Alector Corporate Overview

January 2023

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.

Translating Scientific Insights into a Broad Portfolio of First-in-Class Programs

NOVEL APPROACH

Founded to pioneer a new field of research: **Immuno-neurology**

Informed by **neuroscience, human genetics and immunology**

Substantial IP portfolio established: *41 issued patents, 500+ patent applications*

MULTIPLE CLINICAL TRIALS

PGRN Phase 3 Program for FTD-GRN
TREM2 Phase 2 Program for Early AD

PGRN Phase 2 Program for FTD-C9orf72
MS4A Phase 1 Program for AD

Pre-Clinical Portfolio and Discovery Platform
Multiple immuno-neurology and oncology opportunities

WORLD CLASS PARTNERS

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

GSK

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

abbvie

STRONG FINANCIALS

$758 MILLION IN CASH: RUNWAY THROUGH 2025

alector

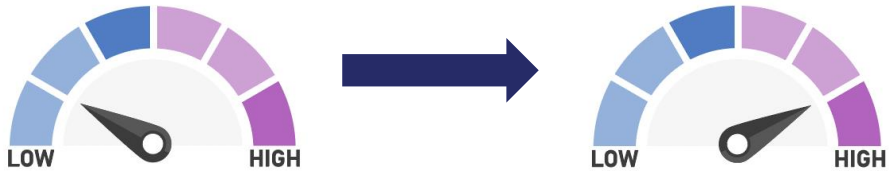
FTD = Frontotemporal dementia, PD = Parkinson's Disease, AD = Alzheimer's Disease

Note: As of September 30, 2022, Alector's cash, cash equivalents and investments totaled $758.3 million.

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

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

Immuno-neurology Therapeutics

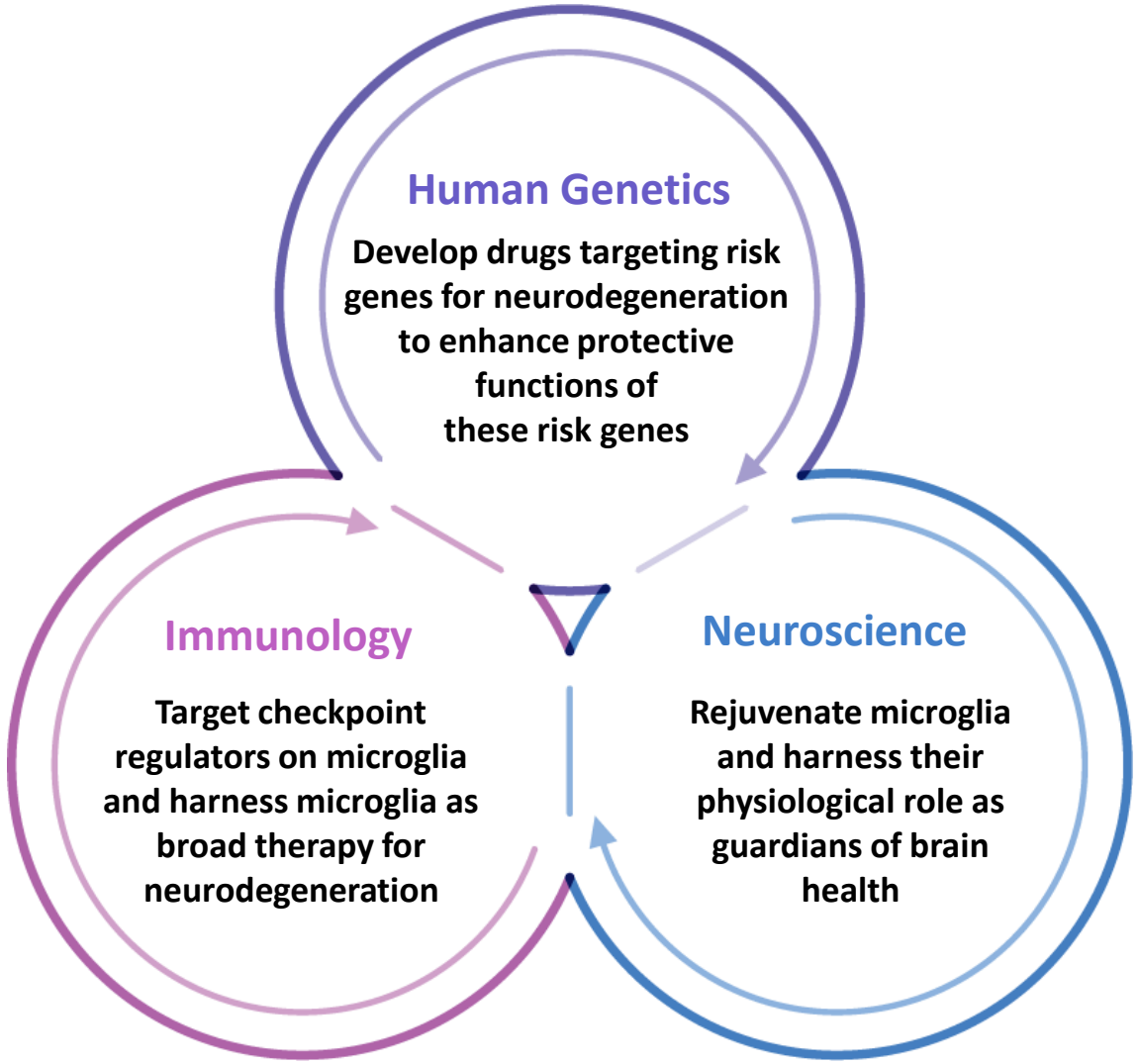


Ineffective and damaging microglia

Effective and beneficial microglia

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

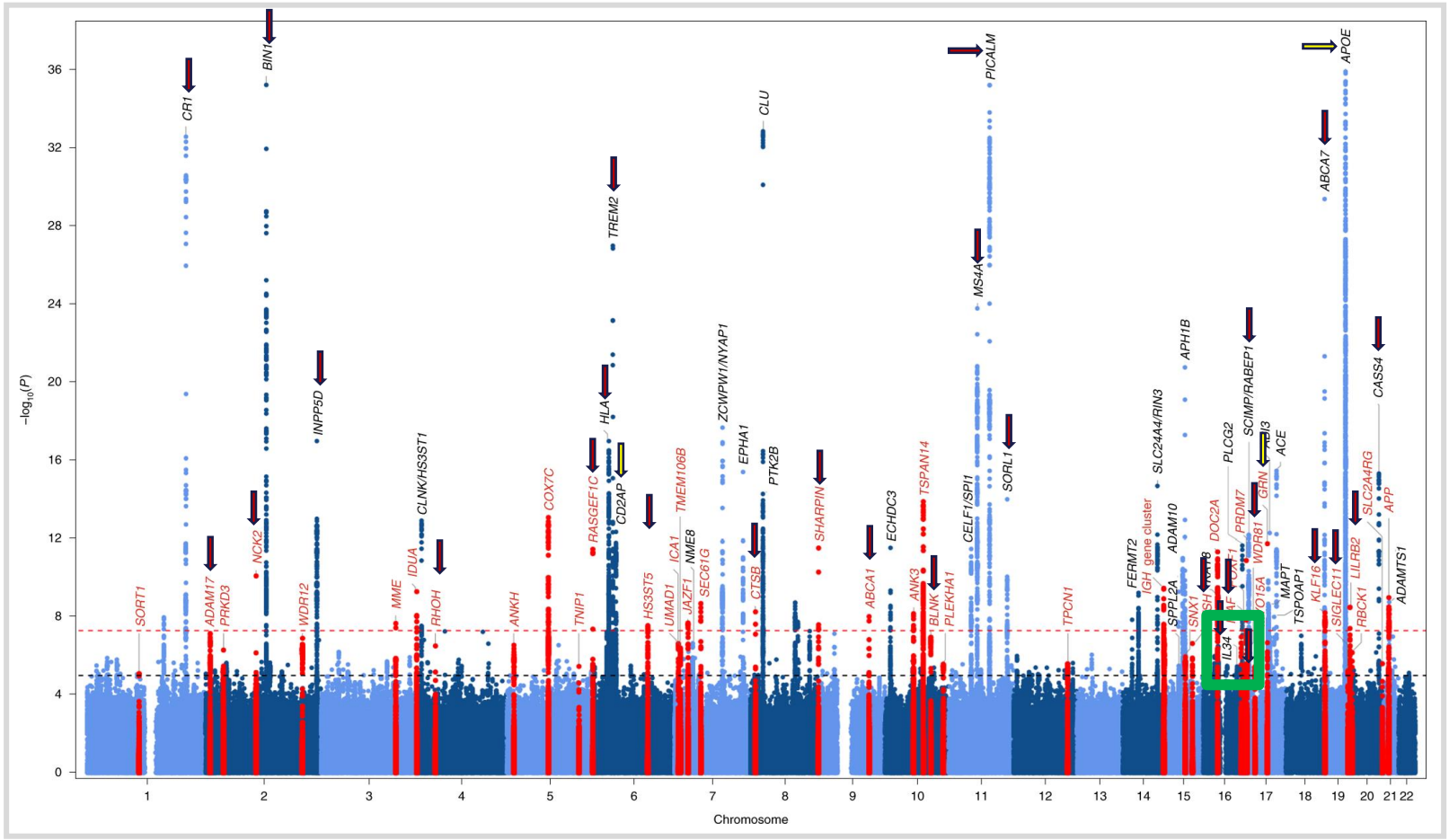
Multiple first-in-class programs are in or entering the clinic for neurodegenerative diseases



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

Genetic Rationale for Immuno-Neurology: Many Familiar Risk Genes for Alzheimer's Disease are Checkpoint Proteins for the Microglia Brain Innate-Immune System

Most AD risk genes are microglia regulators (Arrows)



Chromosome Number

Source *Nature Genetics* volume 54, pages412–436 (2022)

Biological Rationale for Immuno-Neurology: Microglia are Essential for Brain Health in Humans

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

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

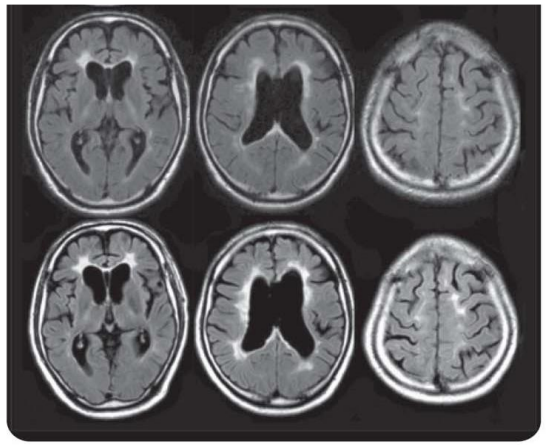
Patients experience range of psychiatric, neurocognitive, and motor symptoms

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

Rapid brain tissue loss

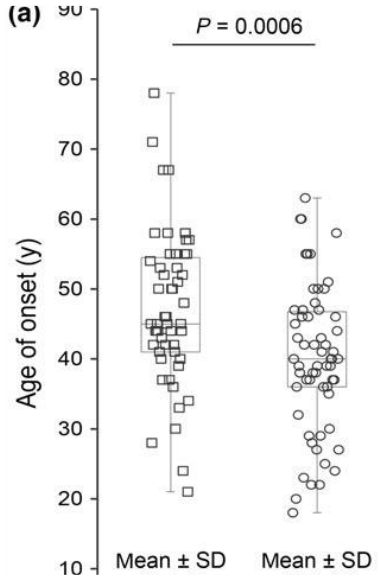
54 yo
1 year after onset

57 yo
4 years after onset

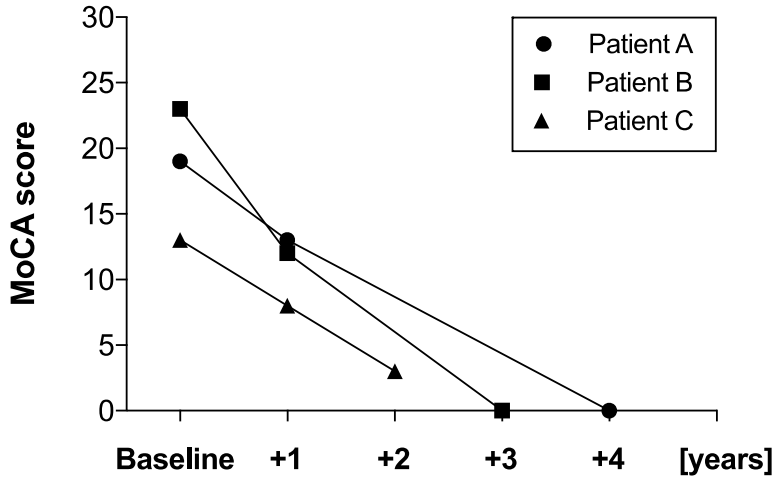


MRI shows dilation of brain ventricles

~ 6 Year Survival Rate



Rapid Cognitive Decline



Source: Konno, Neurology 2014 and Konno, Eur J Neurol 2016.

