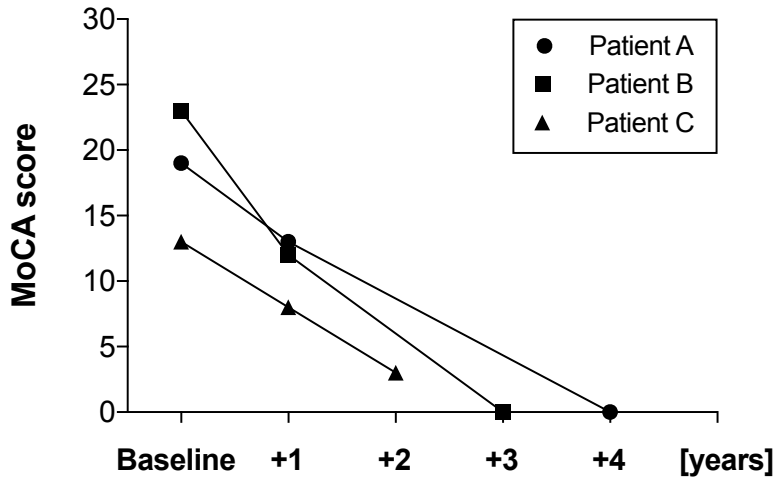


MRI shows brain ventricles dilation

~ 6 Year Survival Rate



Rapid Cognitive Decline



Konno T et al. *Neurology* 2014;82(2):139-48. Konno T et al. *Eur J Neurol*. 2017;24(1):37-45

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*					gsk
		AL001	ALS*					gsk
		AL101	Healthy volunteers for AD and PD					gsk
Alzheimer Programs	**TREM2**	**AL002**	Alzheimer's disease					abbvie
	MS4A	**AL044**	Alzheimer's disease					
		AL044	Orphan neuro indication					
Oncology Programs	**SIRP-alpha**	**AL008**	Solid tumors					
	Multi-Siglec	**AL009**	Solid tumors					
Target indications include ***AD, PD, FTD, MS & cancer***		**12+ programs**						

IP portfolio contains 50+ patent application families, which include 20 issued patents and >450 pending patent applications directed to more than 20 targets and/or technologies

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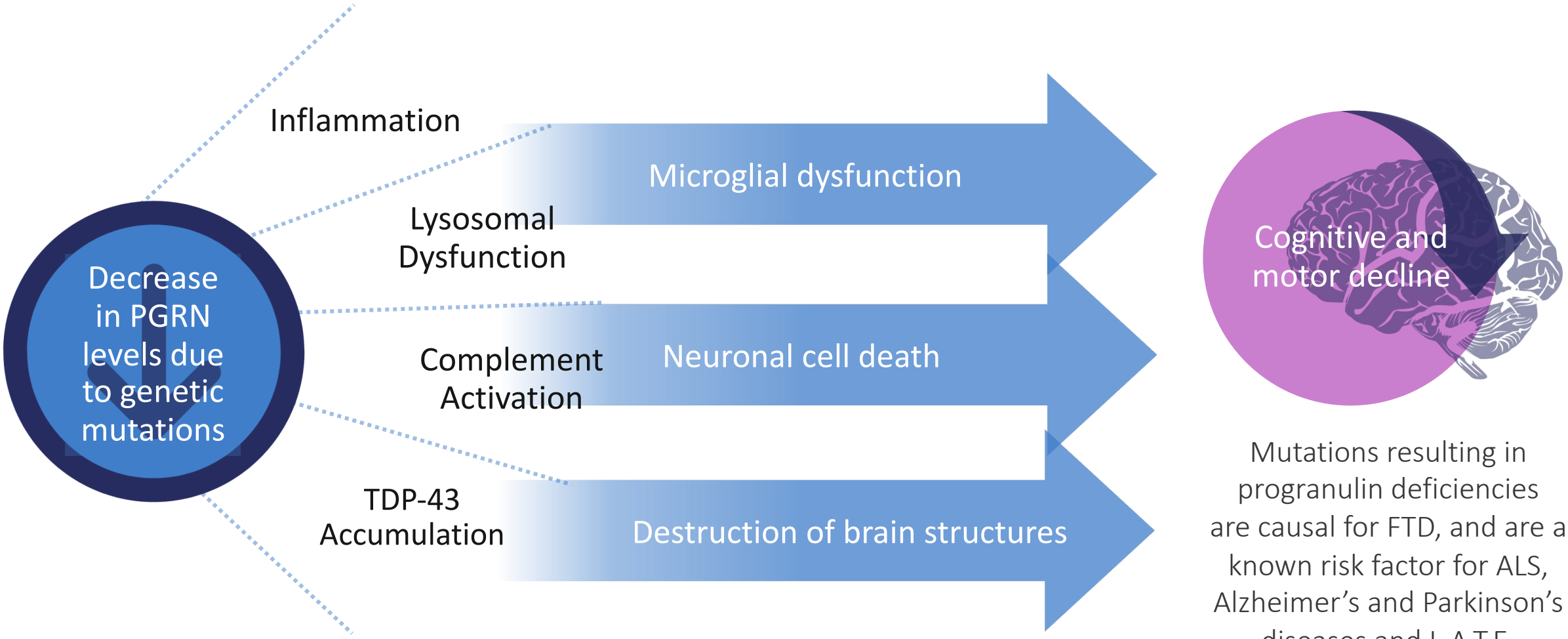
AD = Alzheimer's disease
PD = Parkinson's disease
FTD = Frontotemporal dementia
ALS = Amyotrophic lateral sclerosis
MS = Multiple sclerosis

**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 potential Phase 2b study for patients with all forms of ALS, including the C9orf72 mutation.*

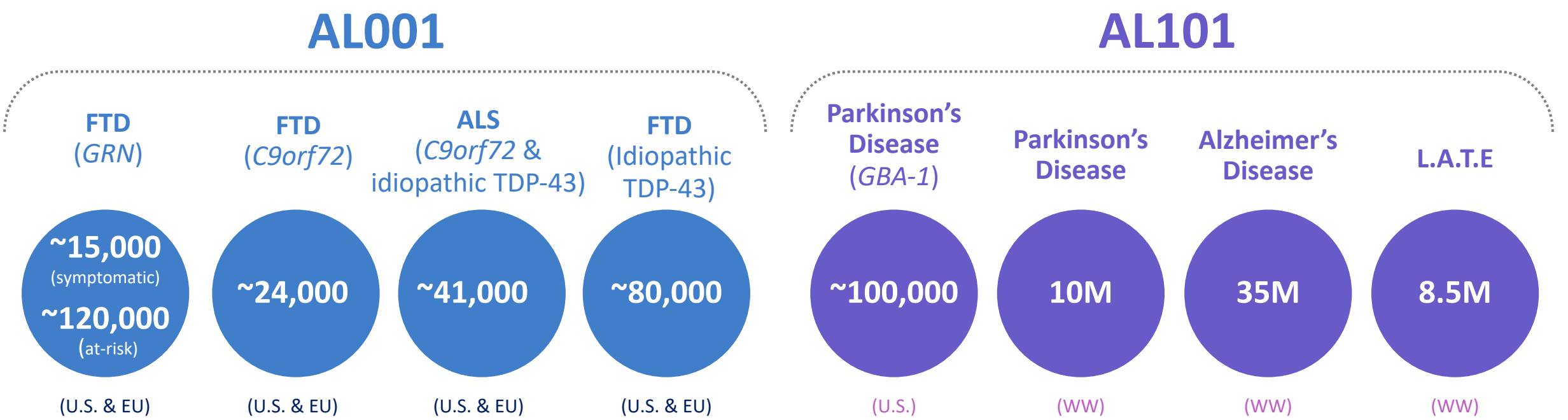
Progranulin Franchise Programs
AL001 / AL101

The Role of Progranulin in Neurodegeneration



Mutations resulting in progranulin deficiencies are causal for FTD, and are a known risk factor for ALS, Alzheimer's and Parkinson's diseases and L.A.T.E.