Alector's Discovery Platform for Genetically Validated Microglia Checkpoint Targets

IDENTIFY FAMILIAL GENETIC RISK VARIANTS FOR NEURO-DEGENERATION

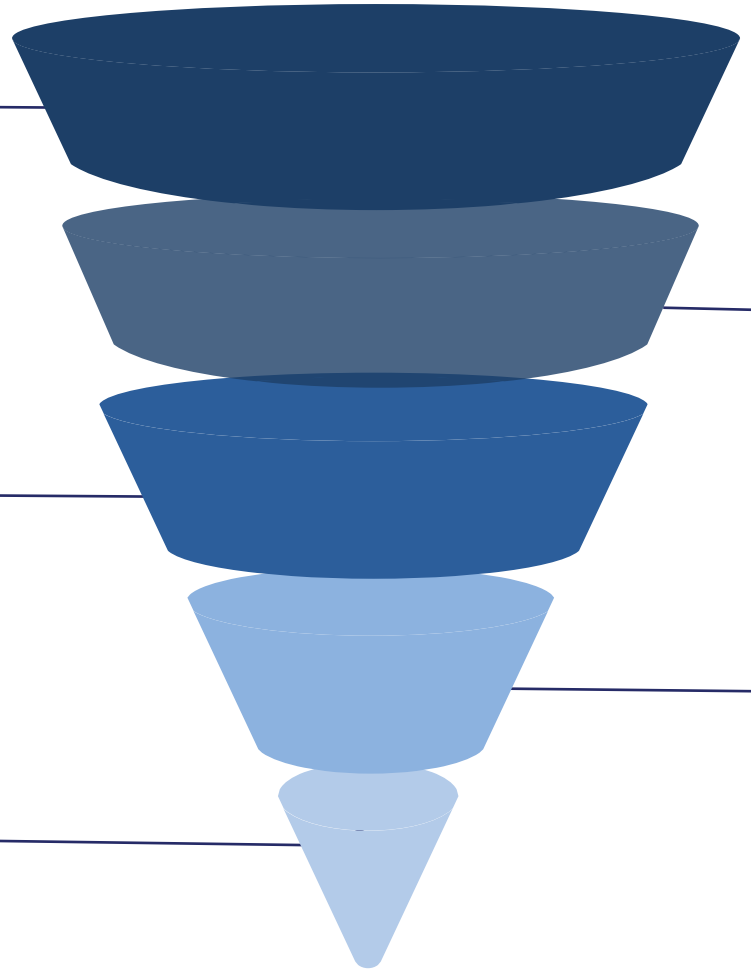
Germline genetics of Alzheimer's, Parkinson's, FTD, ALS, MS

DETERMINE GENE AND PROTEIN EXPRESSION SIGNATURES & KO/KI PHENOTYPE

7k Proteins, 20K genes, IPSC, CRISPR AI in house & public databases

TEST DRUGS IN DISEASE MODELS

Efficacy & safety



SELECT SUBSET THAT REGULATE IMMUNE SYSTEM

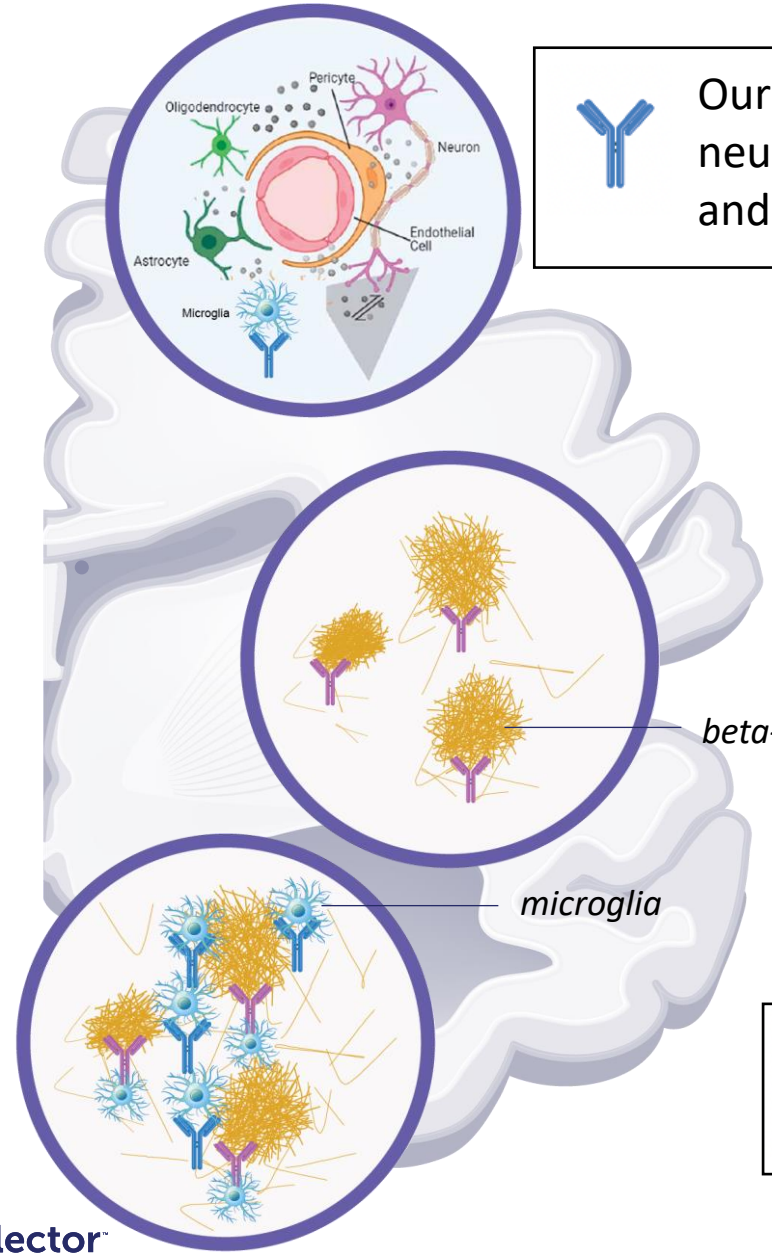
RNAseq, KO in models, IPSC, CRISPR AI

DEVELOP DRUGS THAT MIMIC THE SIGNATURE & FUNCTION OF THE PROTECTIVE GENETIC VARIANT

Drugs expression signature and phenotype

Alector clinical programs

Alector's Checkpoint Therapies Anticipated to Act Independently and in Combination

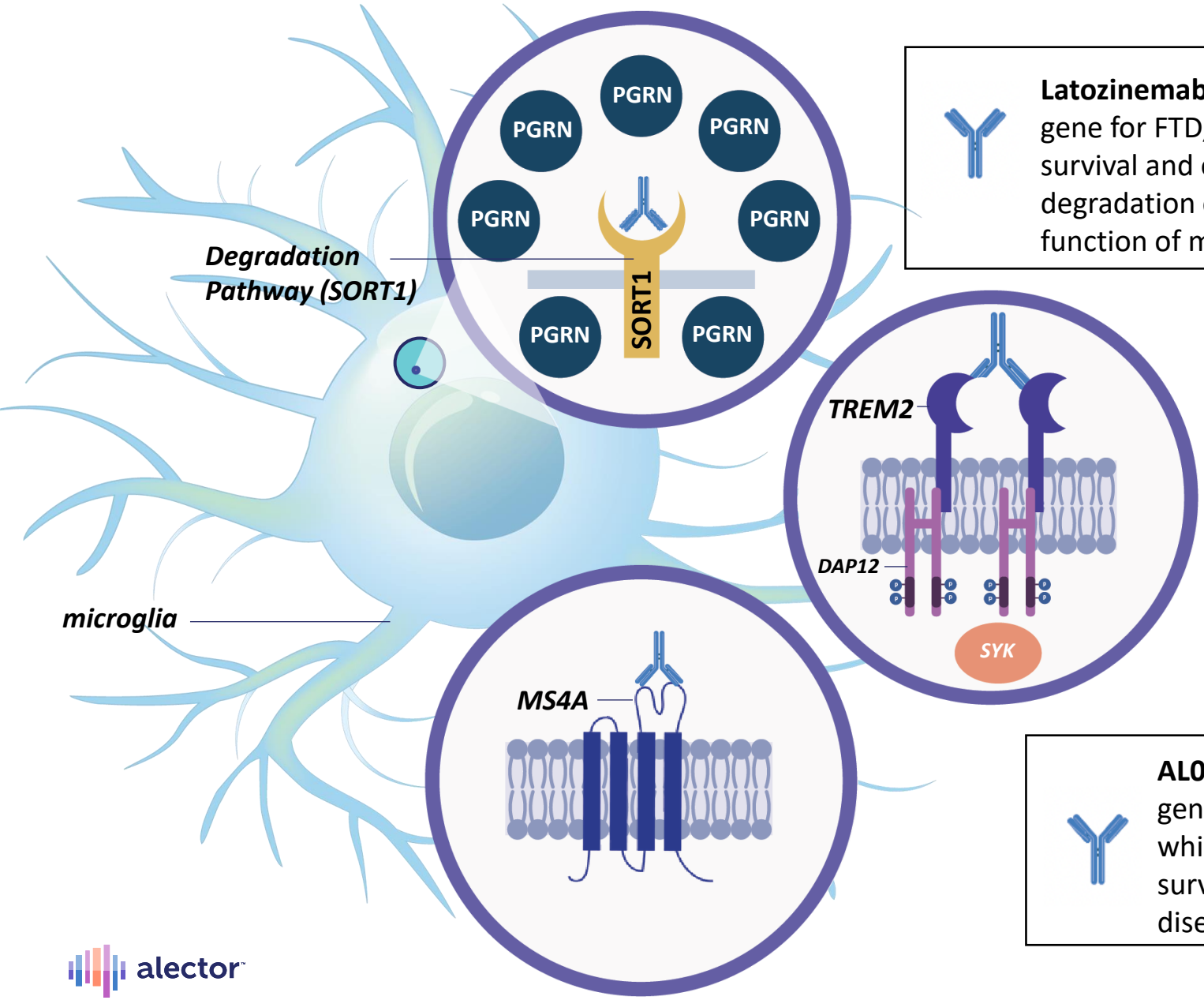


Our therapies seek to harness microglia to improve the functionality of neurons, oligodendrocytes, astrocytes, endothelial cells and blood vessels, and to remove debris, misfolded proteins and recycle damaged synapses.

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

Our therapies are expected to enhance microglia's ability to remove misfolded proteins in conjunction with Abs that tag these proteins.

Alector's Three Clinical Stage Neurodegenerative Disease Programs



Latozinemab (AL001) and AL101 elevate progranulin, a risk gene for FTD, AD, PD, and ALS, which promotes neuronal survival and enhances lysosomal activity, potentially improving degradation of misfolded proteins as well as the overall function of microglia and protecting neurons

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

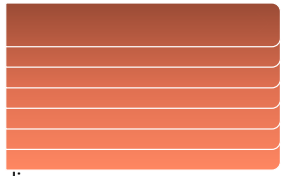
AL044 modulates signaling by MS4A, a risk gene for AD, and elevates sTREM2 levels, which may promote microglia proliferation, survival and functionality in the context of disease signals

First-in-Class Portfolio of Product Candidates Targeting the Innate Immune System

TARGET	CANDIDATE	RESEARCH	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	COMMERCIAL RIGHTS
PGRN	AL001	FTD-*GRN*					GSK
	AL001	FTD-*C9orf72*					GSK
	AL001	ALS*					GSK
	AL101	Healthy volunteers for AD and PD					GSK
TREM2	AL002	Alzheimer's disease					abbvie
MS4A	AL044	Alzheimer's disease					
	AL044	Orphan neuro indication					
Multi-Siglec	AL009	Solid tumors					
SIRP-alpha	AL008	Solid tumors					InnoVent (China)

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

12+ programs



AD = Alzheimer's disease
PD = Parkinson's disease
FTD = Frontotemporal dementia
ALS = Amyotrophic lateral sclerosis
MS = Multiple sclerosis
AL001=latozinemab

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

**In partnership with GSK, the company made a strategic, non-safety related decision to close enrollment in the ALS-C9orf72 Phase 2a biomarker trial and is currently evaluating plans for a new study.*

alector

Progranulin Franchise Programs
Latozinemab (AL001) – Phase 3
AL101 – Phase 1

Latozinemab (AL001) and AL101: Raising Levels of Progranulin for Potential Benefit

Mechanism

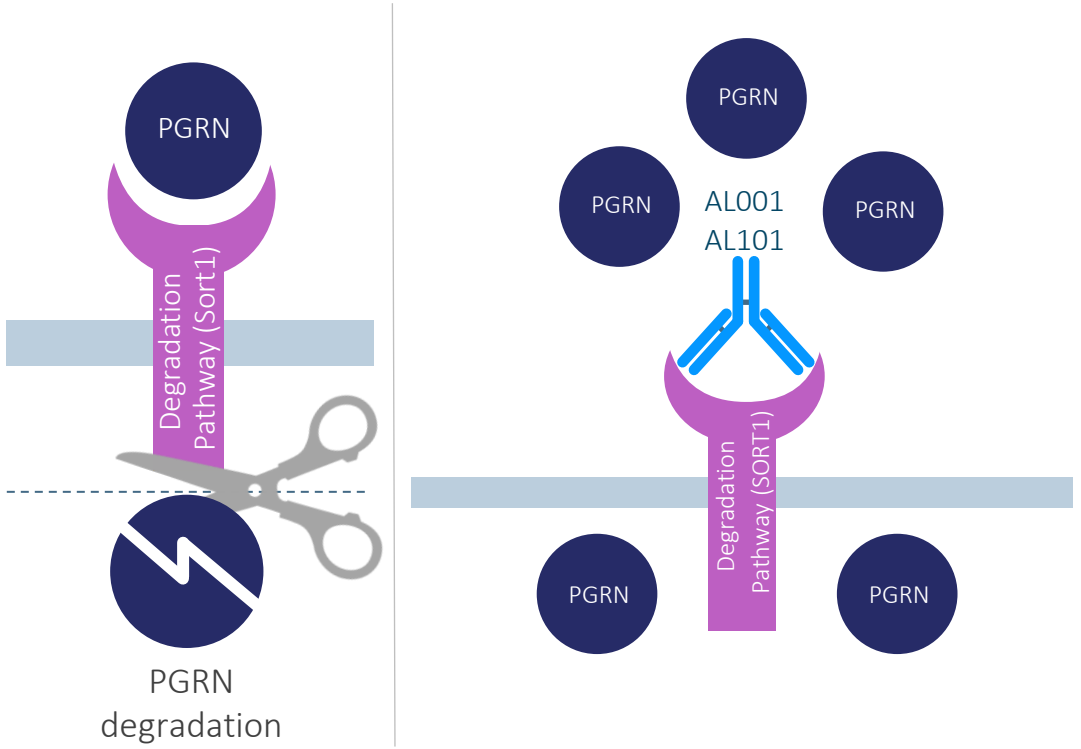
- Increases the half-life of PGRN by blocking Sortilin, a degradation receptor, in order to raise PGRN to normal levels

Latozinemab (AL001) Status

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

AL101 Status

- Phase 1 study of AL101 in healthy volunteers is complete
- Commencing preparatory work for Phase 2 in AD



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

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

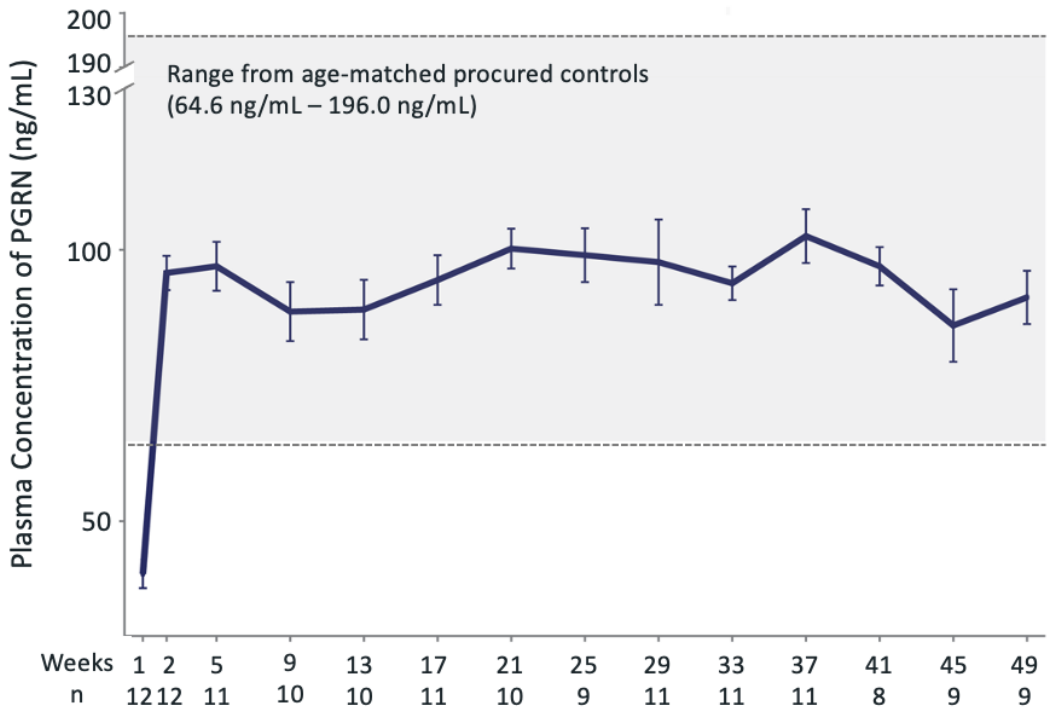
TARGET ENGAGEMENT	BIOMARKERS OF DISEASE ACTIVITY				CLINICAL BENEFIT
PGRN (plasma and CSF)	Lysosomal dysfunction	Complement activation	Astrogliosis	Neuronal health	Clinical Outcome Assessments
PGRN	**e.g. CTSD, LAMP1**	**e.g. C1QB**	**GFAP**	**NfL**	**CDR® plus NACC FTLD-SB**
> 50% reduction in PGRN 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)

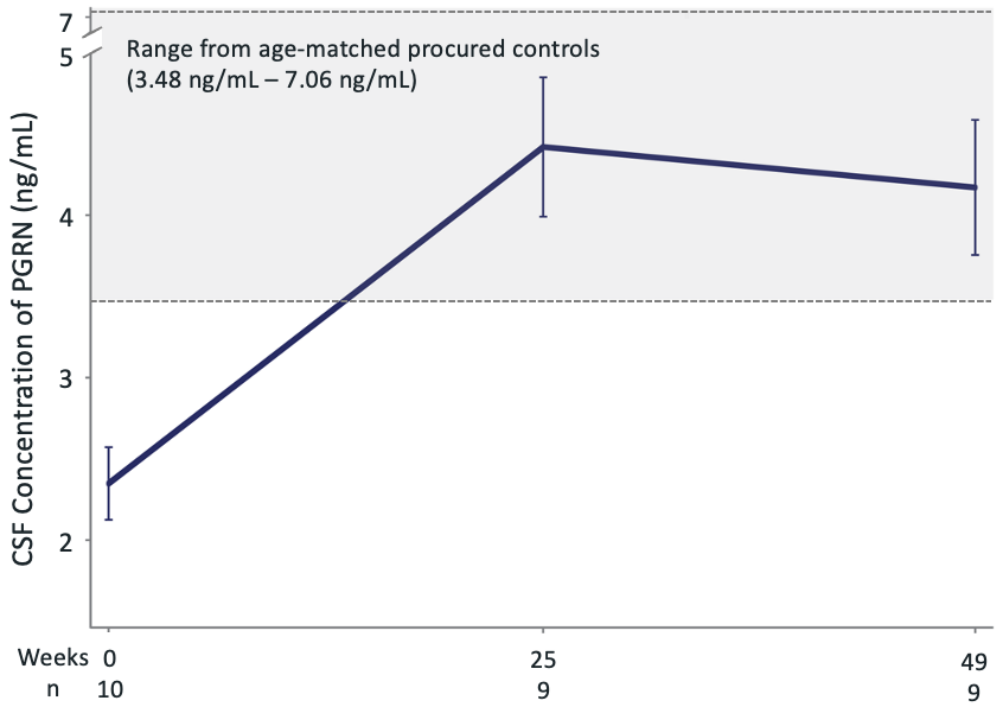
INFRONT-2: Latozinemab Restores PGRN in Plasma and CSF to Normal Levels in Symptomatic FTD-GRN

TARGET ENGAGEMENT

PGRN Plasma Concentration



PGRN CSF Concentration



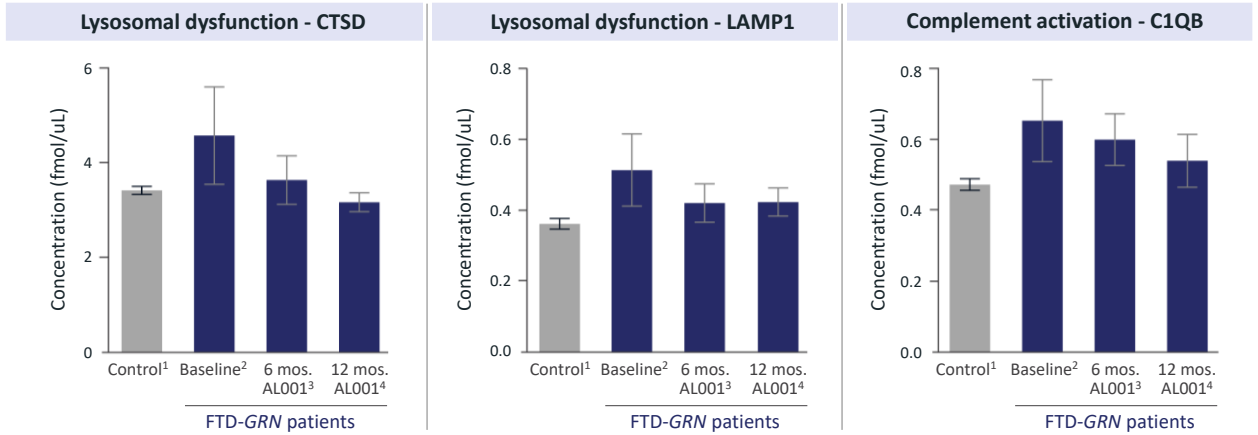
Data cut-off June 15, 2021
Mean +/- SEM
Source: AAIC 2021.

INFRONT-2: Use of Latozinemab Associated with Lowering of Mean Lysosomal and Inflammatory Biomarkers Towards Levels Seen in Control Subjects

FLUID BIOMARKERS OF DISEASE ACTIVITY

Symptomatic FTD-*GRN* patients at 12 months

Normalization of lysosomal and inflammatory biomarkers



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)

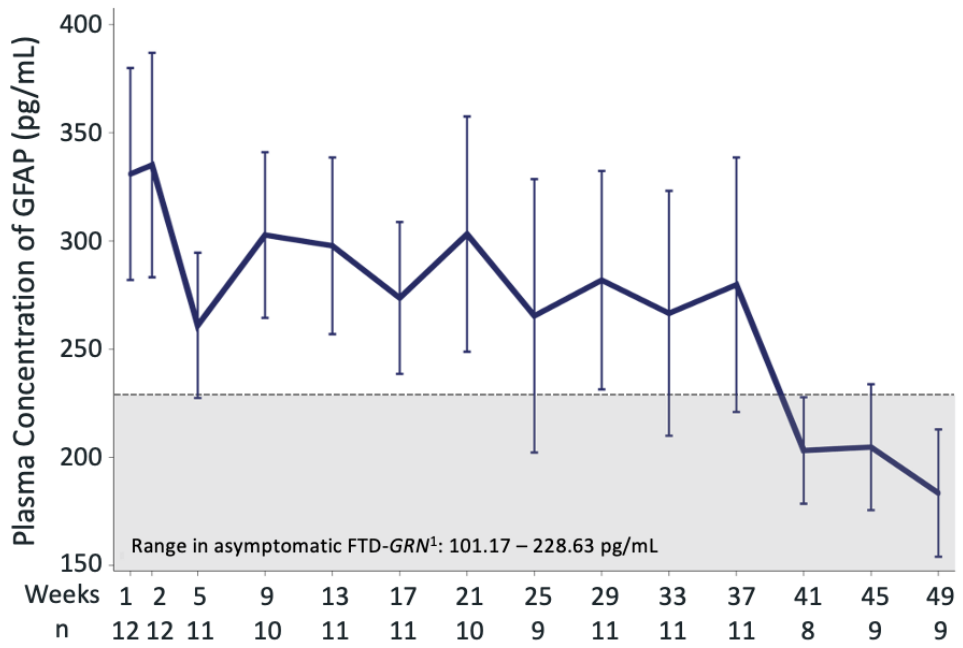
Mean +/- SEM
CTSD = cathepsin D protein
LAMP1= lysosomal-associated membrane protein 1
C1QB = gene that encodes the B-chain polypeptide of serum complement subcomponent C1q
Source: AAIC 2021.

alector

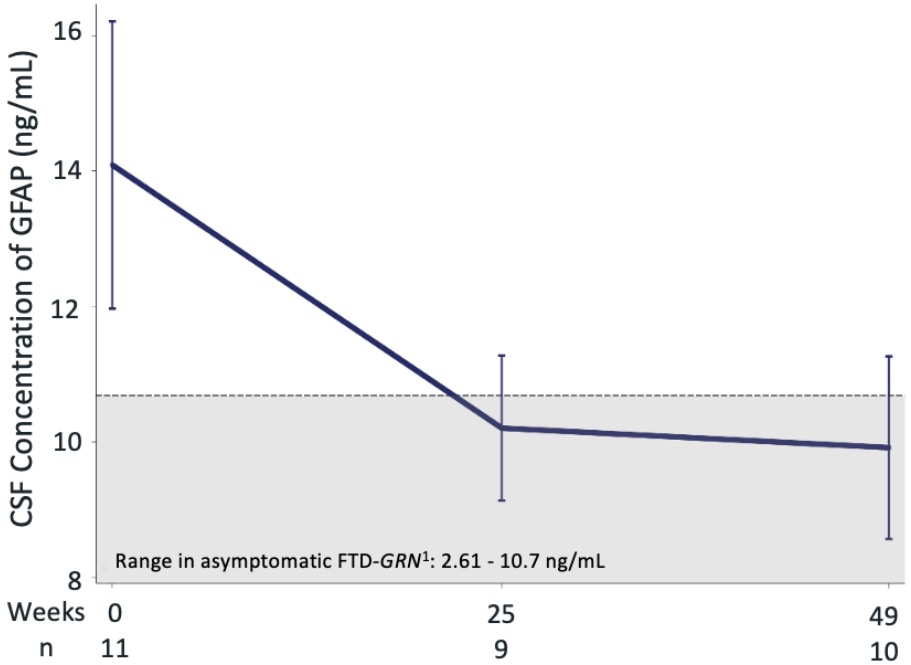
INFRONT-2: Latozinemab Treatment Decreases Glial Fibrillary Acidic Protein (GFAP) Levels Towards Range Seen in Asymptomatic Carriers of FTD-GRN Mutation

BIOMARKERS OF DISEASE ACTIVITY – ASTROGLIOSIS

GFAP Plasma Concentration



GFAP CSF Concentration

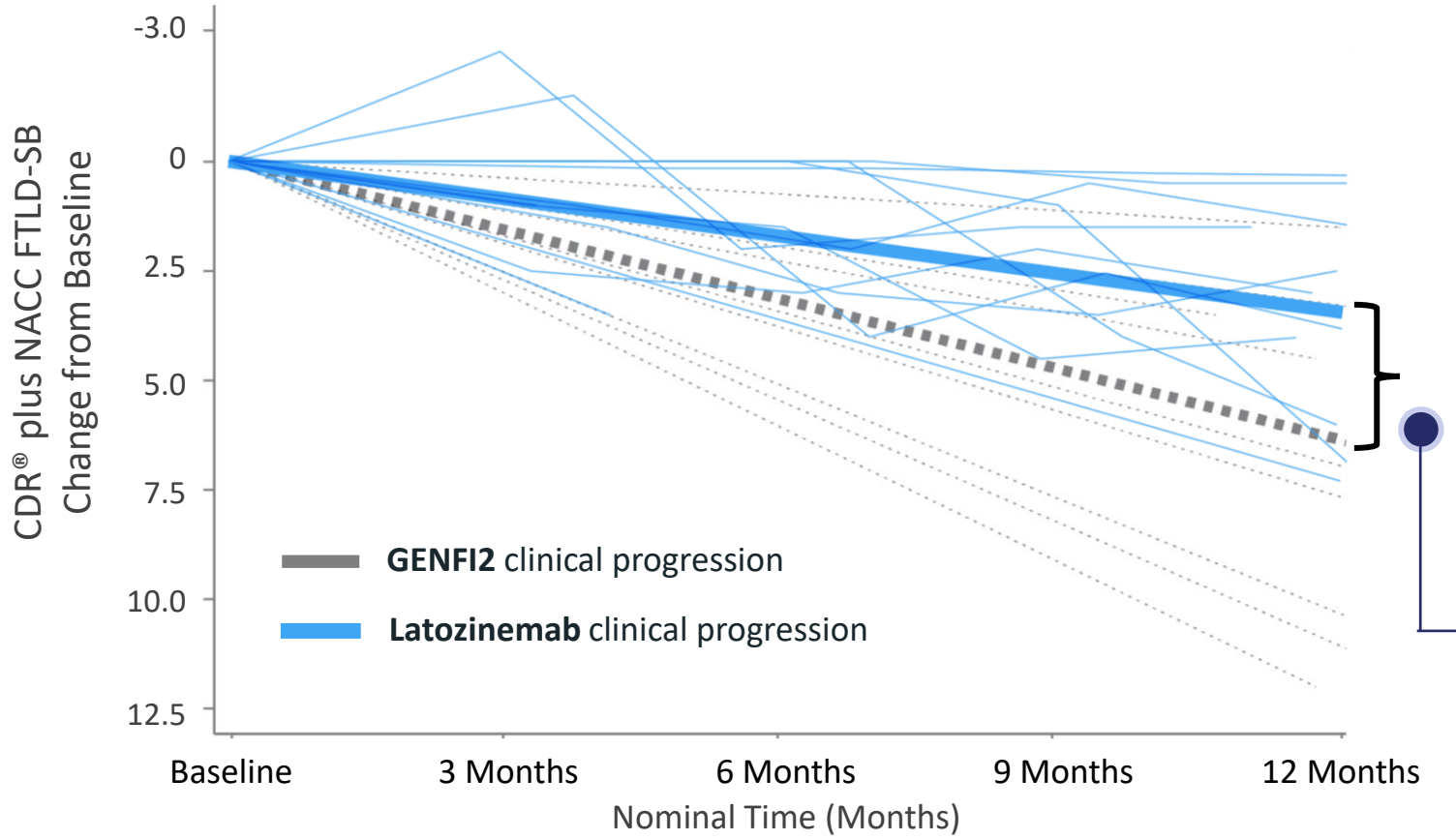


Data cut-off June 15, 2021
Mean +/- SEM
1. Range is of baseline GFAP levels in asymptomatic FTD-GRN patients enrolled in INFRONT-2
Source: AAIC 2021.