Broad Therapeutic Potential Grounded in Genetic Evidence and Animal Models



FTD = Frontotemporal dementia
ALS = Amyotrophic lateral sclerosis
L.A.T.E. = Limbic-predominant age-associated TDP43 encephalopathy

AL001 and AL101: Targeting Progranulin to Restore Function of Microglia

MECHANISM

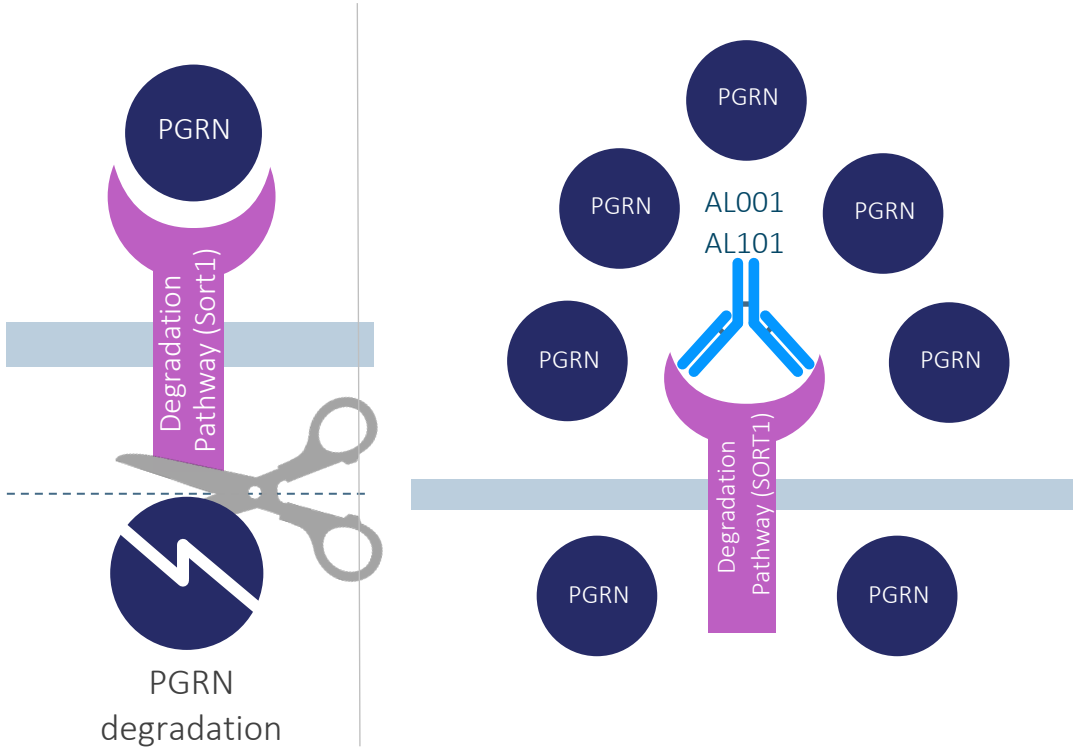
Increases the half-life of PGRN by blocking Sortilin, a degradation receptor, in order to restore PGRN to normal levels

AL001 STATUS

- Orphan Drug and Fast Track Designation
- Phase 1 studies in healthy volunteers complete
- Data presented from ongoing Phase 2 study in FTD-*GRN* and FTD-*C9orf72*
- Currently evaluating study design options for Phase 2b study in patients with all forms of ALS, including the *C9orf72* mutation
- Pivotal Phase 3 study in FTD-*GRN* actively enrolling

AL101 STATUS

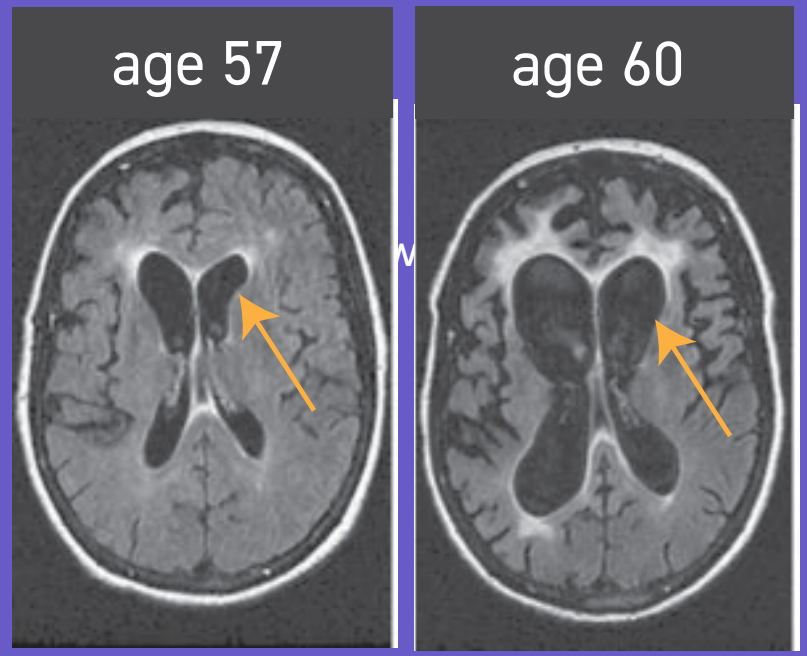
- Ongoing Phase 1 study in healthy volunteers



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*[1]
N = 5
AL001 60 mg/kg q4w for 96 weeks

Symptomatic FTD-*GRN*[1]
N = 12
AL001 60 mg/kg q4w for 96 weeks

Symptomatic FTD-*C9orf72*[1]
N = up to 20
AL001 60 mg/kg q4w for 96 weeks

PRIMARY ENDPOINT

Safety and Tolerability

SECONDARY ENDPOINT

PK, PD

EXPLORATORY ENDPOINTS

CSF and Plasma Biomarkers

Clinical Outcome Assessment (CDR® plus NACC FTLD-SB2)

Volumetric MRI (vMRI)

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

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)

Latozinemab Impacts Key Markers of the Disease Cascade in Symptomatic FTD-GRN Patients

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	Complement activation	Astrogliosis	Neuronal health	Clinical Outcome Assessments
PGRN	**e.g. CTSD, LAMP1**	**e.g. C1QB**	**GFAP**	**NfL**	**CDR® plus NACC FTLD-SB**
> 50% reduction in PGRN levels causal for FTD	Dysfunctional lysosomes are hallmark of FTD-*GRN*	Pathological increases in complement proteins in FTD correlate with cognitive decline	GFAP is increased in conditions characterized by astrogliosis	NfL is a measure of axonal damage	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
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)

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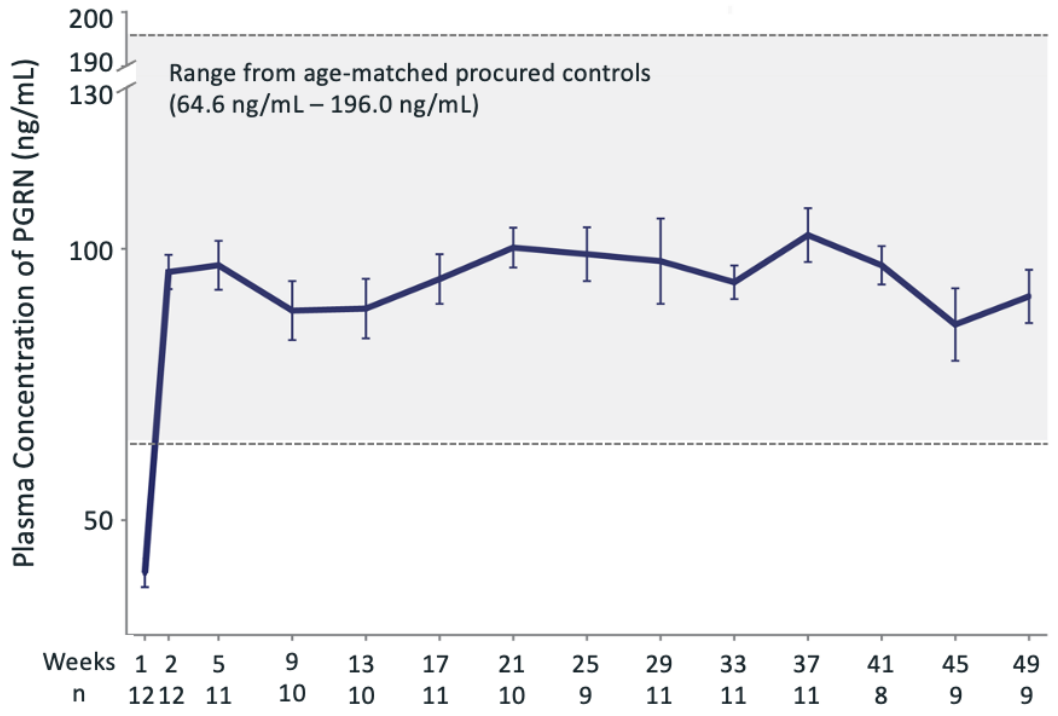
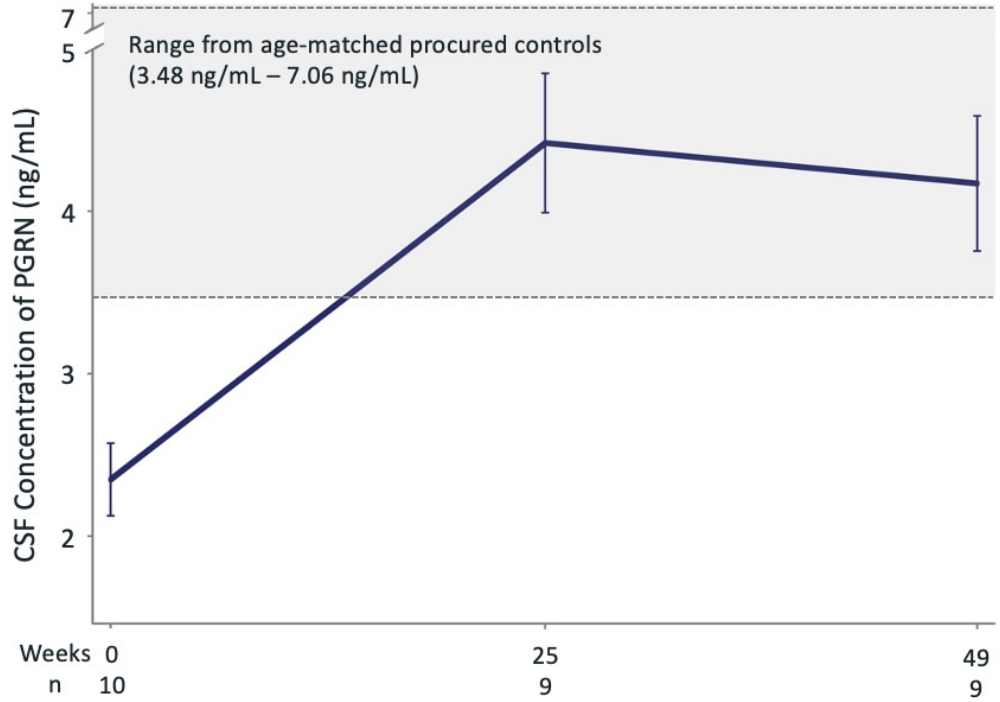
INFRONT-2: AL001 Restores PGRN in Plasma and CSF to Normal Levels