Annual Delay in Disease Progression in Latonizemab-Treated Patients Compared to Matched Historical Controls

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

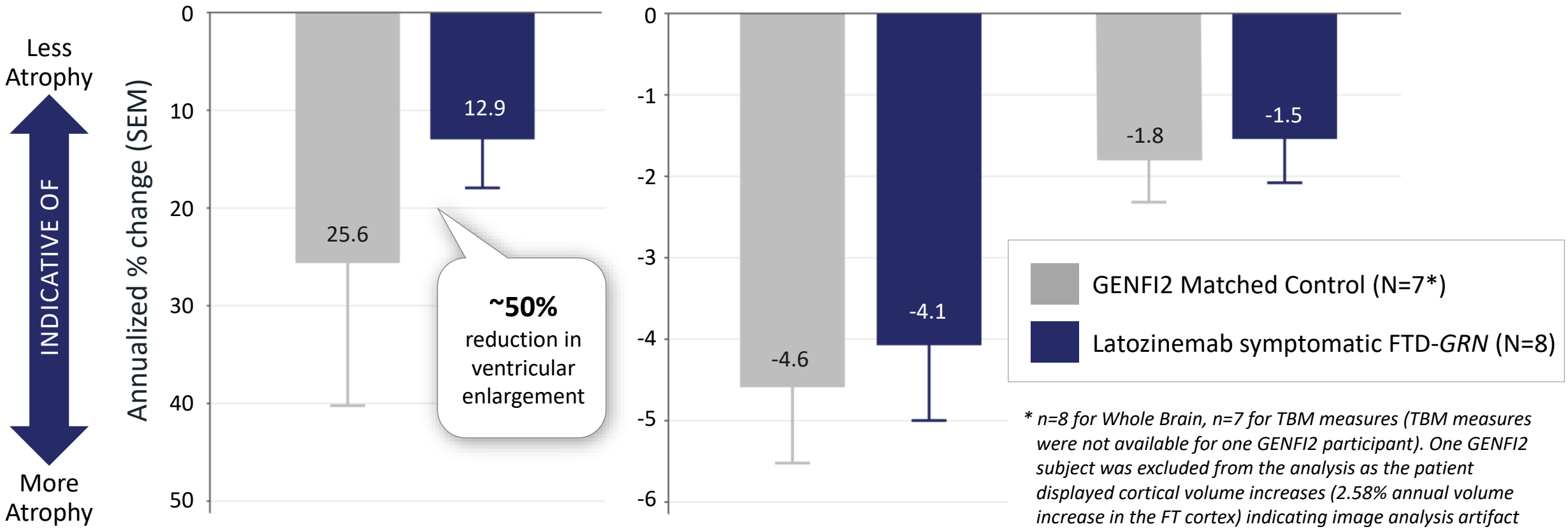
48% slowing of clinical progression (3.1 point change)

1. Random Coefficient Model with Repeated Measurements including baseline & all available post-baseline measurements up to 12 months. Data cut-off Sep 8, 2021.
Phase 2 data presented at CTAD 2021 and ADPD 2022
NCT03987295
GENFI = The Genetic Frontotemporal Initiative
GENFI2 refers to the longitudinal FTD registry dataset

alector

INFRONT-2: vMRI Data Showing Ventricular Enlargement and Brain Atrophy in Latozinemab-Treated FTD-GRN Patients vs. Historic Matched Control

BIOMARKERS OF DISEASE ACTIVITY – BRAIN VOLUME CHANGES



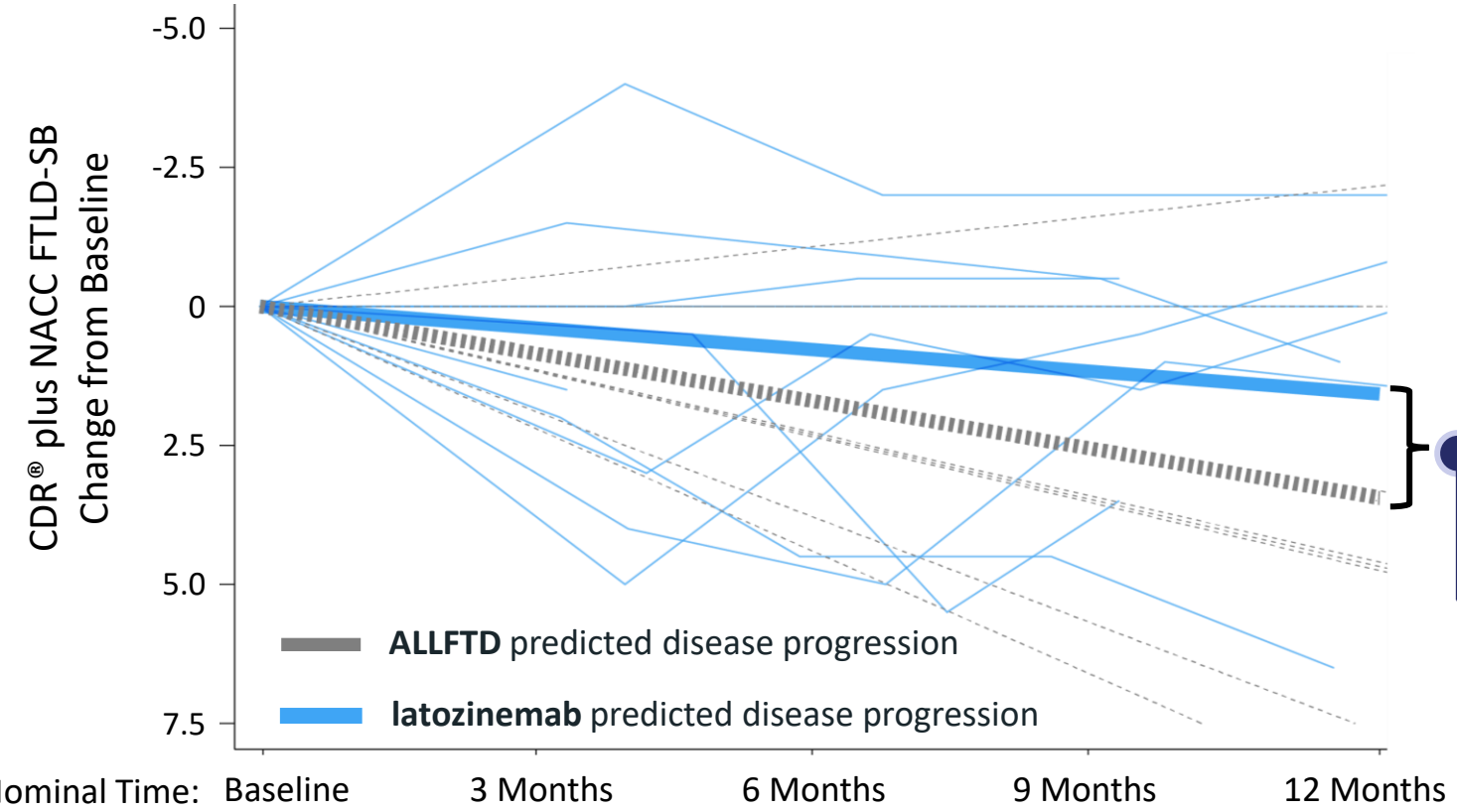
** n=8 for Whole Brain, n=7 for TBM measures (TBM measures were not available for one GENFI2 participant). One GENFI2 subject was excluded from the analysis as the patient displayed cortical volume increases (2.58% annual volume increase in the FT cortex) indicating image analysis artifact*

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

Annual Delay in Disease Progression in Latozinemab-Treated FTD-C9orf72 Participants Compared to the ALLFTD Matched Historical Controls

CLINICAL BENEFIT

CDR® plus NACC FTLD-SB



Parameter	Estimate	95% CI
Annual Change in **ALLFTD** (n=10)[1]	3.4	[1.30,5.60]
Annual Change in **latozinemab** (n=10)[2]	1.6	[-0.63,3.78]
Difference in Annual Change (ALLFTD – latozinemab)[3]	**1.9**	**[-1.21,4.95]**

~54% delay in disease progression

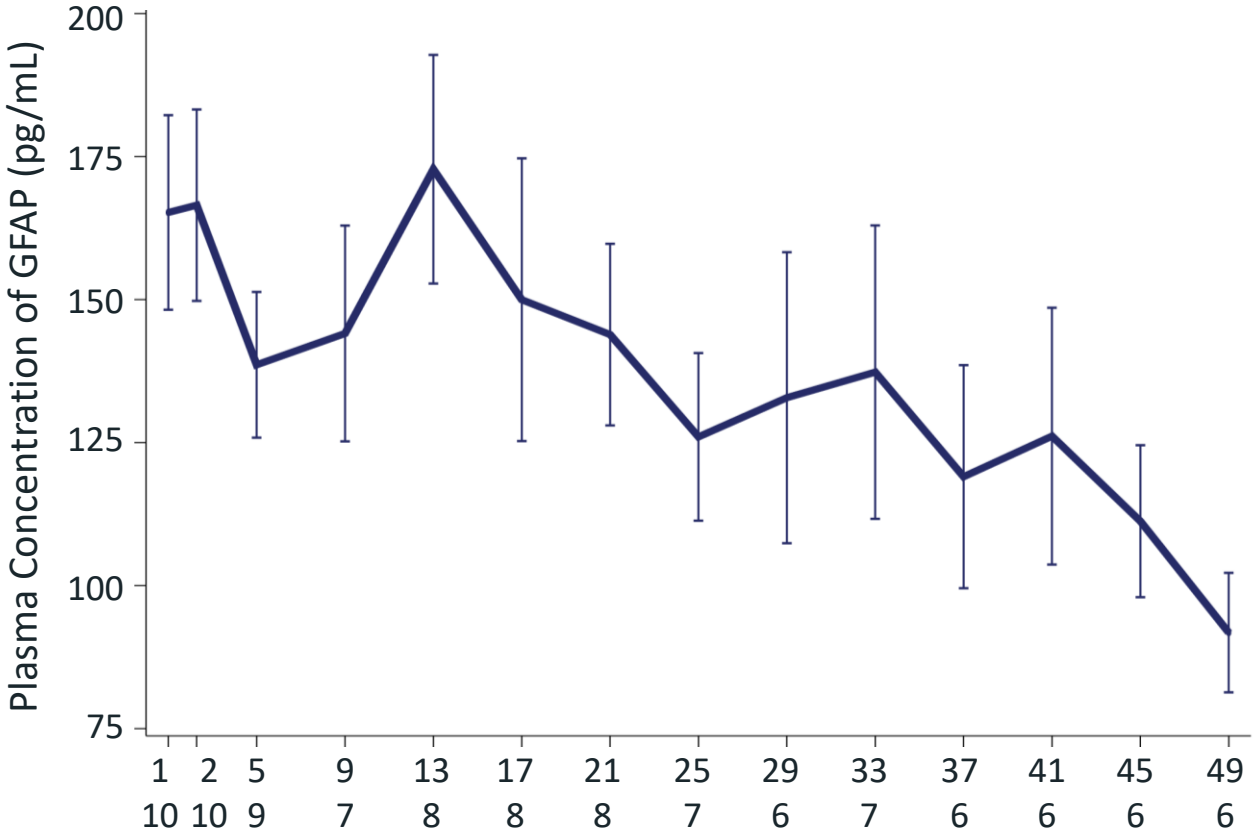
- Analysis of propensity score-matched cohort demonstrated a delay in disease progression of 0.9 points [-1.35,3.21], 36%

1: ALLFTD – one post-baseline timepoint at ~12 months
2: Latozinemab – all available post-baseline assessments (range from 3 to 12 months)
3: Model – Random coefficient model with repeated measurements
ALLFTD= historical observational cohort
Source: AD/PD 2022.

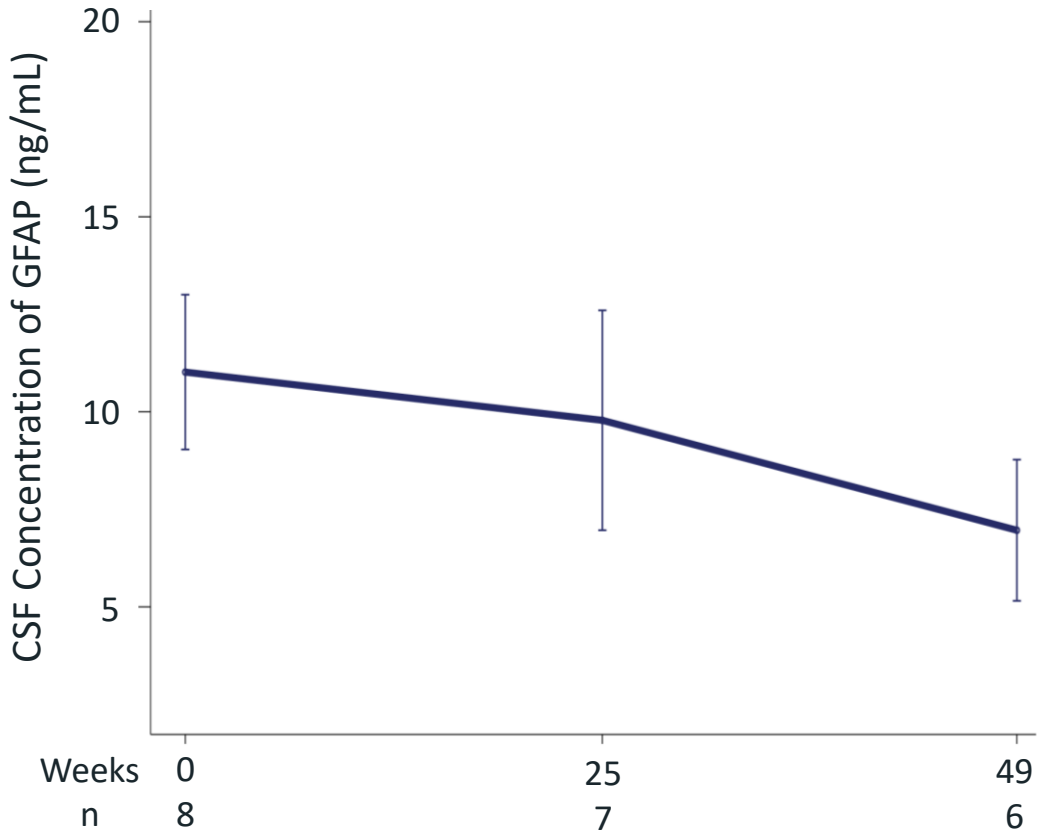
INFRONT-2: GFAP Levels in Plasma and CSF Are Decreased Over 12 Months in Latozinemab-treated FTD-C9orf72 Participants

EXPLORATORY BIOMARKER – Glial Fibrillary Acidic Protein (GFAP)

GFAP Plasma Concentration

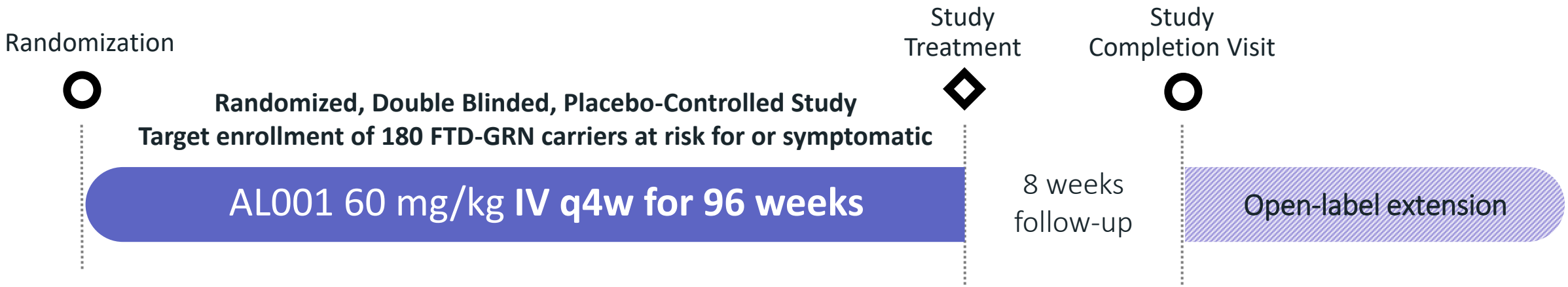


GFAP CSF Concentration



Data cut-off June 15, 2021
Mean +/- SEM
Source: AD/PD 2022.