TARGET ENGAGEMENT

PGRN Plasma Concentration



PGRN CSF Concentration



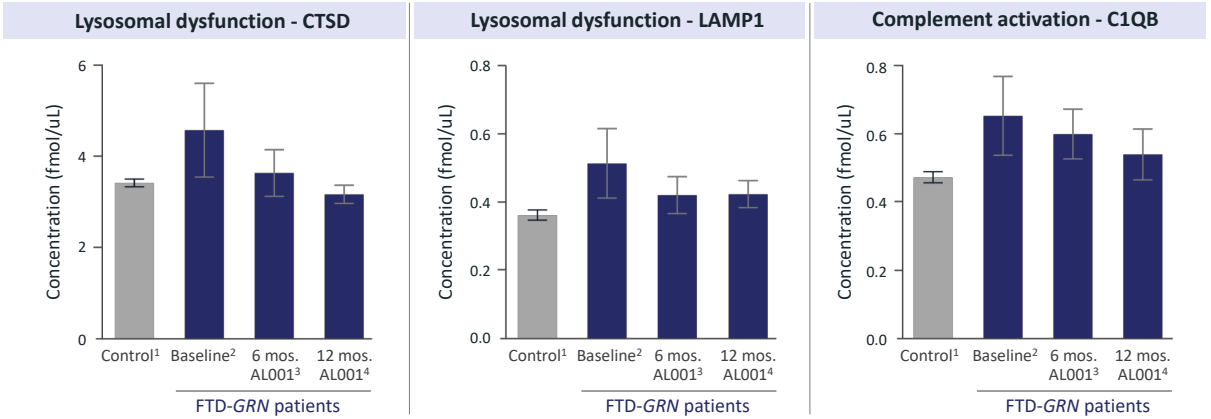
Data cut-off June 15, 2021
Mean +/- SEM

INFRONT-2: Latozinemab Demonstrated Consistent Effects on Disease Biomarkers

FLUID BIOMARKERS OF DISEASE ACTIVITY

Symptomatic FTD-*GRN* patients at 12 months

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)

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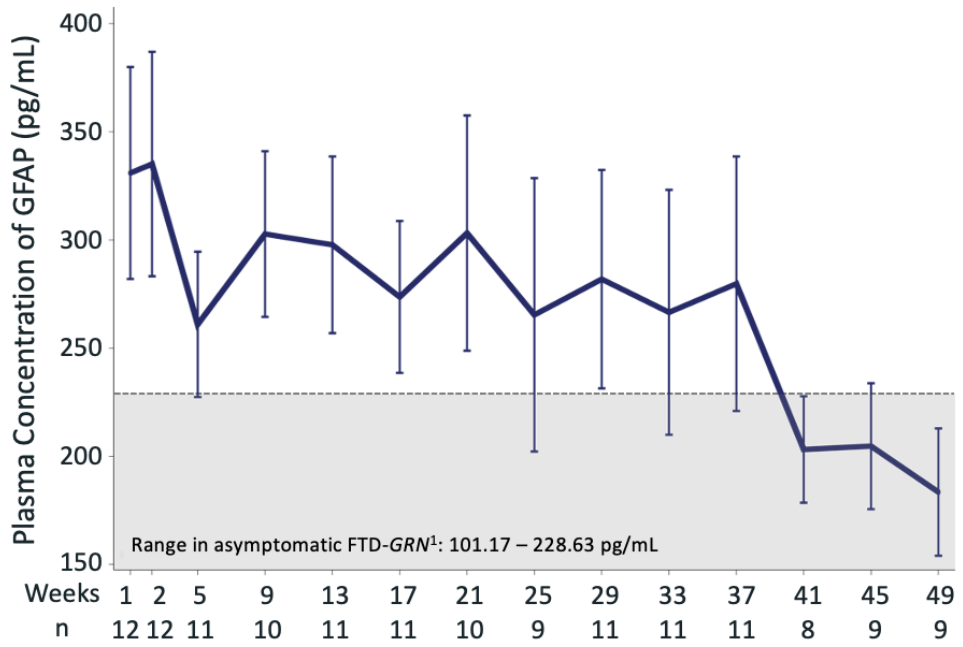
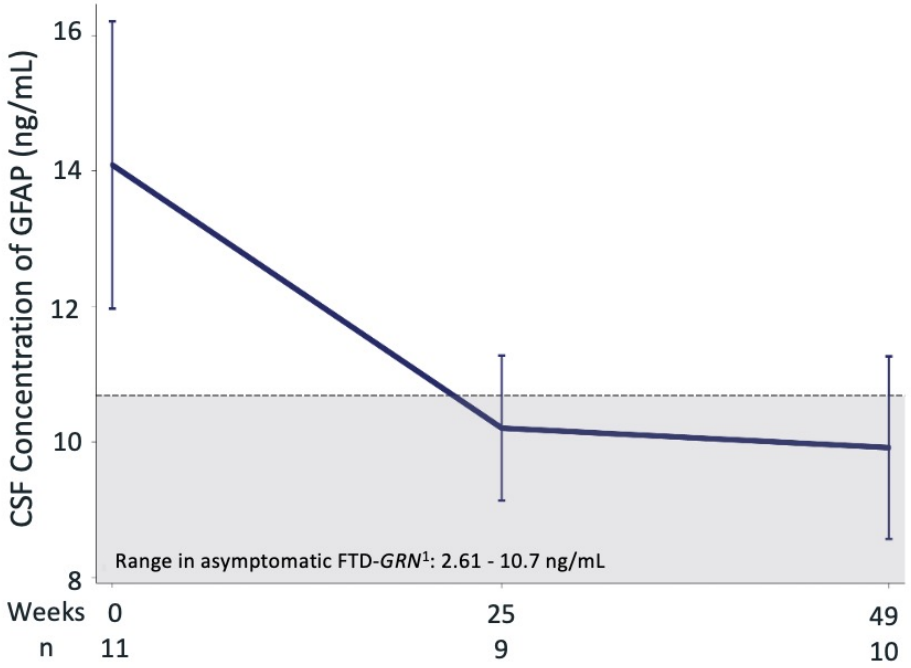
INFRONT-2: AL001 Treatment Decreases Glial Fibrillary Acidic Protein (GFAP) Levels Towards Normal Levels

BIOMARKERS OF DISEASE ACTIVITY – ASTROGLIOSIS

GFAP Plasma Concentration



GFAP CSF Concentration

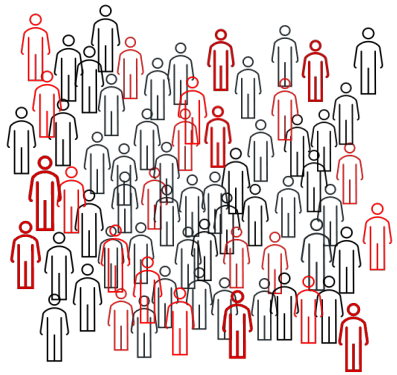


Data cut-off June 15, 2021
Mean +/- SEM
1. Range is of baseline GFAP levels in asymptomatic FTD-GRN patients enrolled in INFRONT-2

INFRONT-2: A two-step Matching Strategy to Eliminate Potential Confounding Factors in Constructing the GENFI2 Historical Control Cohort

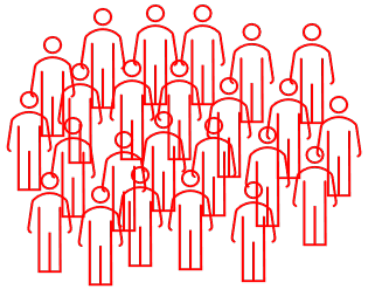
Step 1

GENFI2 FTD-*GRN* participants with at least one post-baseline CDR® plus NACC FTLD-SB (n=102)



Propensity score matching by baseline CDR® plus NACC FTLD-SB

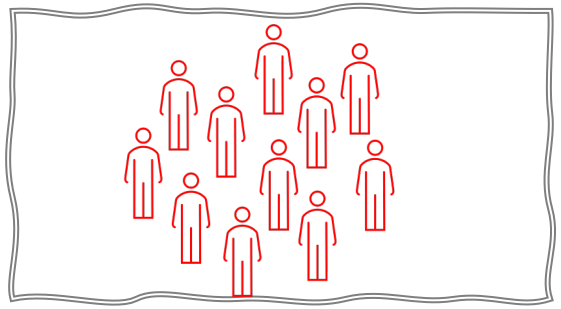
Potential GENFI2 matches using propensity score matching based on CDR® plus NACC FTLD-SB (n=25)



Step 2

Blinded clinical adjudication matching by NfL at baseline, age, diagnosis and gender

GENFI2 matched historical control cohort (n=10)



- Propensity scores were computed using a logistic regression including the most important covariate, cognition, measured at baseline using the CDR® plus NACC FTLD-SB
- Matching was done by comparing the logit propensity score

- To further increase the chances that the matched historical control cohort would mimic a placebo group in a randomized experiment, clinical adjudication of secondary covariates, including NfL at baseline, age, diagnosis and gender were used to refine and construct the final matched historical control cohort
- This step was done on a blinded basis without knowing the progression rate.

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Note: Figures are illustrative - do not correspond to exact patient numbers

INFRONT-2: Contextualizing vMRI and Clinical Results with GENFI2 Matched Controls

- INFRONT-2 vMRI and clinical results compared against comparable, matched GENFI2 controls
- Comparable baseline characteristics established between INFRONT-2 FTD-*GRN* symptomatic cohort and GENFI2 controls in two-steps:
  - Propensity score matching[1] based on CDR® plus NACC FTLD-SB at baseline
  - Matching refined by age, gender, baseline plasma NfL levels, and FTD disease variant at baseline[2]

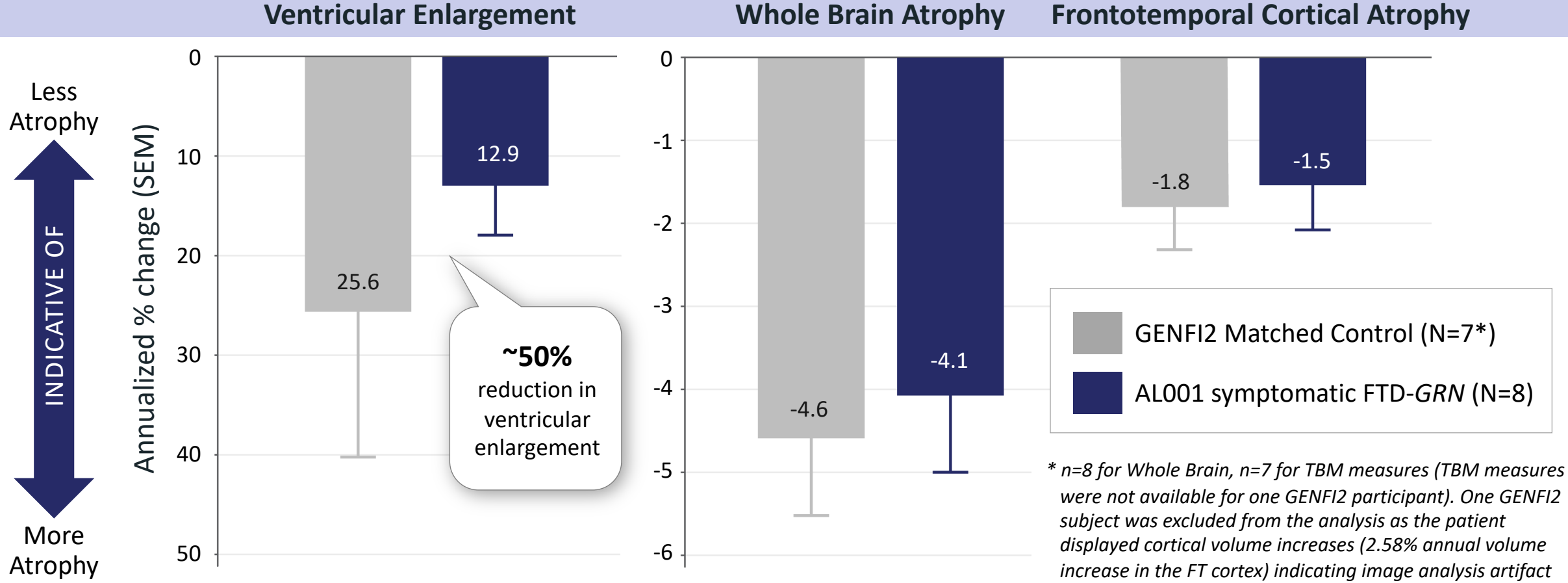
Baseline characteristics		INFRONT-2 (N=12)	GENFI2 Matched Controls (N=10)
CDR® plus NACC FTLD-SB	**Mean (SD)**	**5.9 (3.74)**	**5.2 (3.60)**
	Min, Max	**0.5, 11**	**0.5, 11.5**
AGE (Years)	Mean (SD)	63.2 (9.71)	62.1 (6.74)
	Min, Max	49, 79	52, 72
GENDER	Male	8 (67%)	3 (30%)
PLASMA NfL (pg/mL)	N	12	9
	Mean (SD)	62.8 (47.00)	40.3 (27.28)
	Min, Max	11.2, 148.8	9.3, 99.9
FTD DISEASE VARIANT	bvFTD	5 (42%)	5 (50%)
	PPA	3 (25%)	3 (30%)
	Both	3 (25%)	0
	Other	1 (8%)	1 (10%)

GENFI = The Genetic Frontotemporal Initiative
GENFI2 refers to the longitudinal FTD registry dataset
1. Propensity score matching is a well-established statistical method intended to mimic randomization
2. Clinical reviewers blinded to outcome data

alector

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

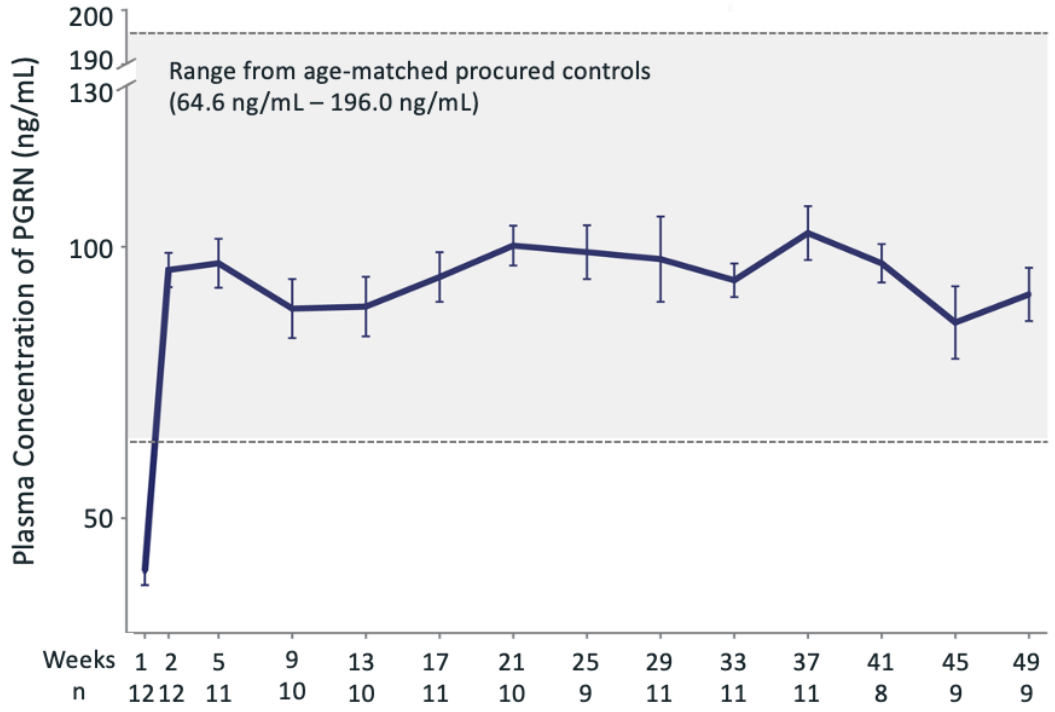


** n=8 for Whole Brain, n=7 for TBM measures (TBM measures were not available for one GENFI2 participant). One GENFI2 subject was excluded from the analysis as the patient displayed cortical volume increases (2.58% annual volume increase in the FT cortex) indicating image analysis artifact*