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



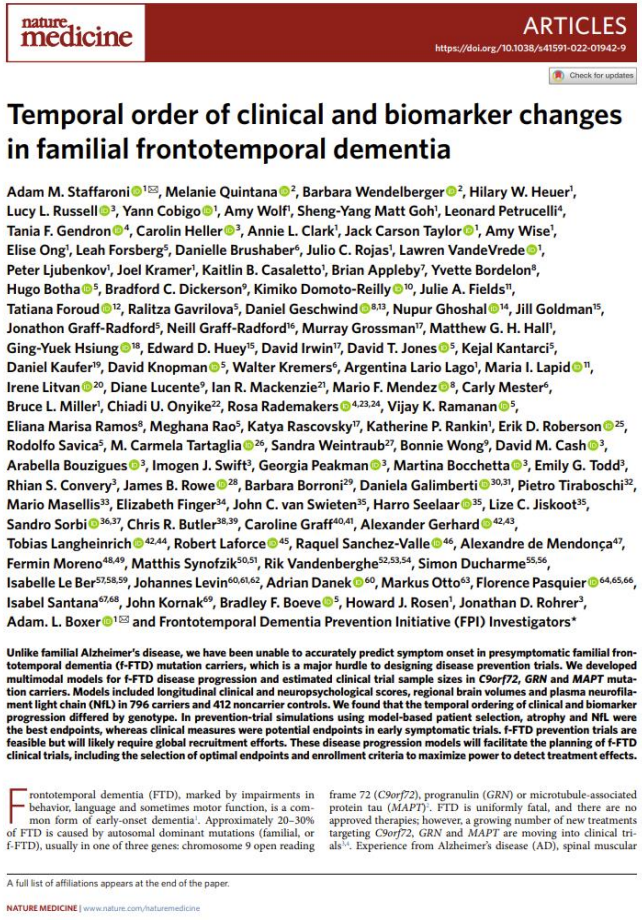
PRIMARY ENDPOINT	SECONDARY CLINICAL OUTCOMES ASSESSMENTS:	EXPLORATORY ENDPOINTS
CDR® plus NACC FTLD-SB	CGI-S, CGI-I, FRS, RBANS	vMRI, CSF and Plasma Biomarkers

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

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

Latozinemab: Recent Updates and Considerations for Path Forward in FTD-GRN

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



nature medicine ARTICLES
https://doi.org/10.1038/s41591-022-01942-9
Check for updates

Temporal order of clinical and biomarker changes in familial frontotemporal dementia

Adam M. Staffaroni[1✉], Melanie Quintana[2], Barbara Wendelberger[2], Hilary W. Heuer[1], Lucy L. Russell[3], Yann Cobigo[1], Amy Wolf[1], Sheng-Yang Matt Goh[1], Leonard Petrucelli[4], Tania F. Gendron[4], Carolin Heller[3], Annie L. Clark[1], Jack Carson Taylor[1], Amy Wise[1], Elise Ong[1], Leah Forsberg[5], Danielle Brushaber[6], Julio C. Rojas[1], Lawren VandeVrede[1], Peter Ljubenkov[1], Joel Kramer[1], Kaitlin B. Casaletto[1], Brian Appleby[7], Yvette Bordelon[8], Hugo Botha[5], Bradford C. Dickerson[9], Kimiko Domoto-Reilly[10], Julie A. Fields[11], Tatiana Foroud[12], Ralitza Gavrilova[5], Daniel Geschwind[8,13], Nupur Ghoshal[14], Jill Goldman[15], Jonathon Graff-Radford[5], Neill Graff-Radford[16], Murray Grossman[17], Matthew G. H. Hall[1], Ging-Yuek Hsiung[18], Edward D. Huey[15], David Irwin[17], David T. Jones[5], Kejal Kantarci[5], Daniel Kaufer[19], David Knopman[5], Walter Kremers[6], Argentina Lario Lago[1], Maria I. Lapid[11], Irene Litvan[20], Diane Lucente[9], Ian R. Mackenzie[21], Mario F. Mendez[8], Carly Mester[6], Bruce L. Miller[1], Chiadi U. Onyike[22], Rosa Rademakers[4,23,24], Vijay K. Ramanan[5], Eliana Marisa Ramos[8], Meghana Rao[5], Katya Rascovsky[17], Katherine P. Rankin[1], Erik D. Roberson[25], Rodolfo Savica[5], M. Carmela Tartaglia[26], Sandra Weintraub[27], Bonnie Wong[9], David M. Cash[3], Arabella Bouzigues[3], Imogen J. Swift[3], Georgia Peakman[3], Martina Bocchetta[3], Emily G. Todd[3], Rhian S. Convery[3], James B. Rowe[28], Barbara Borroni[29], Daniela Galimberti[30,31], Pietro Tiraboschi[32], Mario Masellis[33], Elizabeth Finger[34], John C. van Swieten[35], Harro Seelaar[35], Lize C. Jiskoot[35], Sandro Sorbi[36,37], Chris R. Butler[38,39], Caroline Graff[40,41], Alexander Gerhard[42,43], Tobias Langheinrich[42,44], Robert Laforce[45], Raquel Sanchez-Valle[46], Alexandre de Mendonça[47], Fermin Moreno[48,49], Matthis Synofzik[50,51], Rik Vandenberghe[52,53,54], Simon Ducharme[55,56], Isabelle Le Ber[57,58,59], Johannes Levin[60,61,62], Adrian Danek[60], Markus Otto[63], Florence Pasquier[64,65,66], Isabel Santana[67,68], John Kornak[69], Bradley F. Boeve[5], Howard J. Rosen[1], Jonathan D. Rohrer[3], Adam. L. Boxer[1✉] and Frontotemporal Dementia Prevention Initiative (FPI) Investigators*

Unlike familial Alzheimer's disease, we have been unable to accurately predict symptom onset in presymptomatic familial frontotemporal dementia (f-FTD) mutation carriers, which is a major hurdle to designing disease prevention trials. We developed multimodal models for f-FTD disease progression and estimated clinical trial sample sizes in *C9orf72*, *GRN* and *MAPT* mutation carriers. Models included longitudinal clinical and neuropsychological scores, regional brain volumes and plasma neurofilament light chain (NfL) in 796 carriers and 412 noncarrier controls. We found that the temporal ordering of clinical and biomarker progression differed by genotype. In prevention-trial simulations using model-based patient selection, atrophy and NfL were the best endpoints, whereas clinical measures were potential endpoints in early symptomatic trials. f-FTD prevention trials are feasible but will likely require global recruitment efforts. These disease progression models will facilitate the planning of f-FTD clinical trials, including the selection of optimal endpoints and enrollment criteria to maximize power to detect treatment effects.

Frontotemporal dementia (FTD), marked by impairments in behavior, language and sometimes motor function, is a common form of early-onset dementia[1]. Approximately 20–30% of FTD is caused by autosomal dominant mutations (familial, or f-FTD), usually in one of three genes: chromosome 9 open reading frame 72 (*C9orf72*), progranulin (*GRN*) or microtubule-associated protein tau (*MAPT*)[2]. FTD is uniformly fatal, and there are no approved therapies; however, a growing number of new treatments targeting *C9orf72*, *GRN* and *MAPT* are moving into clinical trials[3,4]. Experience from Alzheimer's disease (AD), spinal muscular

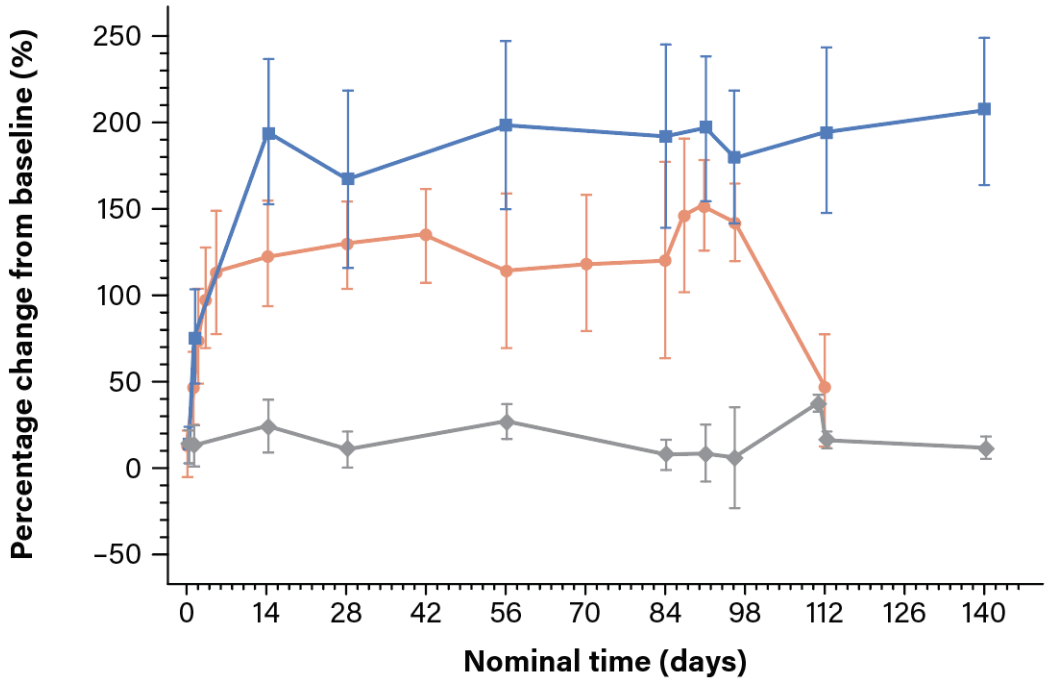
A full list of affiliations appears at the end of the paper.

AL101 Elevated Progranulin Levels in Plasma and CSF in Phase 1

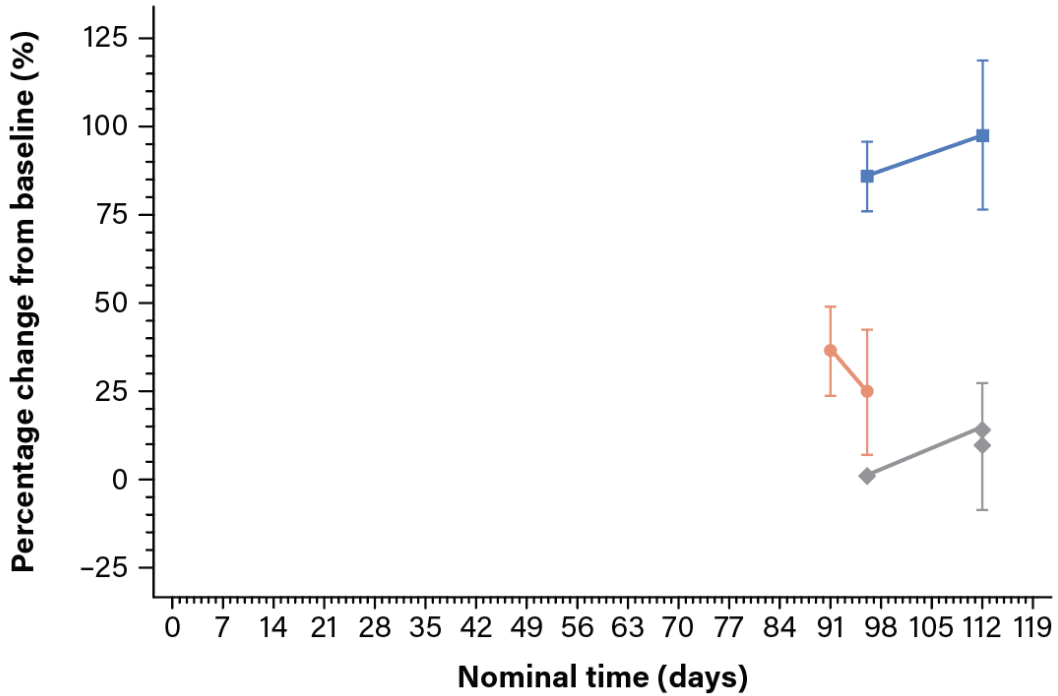
Data supports development of AL101, which has higher potency and a longer half-life that enables the potential for lower and less frequent dosing, for larger indications such as Alzheimer's disease

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

Plasma PGRN



CSF PGRN



AL101 300 mg MD SC AL101 30 mg/kg MD IV Pooled Placebo MD IV

CSF =cerebrospinal fluid; IV = intravenous; MD = multiple-dose; PGRN = progranulin; SC = subcutaneous; SD = standard deviation
Source: Ward et al. CTAD 2022.