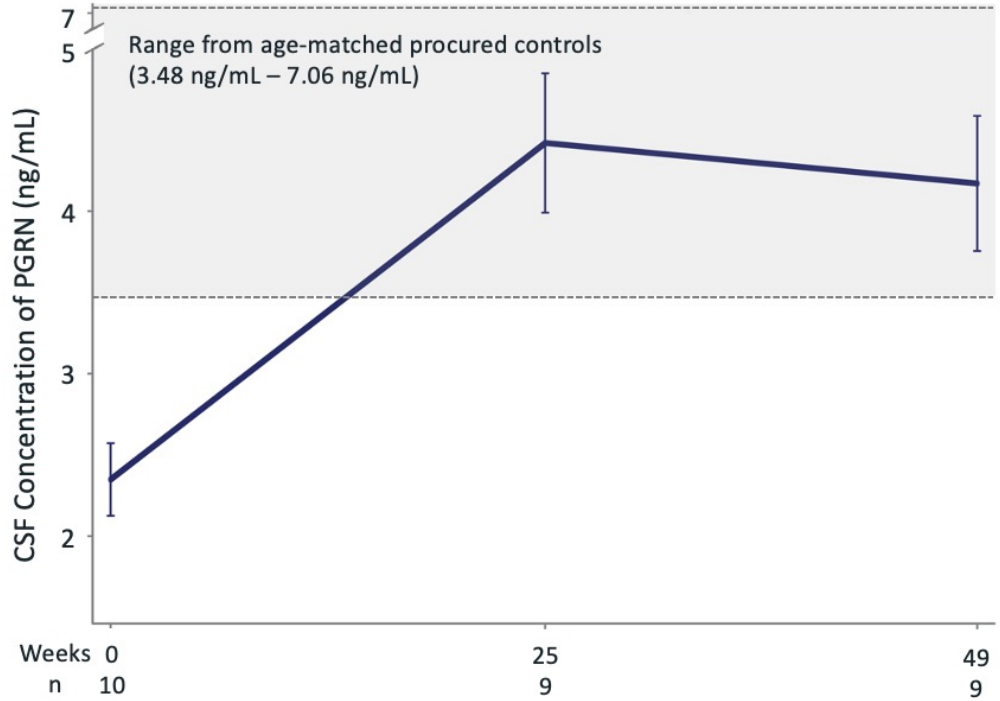
INFRONT-2: Al001 Restores PGRN in Plasma and CSF to Normal Levels

TARGET ENGAGEMENT

PGRN Plasma Concentration



PGRN CSF Concentration



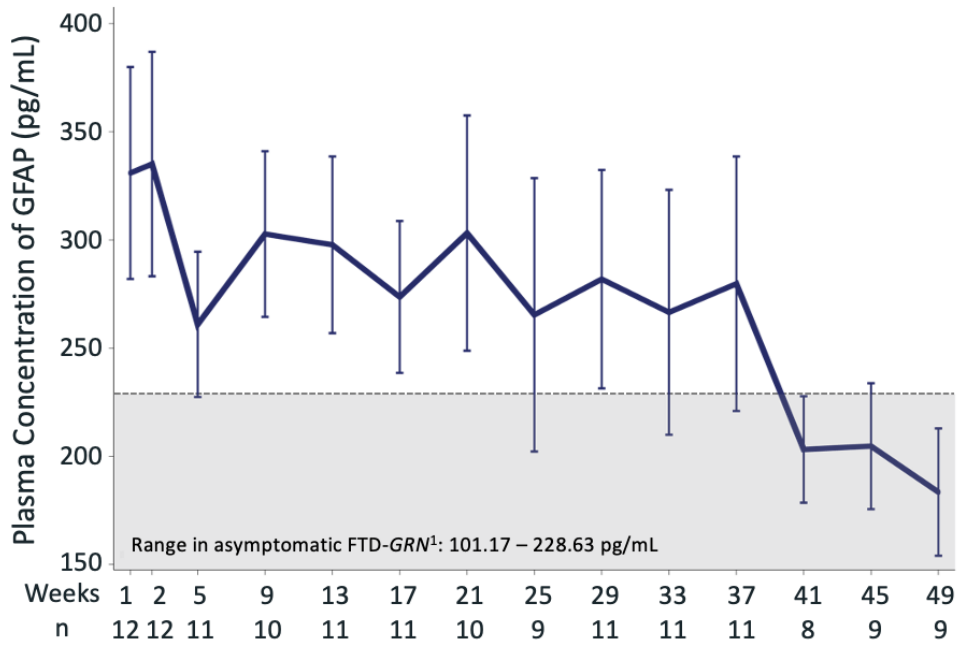
Data cut-off June 15, 2021
Error bars represent mean +/- SEM
Phase 2 data presented at CTAD 2021
NCT03987295

Add after current slide 23

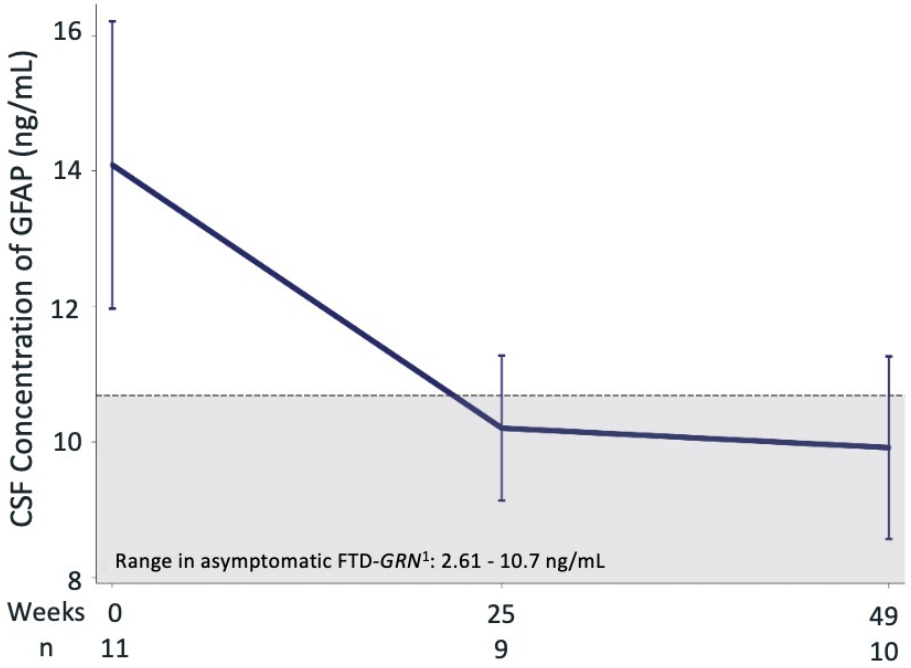
INFRONT-2: AL001 Treatment Decreases Glial Fibrillary Acidic Protein (GFAP) Levels Towards Normal Levels

BIOMARKERS OF DISEASE ACTIVITY – ASTROGLIOSIS

GFAP Plasma Concentration



GFAP CSF Concentration



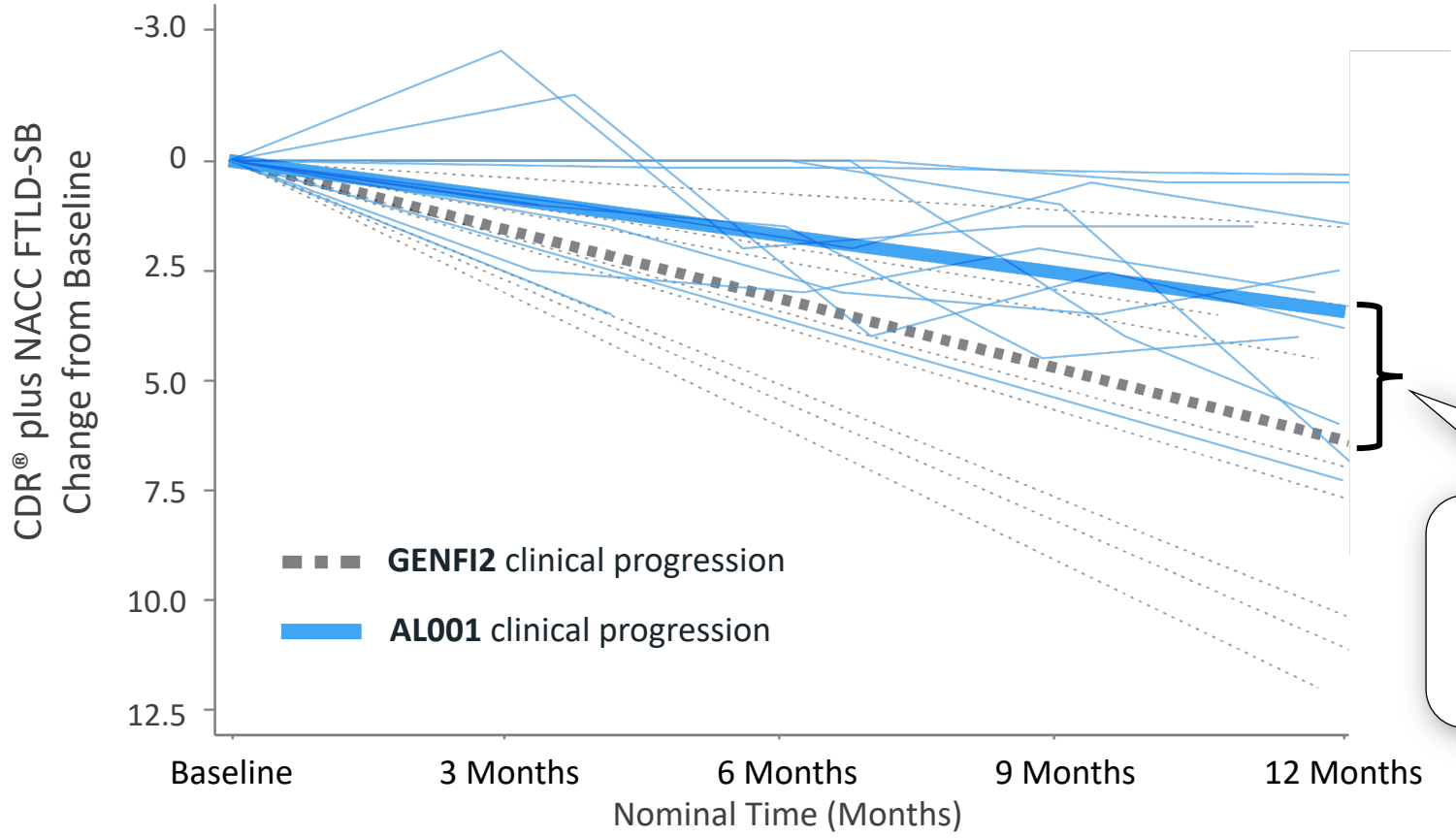
Data cut-off June 15, 2021
Error bars represent mean +/- SEM
[1]Range is of baseline GFAP levels in asymptomatic FTD-GRN patients enrolled in INFRONT-2
Phase 2 data presented at CTAD 2021
NCT03987295