TREM2 Alzheimer's Disease Program
AL002 – Phase 2

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

Rationale

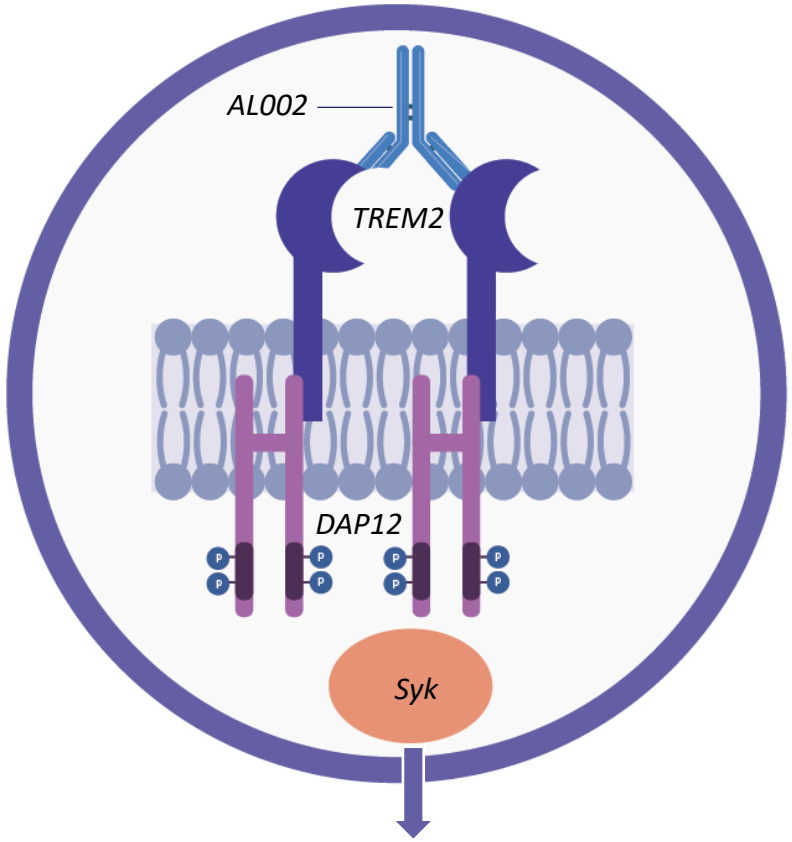
- TREM2 signaling controls critical microglial activity
- TREM2 is a prominent risk gene for Alzheimer's disease
  - Homozygous mutations cause dementia (NHD, FTD)
  - Heterozygous mutations increase risk for Alzheimer's disease by 3x
  - Ligands include APOE, an Alzheimer's risk gene

Mechanism

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

Status

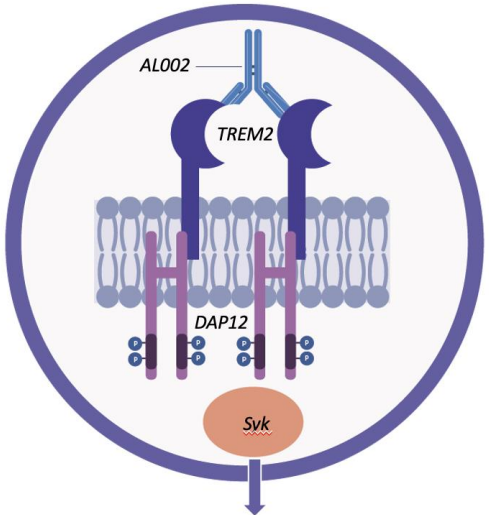
- INVOKE-2 Phase 2 double-blind, randomized, placebo-controlled clinical trial on-going



Intended to improve survival, proliferation, function of microglia

NHD = Nasu-Hakola disease
APOE = Apolipoprotein E

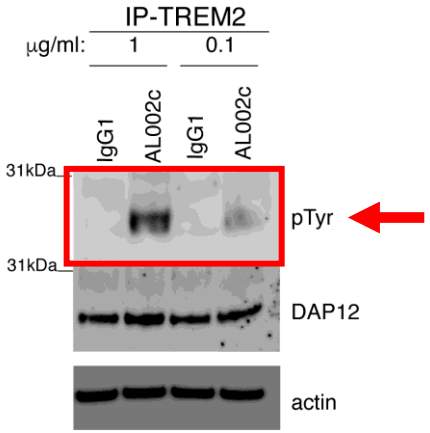
AL002 Demonstrated Biological Activity in Multiple *in vitro* Assays



Intracellular signaling

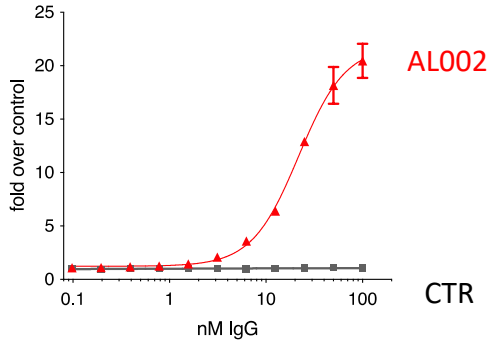
Macrophage survival

Receptor activation



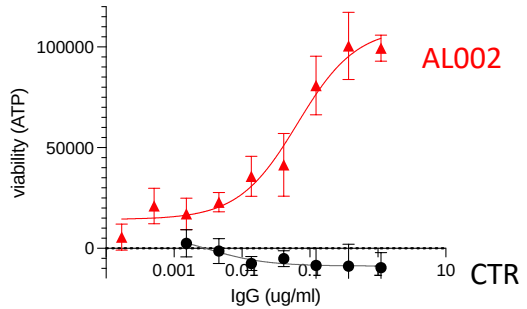
AL002 promotes TREM2-mediated DAP12 phosphorylation

Downstream effects



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

Macrophage function



AL002 increases human macrophage survival under cellular stress

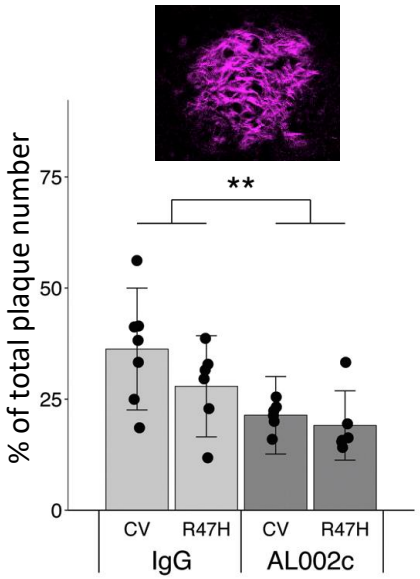
alector

Alector data on file

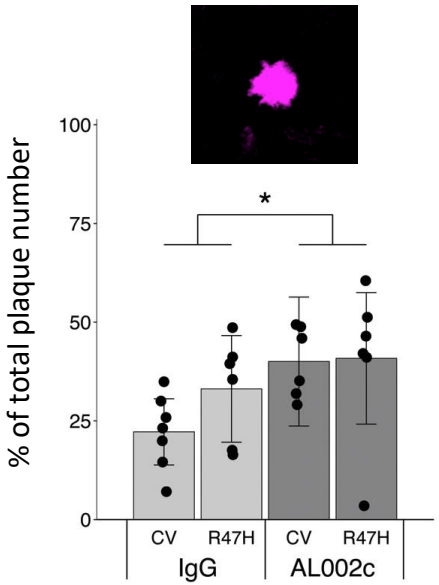
TREM2 Activation Appears to Reduce Toxic Plaques and Neuronal Damage in a Mouse Model of AD

Compaction of amyloid plaque

Filamentous Plaque



Inert Plaque



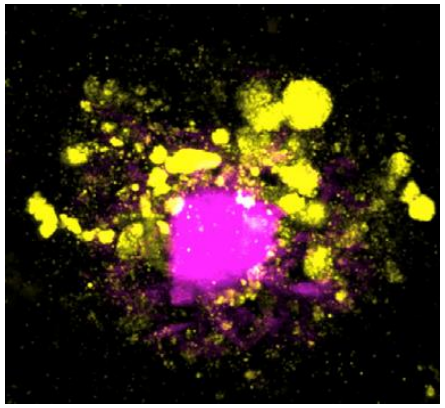
- Filamentous Plaque is considered detrimental

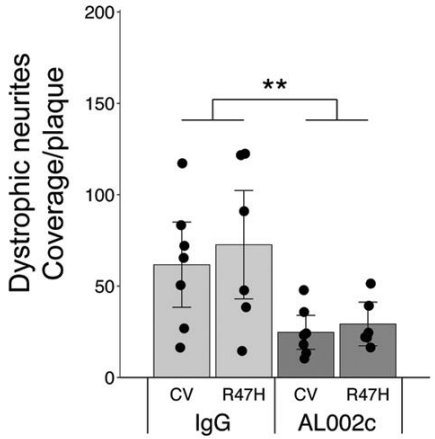
CV- mice expressing WT human TREM2

R47H- mice expressing R47H mutant TREM2

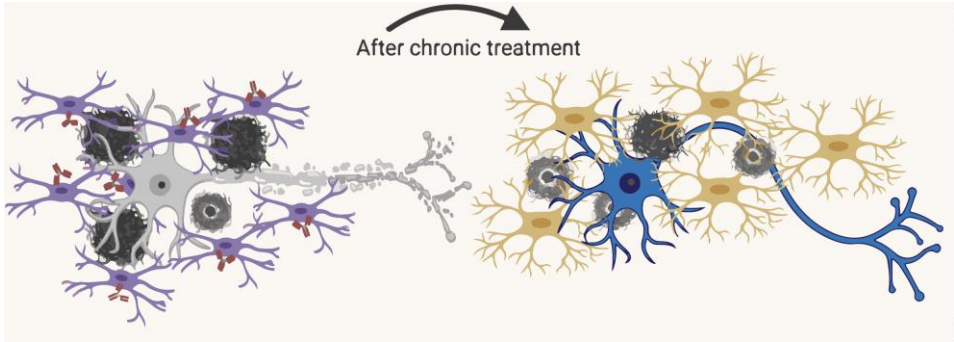
Reduction of neuronal damage

Neurite dystrophy surrounding a plaque





Alteration of pathology in the mouse

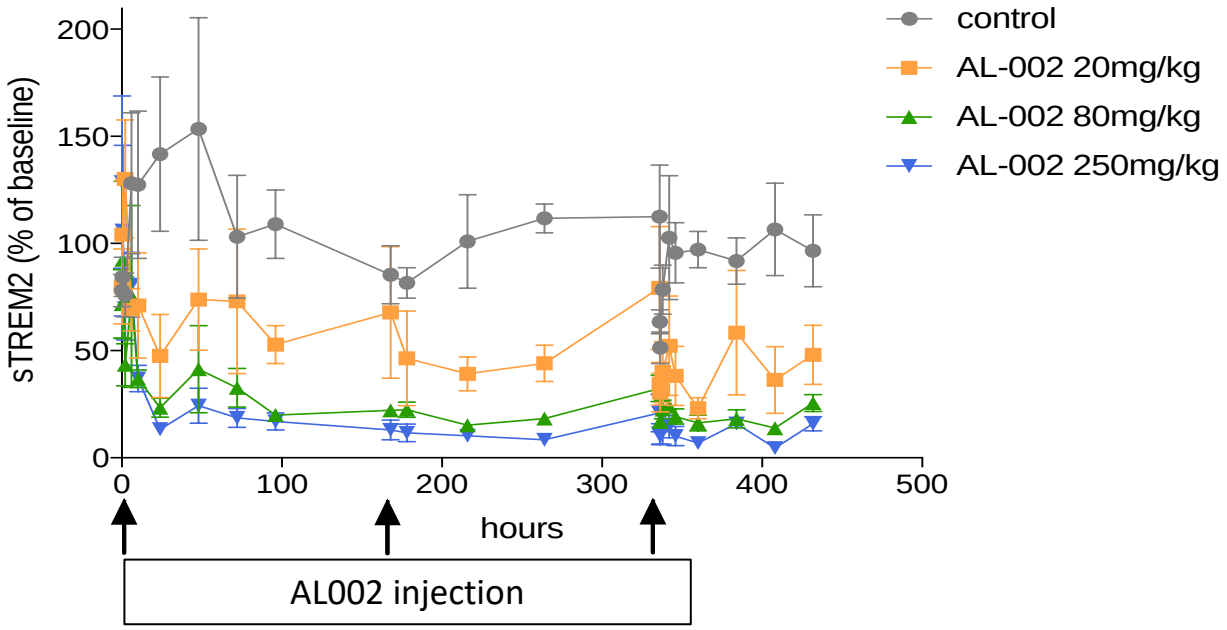


Source: Wang, Mustafa, JEM, 2020 and Yuan, Neuron 2016.
Studies conducted with AL002c, a murine version of AL002.

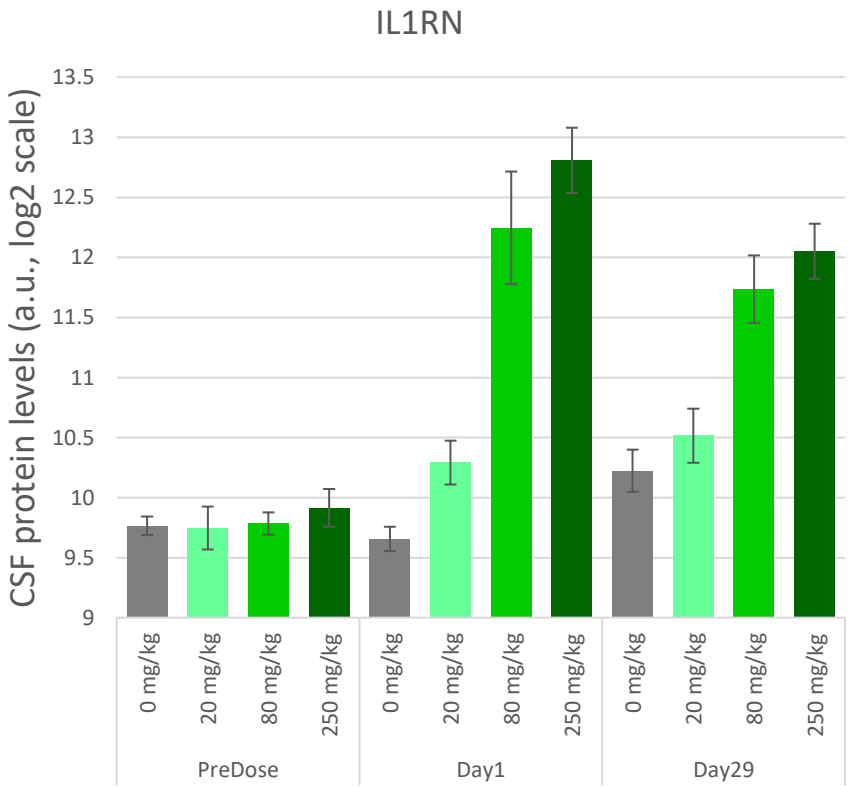
AL002 Shows Evidence of Target Engagement and Microglia Activation with Decreases in sTREM2 and Increases in IL1RN in the CSF of NHPs

Preclinical results consistent with subsequent human data

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



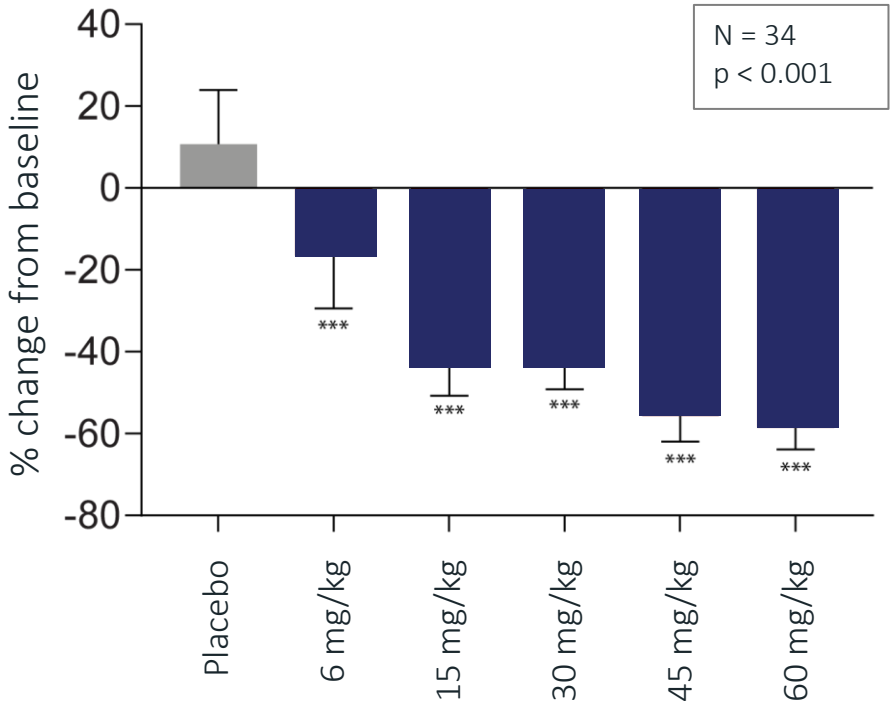
AL002 increases IL1RN in the CSF of **non-human primates** in a dose-dependent manner