Latozinemab-Treated FTD-GRN Parcipipants Experience a ~48% Annual Delay in Disease Progression Compared to Matched Historical Controls

Similar findings of ~54% delay in disease progression for C9-orf72 FTD patients: Latozinemab was well tolerated in INFRONT-2

CLINICAL BENEFIT

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 **AL001** (n=12)	3.3	[1.38,5.28]
Difference in Annual Change (GENFI2 – AL001)	**3.1**	**[0.24,5.88]**

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

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

Enrollment Ongoing for Pivotal INFRONT-3 Phase 3 Study of AL001

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 approximately 45 clinical centers in US, Canada, Europe and Australia

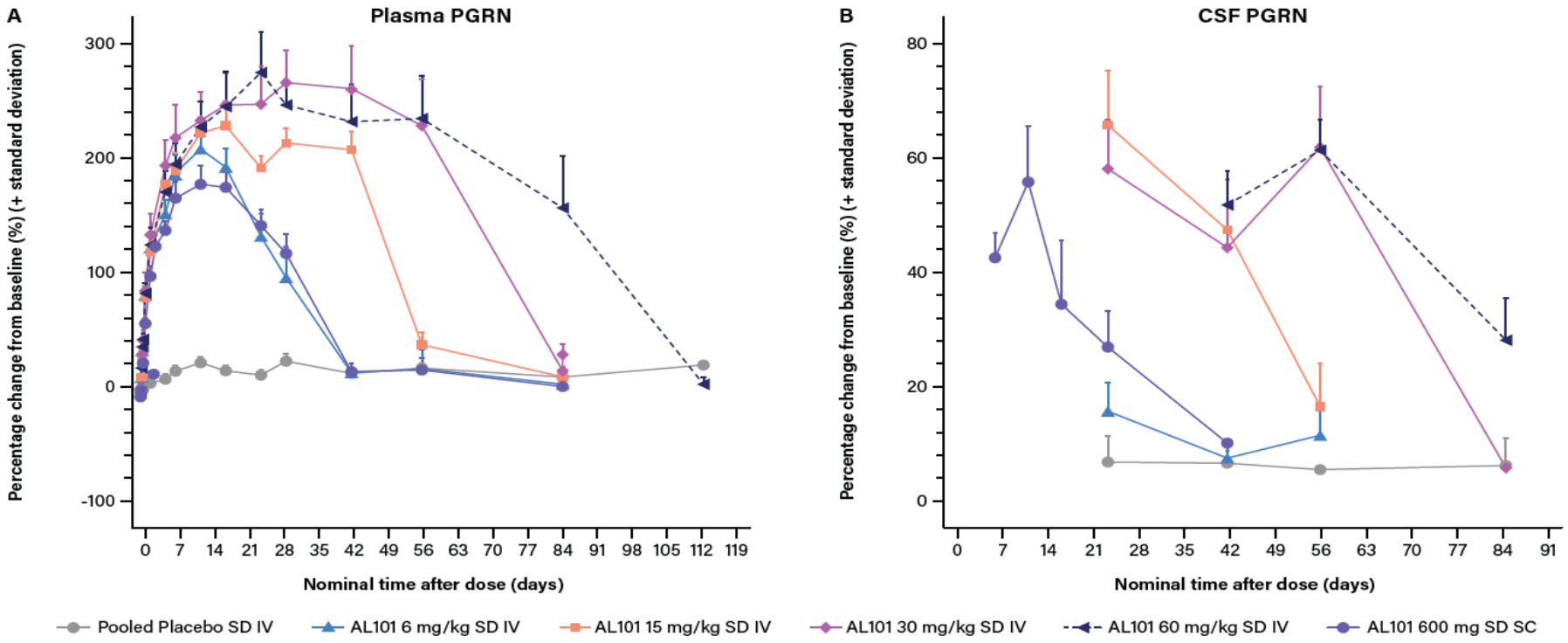
Initial data read out after 96-week treatment period

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

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 Candidate: AL002

AL002: Designed to Activate TREM2 in Order to Enhance Microglia Function

RATIONALE

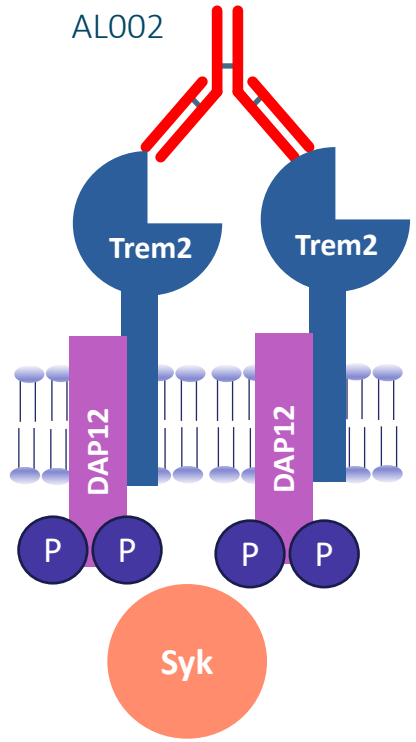
- TREM2 signaling controls critical microglial activity
- TREM2 is a prominent risk gene for Alzheimer's disease
  - Homozygous mutations cause dementia (NHD, FTD)
  - Heterozygous mutations increase risk for Alzheimer's disease by 3x
  - Ligands include APOE, an Alzheimer's risk gene

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

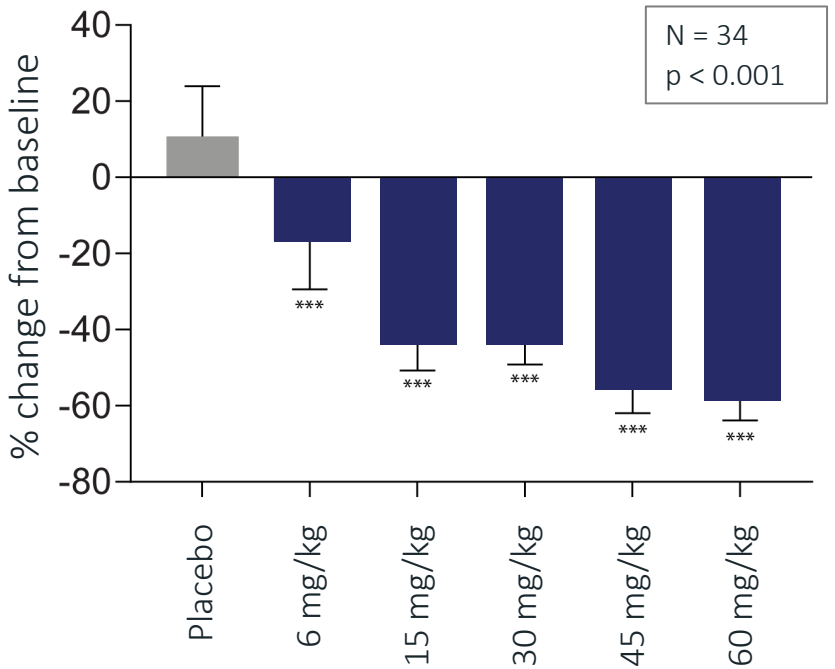


Intended to improve survival, proliferation, function of microglia

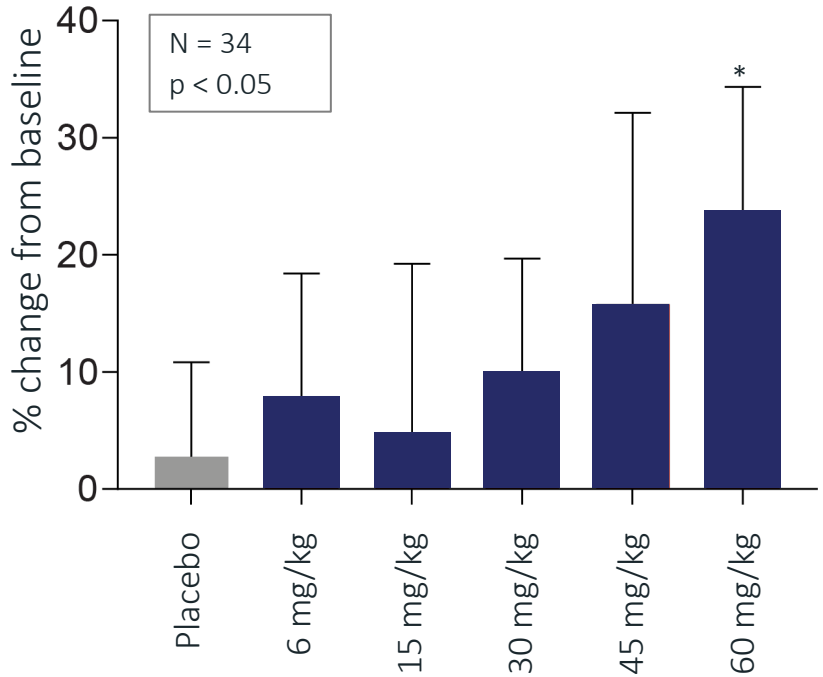
AL002 Target and Microglia Engagement Achieved in Phase 1

Generally well-tolerated in healthy volunteers[1]

Dose-Dependent Reduction in Soluble TREM2[2]

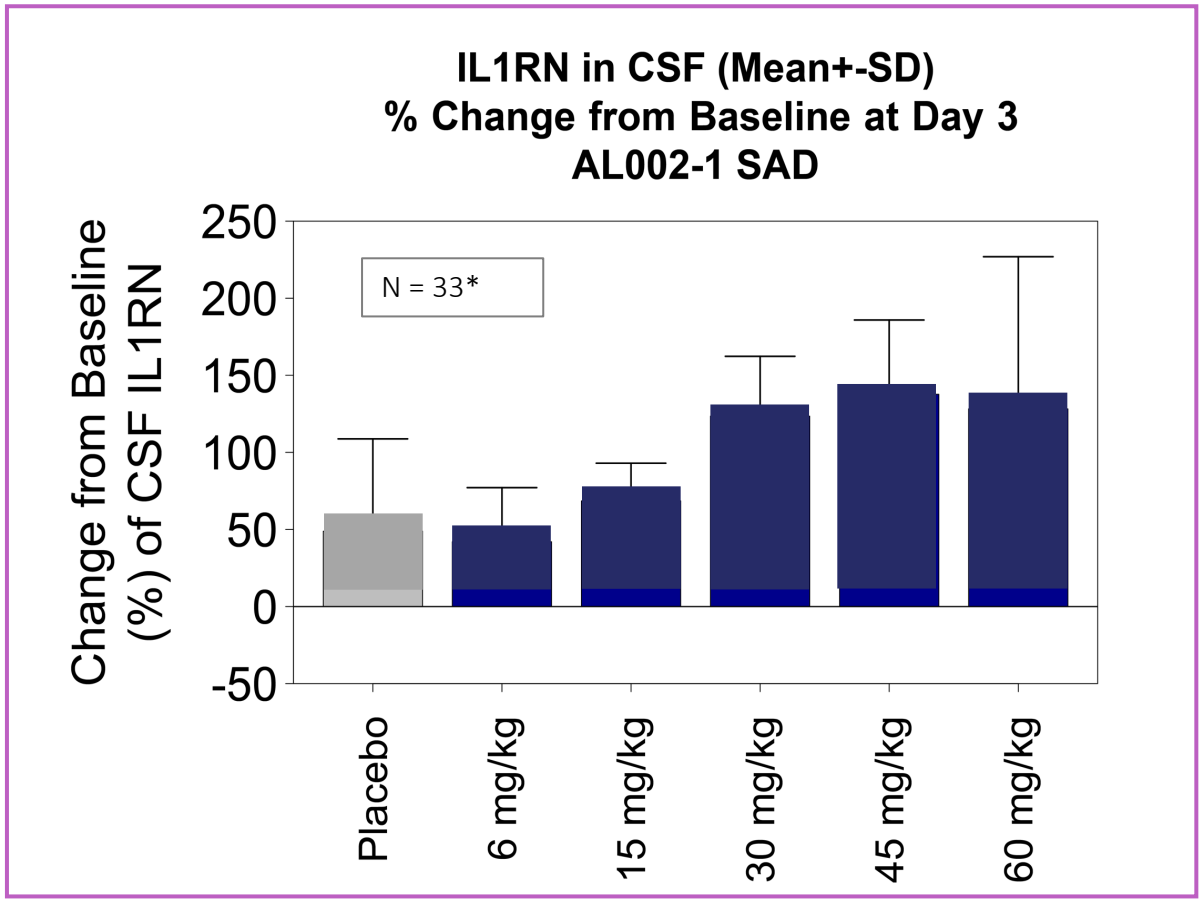


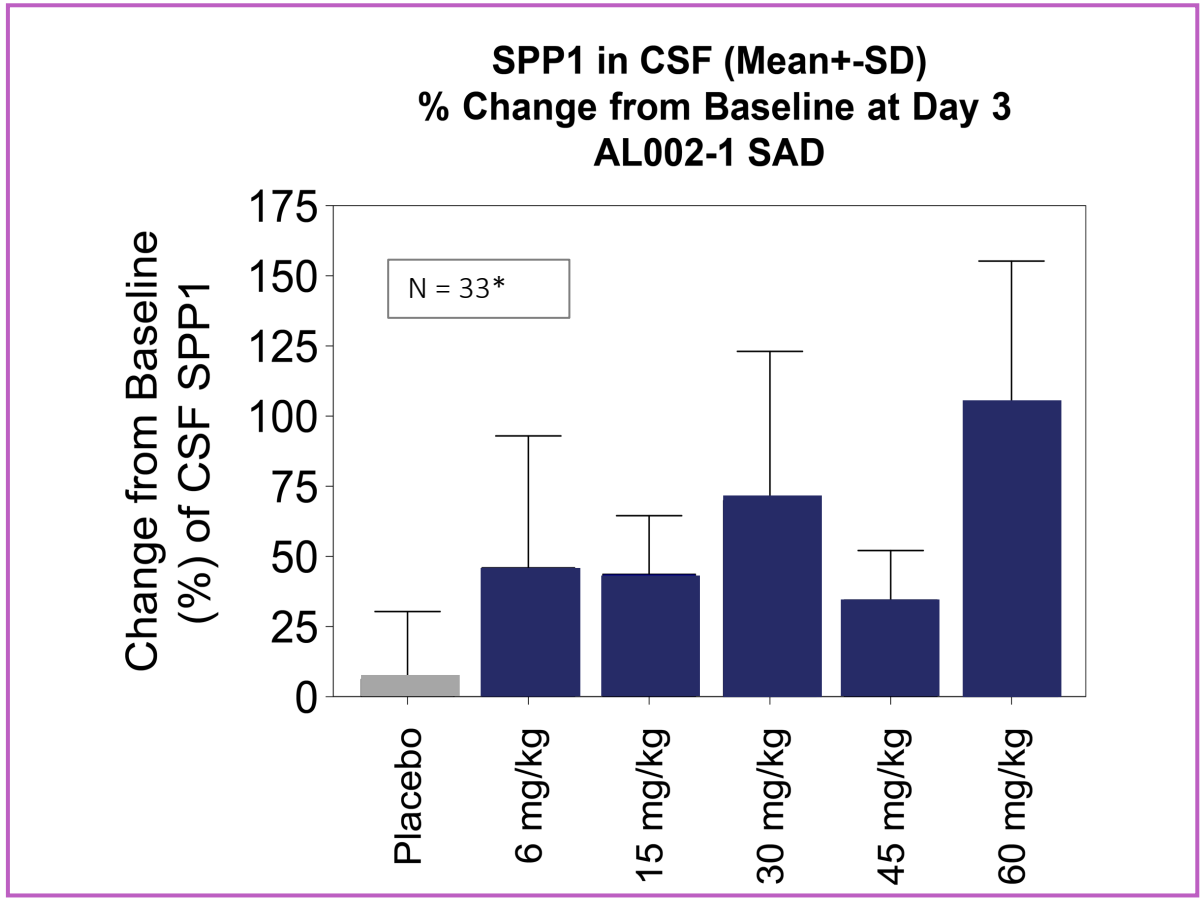
Dose-Dependent Elevation in sCSF-1R, Associated with Microglia Activation[2]



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.