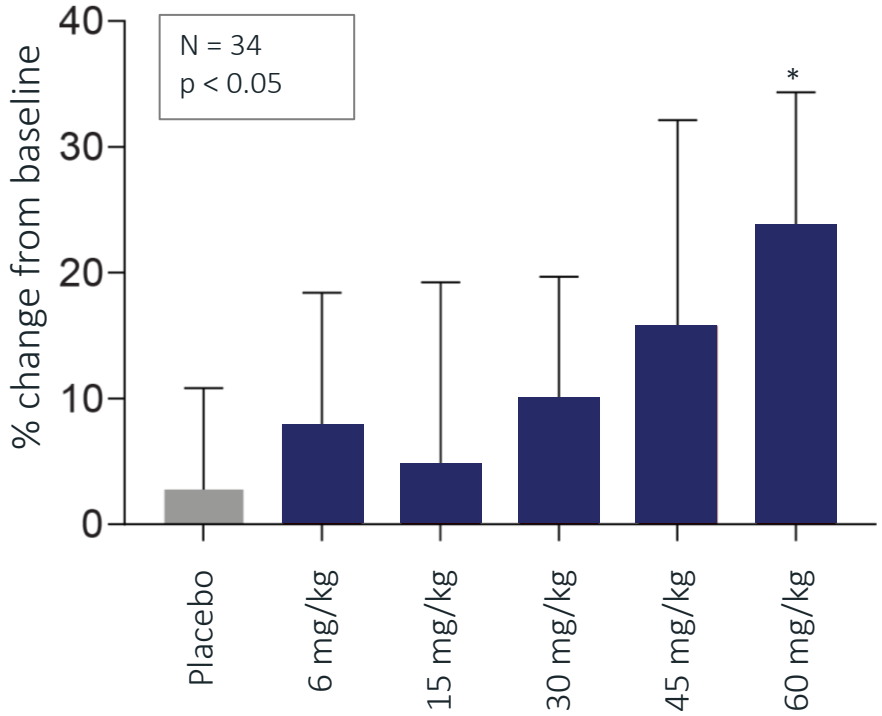
AL002 Target Engagement and Evidence of Microglia Activation Achieved in Phase 1

AL002 was generally well-tolerated and demonstrated dose-dependent target engagement and activation of microglia in healthy volunteers consistent with preclinical results[1]

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



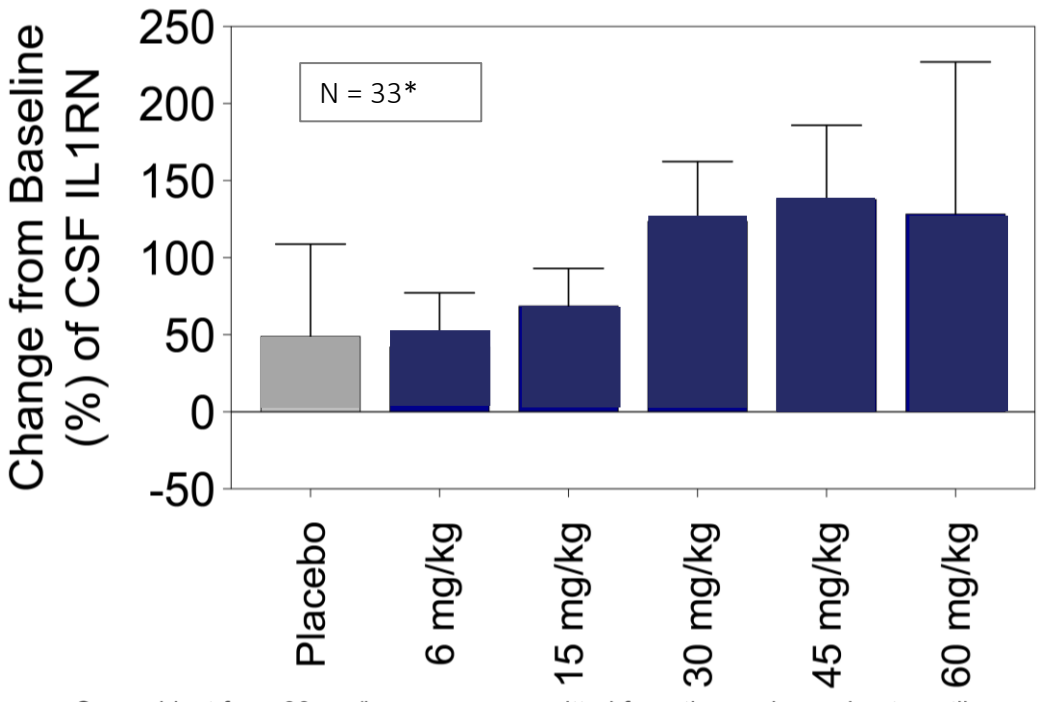
Dose-Dependent Elevation in CSF sCSF-1R (Mean +-SD), Associated with Microglia Activation[2]



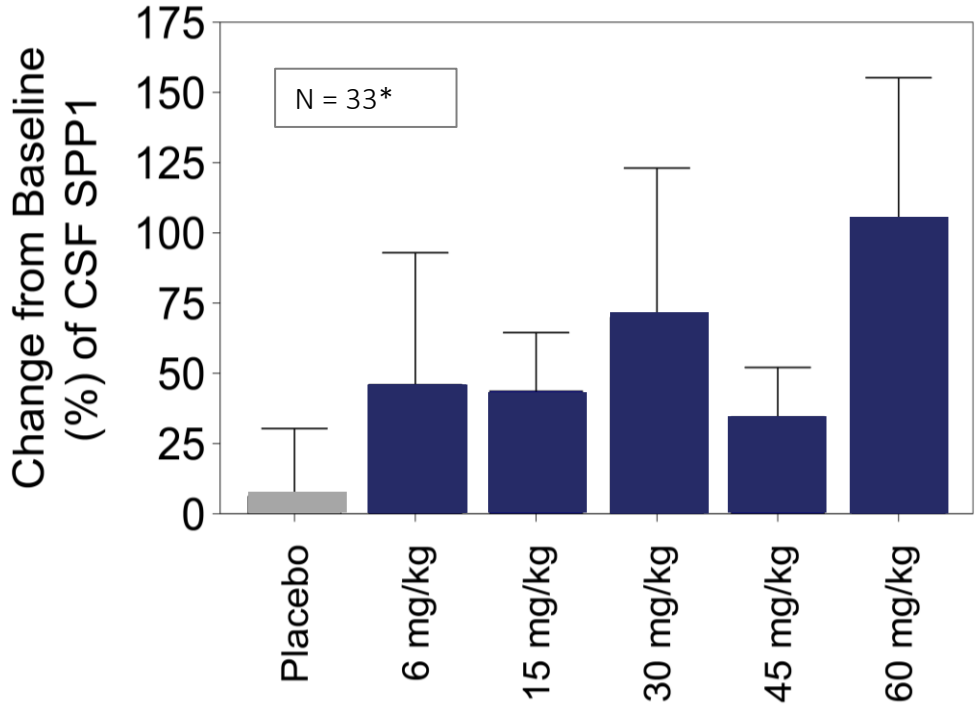
Data are presented as mean ±SD; cohort n = 6 (placebo, 6 mg/kg, 15 mg/kg, 30 mg/kg) and 5 (45 mg/kg, 60 mg/kg).
***P = 0.0001 for 6 mg/kg and P < 0.0001 for all other doses vs. pooled placebo control. *P = 0.026 at 60 mg/kg vs. pooled placebo.
[1]Phase 1 data presented at AAIC 2021; NCT03635047. [2]Wang 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

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

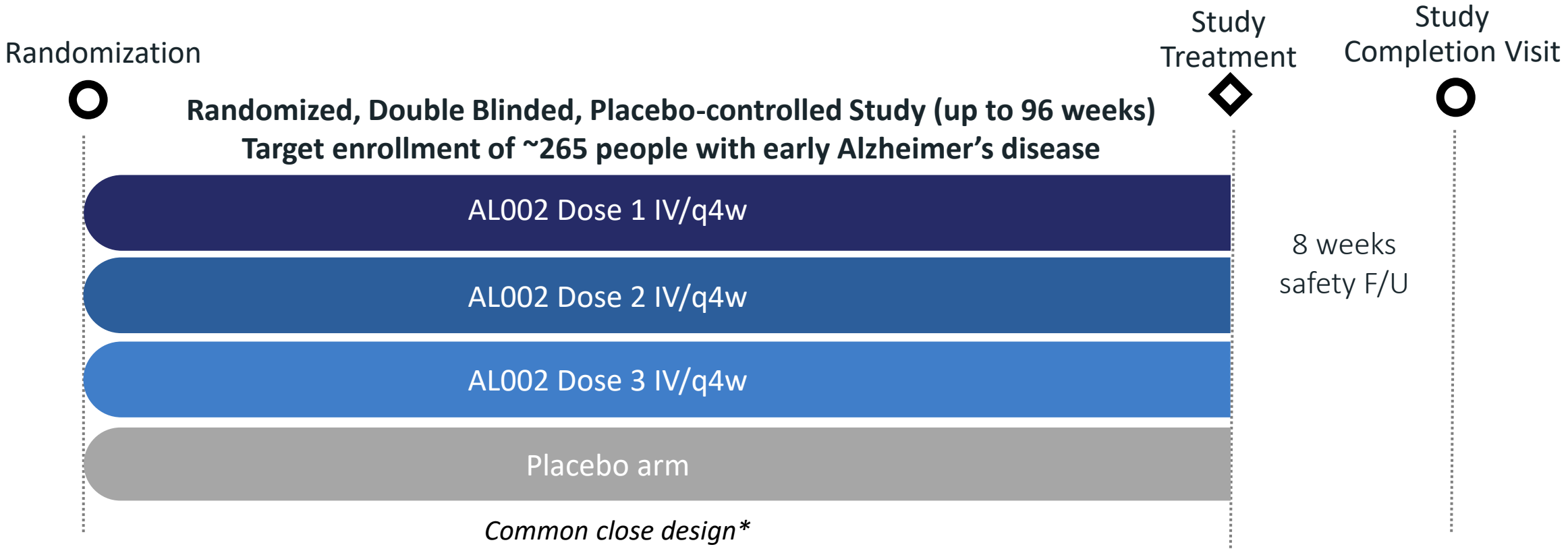


Elevation of SPP1 in CSF (Mean +-SD)
After Treatment with AL002



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.

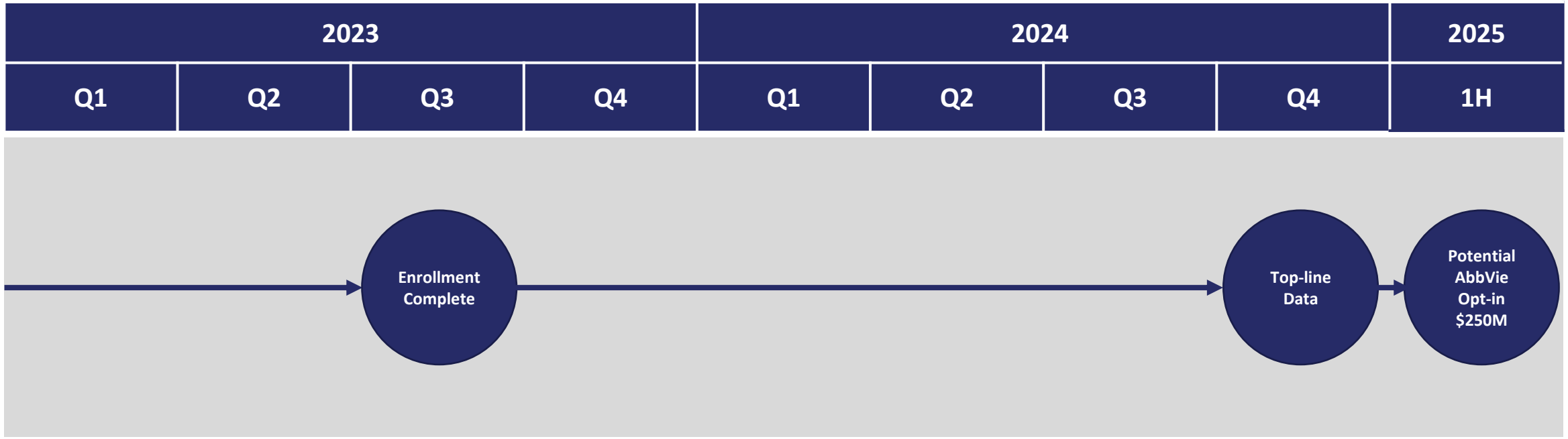
INVOKE-2 Phase 2 AL002 Study in Individuals with Early Alzheimer's Disease



PRIMARY ENDPOINT	SECONDARY CLINICAL OUTCOMES ASSESSMENTS:	EXPLORATORY ENDPOINTS
CDR-SB	RBANS, ADAS-Cog13, ADCS-ADL-MCI	vMRI, CSF, Plasma Biomarkers and PET scans

* Common close design, while treatment is up to 96 weeks, the study is completed when the last patient reaches 48 weeks of therapy (plus 8 weeks of safety follow-up).