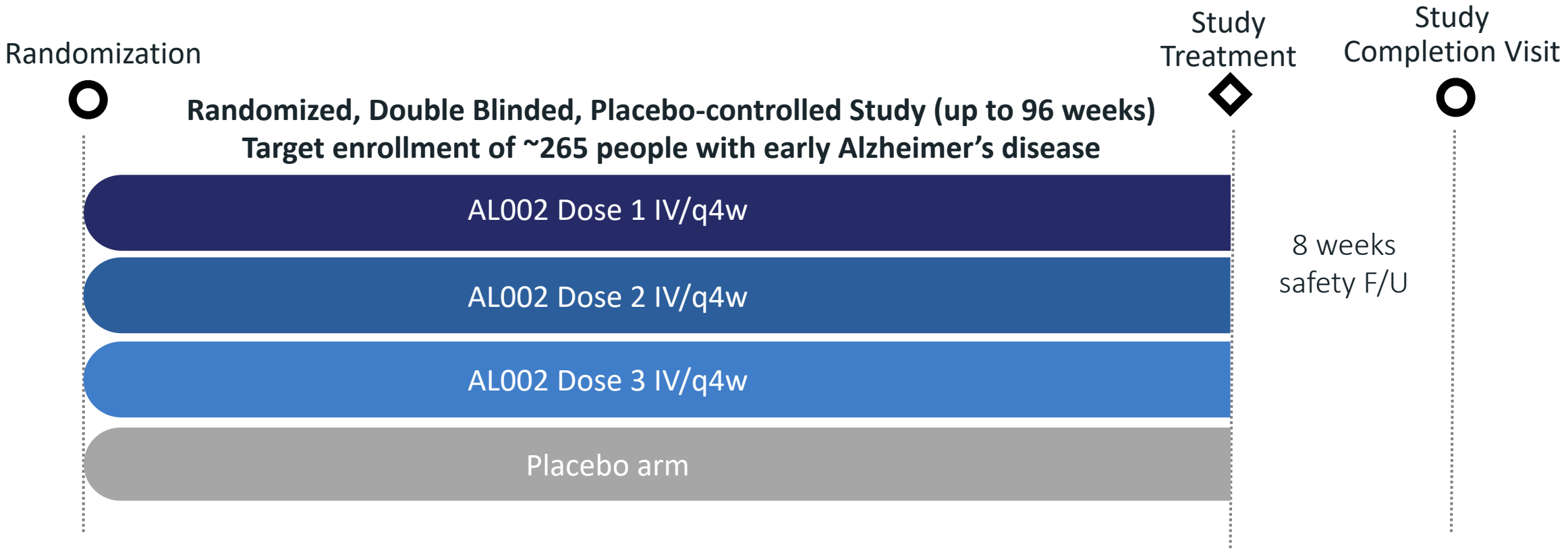
AL002 Treatment in Phase 1 Also Caused An Increase in CSF Levels of IL1RN and SPP1, Indicating Further Evidence of Microglial Activation





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 AAIC 2021

INVOKE-2 Phase 2 AL002 Study in Individuals with Early Alzheimer's Disease



PRIMARY ENDPOINT:
CDR-SB

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

EXPLORATORY ENDPOINTS:
vMRI, CSF and Plasma Biomarkers, PET scans

Note: 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).

Preclinical Program for Alzheimer's Disease:

AL044

Background on AL044 Targeting a Candidate Master Regulator of Microglia

Key Features of MS4A and AL044

- MS4A Member of ~22 membrane-tetra spanning 4A family, structurally related to CD20
- Expressed on microglia, CNS perivascular macrophages
- Modulate multiple aspects of AD disease risk, age of onset, progression and survival
- **AL044 our drug candidate functionally phenocopies and exceeds activities of the protective MS4A variant**
- AL044 Regulates the levels of key signaling systems in microglia; Trem2/sTrem2, CSF1R, Dectin1
- AL044 regulate microglia , proliferation, survival migration lysosomal function, immune response and energetics, genes and/or proteins
- **IND filed following pre-IND alignment**

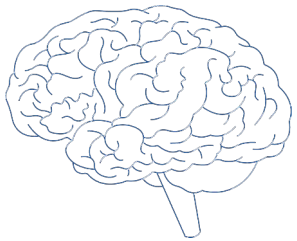
Effects of MS4A on AD

Protective Allele	Effects on AD	Risk Allele
↓	AD Risk	↑
↑	Age of onset and survival	↓
↓	Rate of cognitive decline	↑
↑	CSF Soluble TREM2	↓
↓	Aβ Plaques & CSF Tau	↑
↓	Rate of Cortical and hippocampal Shrinkage	↑
↓	Rate of Conversion from MCI to AD	↑
↑	Protective Interactions with APOE4	↓

Source: doi:10.1126/scitranslmed.aau2291, Sci Transl Med, 2019.; NATURE IMMUNOLOGY | VOL 20 | AUGUST 2019 | 1012–1022; DOI: 10.1016/j.jalz.2016.06.005; Michael Ewers et al., Sci Transl Med 2019;11:eaav6221.

Alector Oncology Overview

Neurodegeneration and Cancer Converge at the Innate Immune System

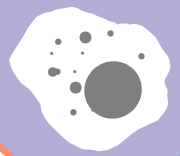


NEURODEGENERATION

Harness the innate immune system to attack brain pathology

Microglia

Tumor Macrophage



CANCER

Harness the innate immune system to attack tumor

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
IND Submission expected later this year

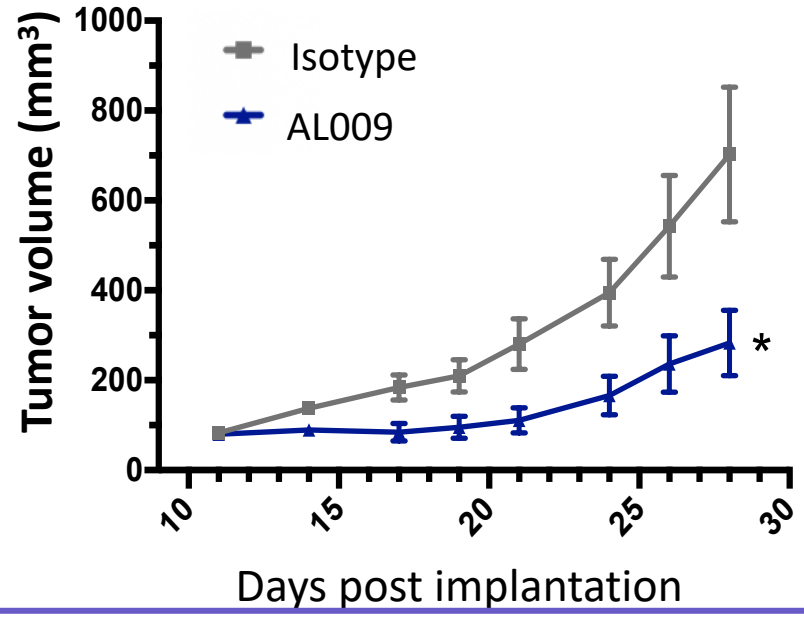
PRODUCT CANDIDATE

- 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



AL008: Potential Best-in-Class Dual Function SIRPα-CD47 Pathway Activator

TARGET
SIRPα - CD47 pathway

SCIENTIFIC RATIONALE
Tumors leverage pathway to hide from immune system

STATUS
Re-acquiring rights granted to Innovent Biologics

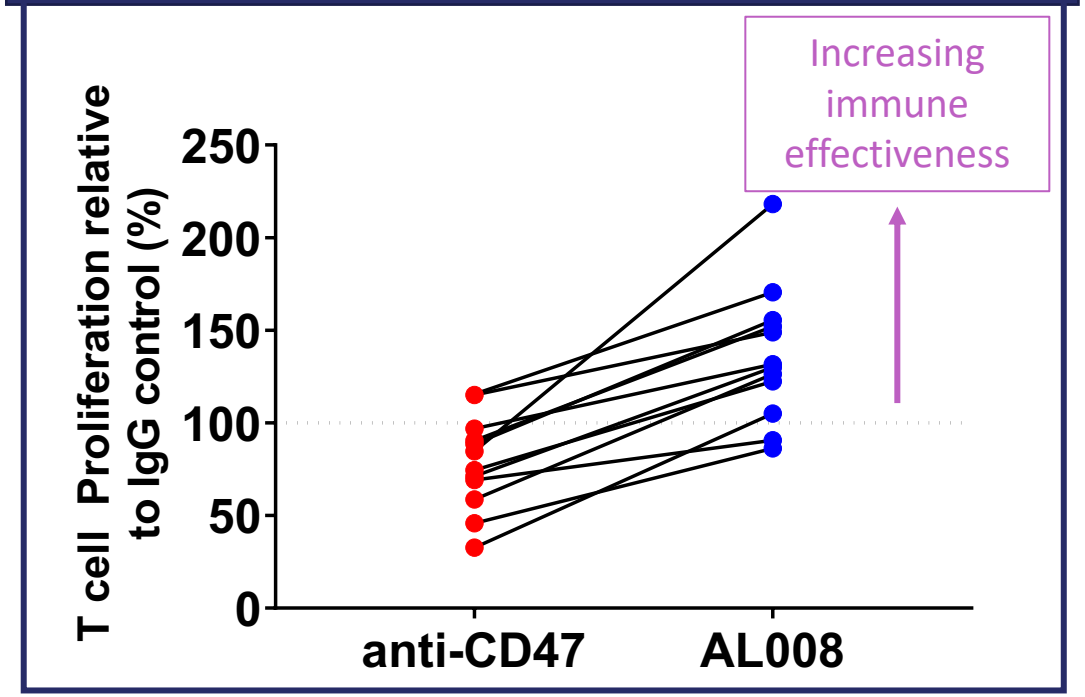
PRODUCT CANDIDATE

- Selectively binds to multiple SIRPα variants
- Does not inhibit T-cell activator SIRPα

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

AL008 enablesT-Cell Activation



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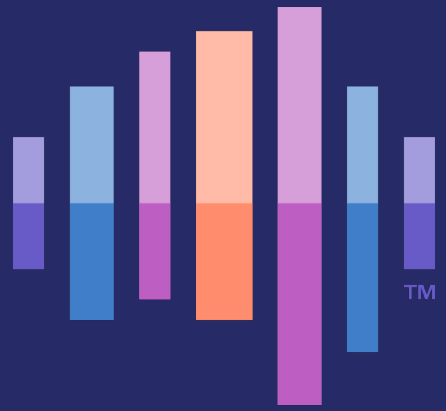

Thank You