AL002: The Most Advanced Clinical Program Targeting TREM2



- Active engagement with sites and investigators (post removal of ApoE e4 homozygous population)
- Significant momentum in engagement (increasingly recognized as a program with transformative potential)
- ARIA events being actively monitored and managed (potential biomarker for amyloid modulation)

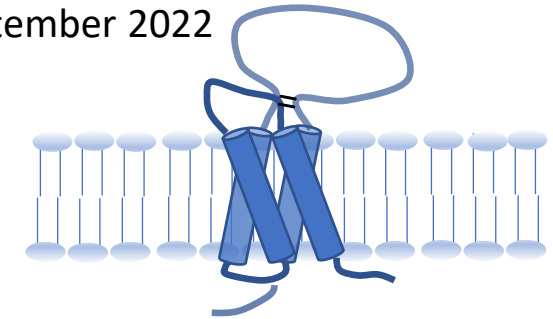
MS4A Alzheimer's Disease Program
AL044 – Phase 1

Background on AL044: Targeting a Candidate Master Regulator of Microglia

Overview of MS4A Target and AL044 Candidate

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

MS4A Protein Structure



Effects of MS4A on AD

Protective Allele	Effects on AD	Risk Allele
↓	AD Risk	↑
↓	Rate of cognitive decline	↑
↓	Ab Plaques & CSF Tau	↑
↓	Rate of brain Tissue Loss	↑
↓	Rate of Conversion from MCI to AD	↑
↑	Age of onset and survival	↓
↑	CSF Soluble TREM2	↓
↑	Protective Interactions with APOE4	↓

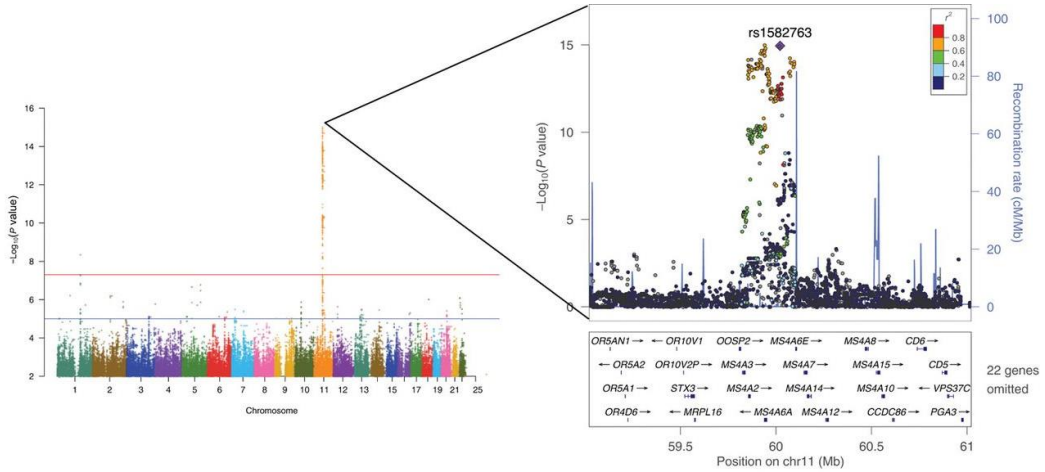
Source: doi:10.1126/scitranslmed.aau2291, Sci Transl Med, 2019.; NATURE IMMUNOLOGY | VOL 20 | AUGUST 2019 | 1012–1022; DOI: 10.1016/j.jalz.2016.06.005; Michael Ewers et al., Sci Transl Med 2019;11:eaav6221.

MS4A Regulates Level of Soluble TREM2 in the CSF

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

GWAS of CSF sTREM2 Level

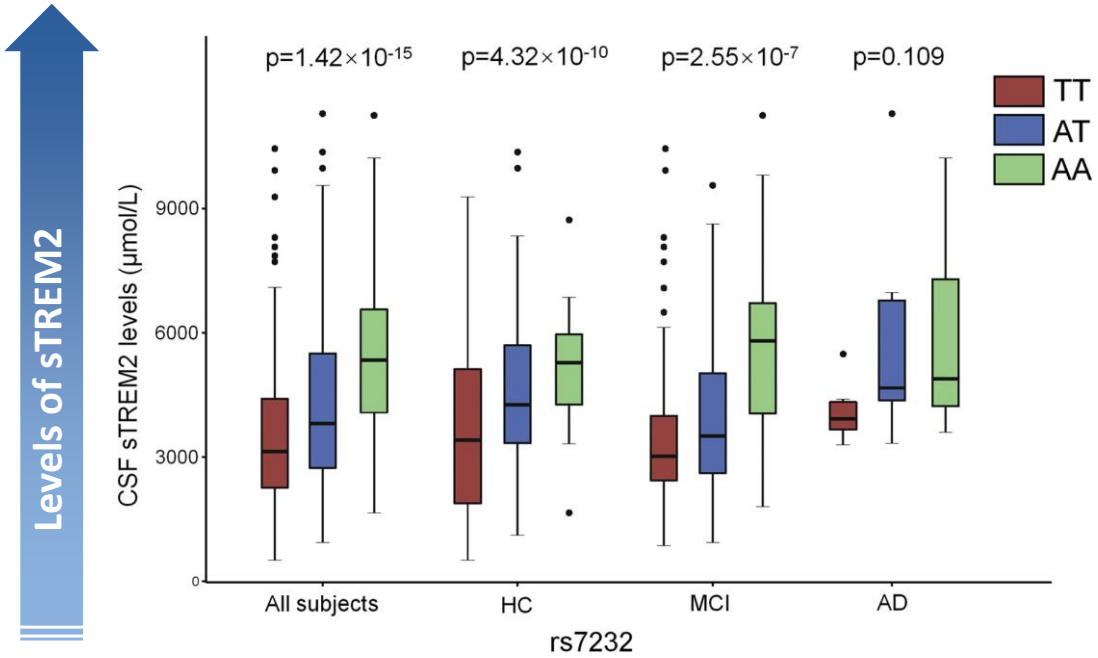
Manhattan and regional plot of the results from QTL analysis for CSF sTREM2 levels.



The same MS4A SNP's/eQTLs associated with protection from AD also regulate the level of sTREM2 in the human CSF

Effect of MS4A SNPs on sTREM2 Expression

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



MS4A AD Risk Variants HC, MCI and AD

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

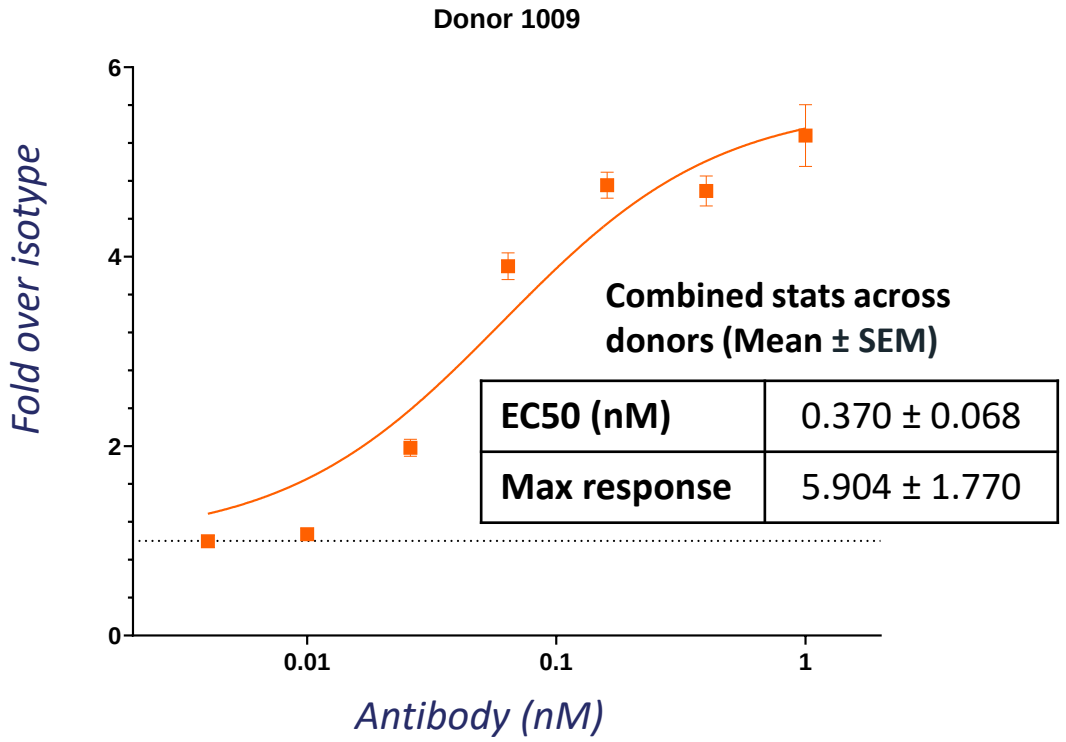
Source: Deming et al., Sci. Transl. Med. 11, eaau2291 (2019). Front Aging Neurosci . 2019 Oct 25;11:297; Neurobiology of Aging Volume 84, December 2019, Pages 241.

;

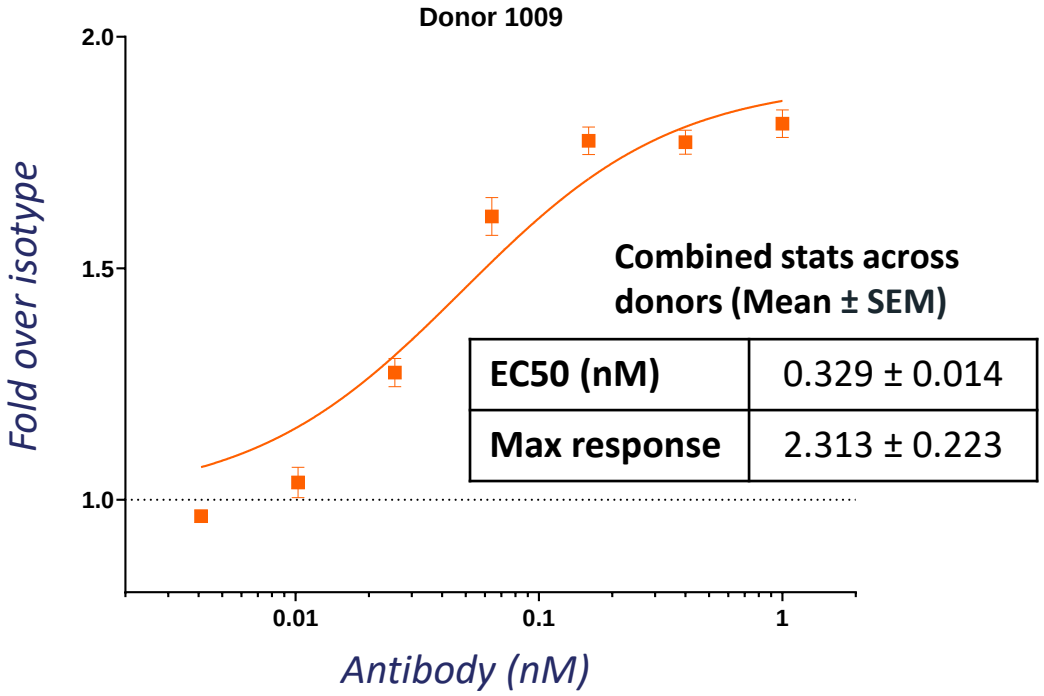
AL044 Phenocopies and Exceeds the Elevation of Soluble and Membrane TREM2 by the Protective Allele

The protective allele of MS4A increases sTREM2 by ~20%

sTREM2 Levels After Treatment with AL044 for 48 Hours



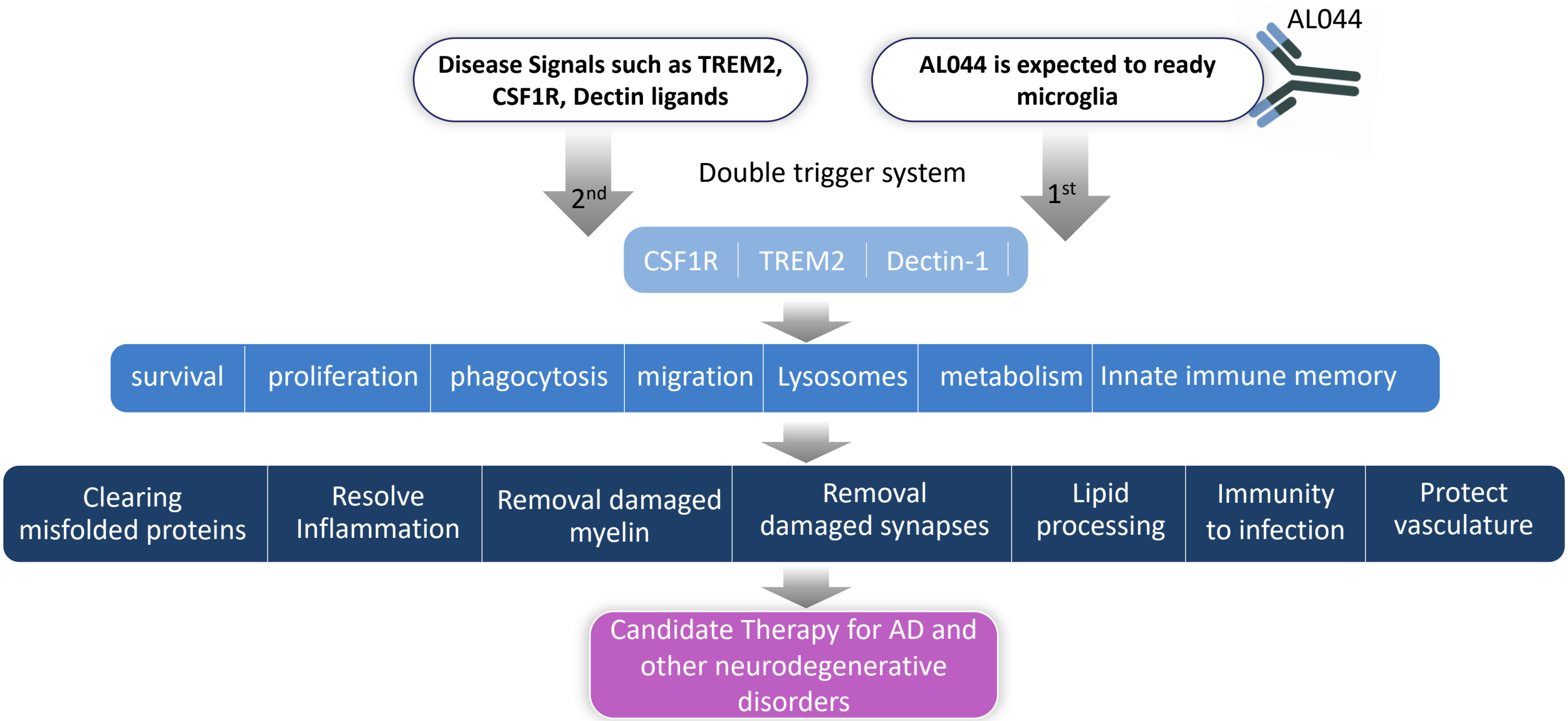
Membrane TREM2 Levels After Treatment with AL044 for 48 Hours



Source: RTR-AL044-012

Note: Monocyte-derived macrophages. Treated for 48 hours. Membrane TREM2 measured by flow cytometry. Soluble TREM2 measured by MSD.

AL044: Targeting a Candidate Master Immune Checkpoint Regulator of Microglia



Alector Oncology Overview

Neurodegeneration and Cancer Converge on Innate Immunity

Innate immunity plays critical role in both neurodegeneration and cancer

NEURODEGENERATION

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

Tumor associated Macrophage (TAMs)

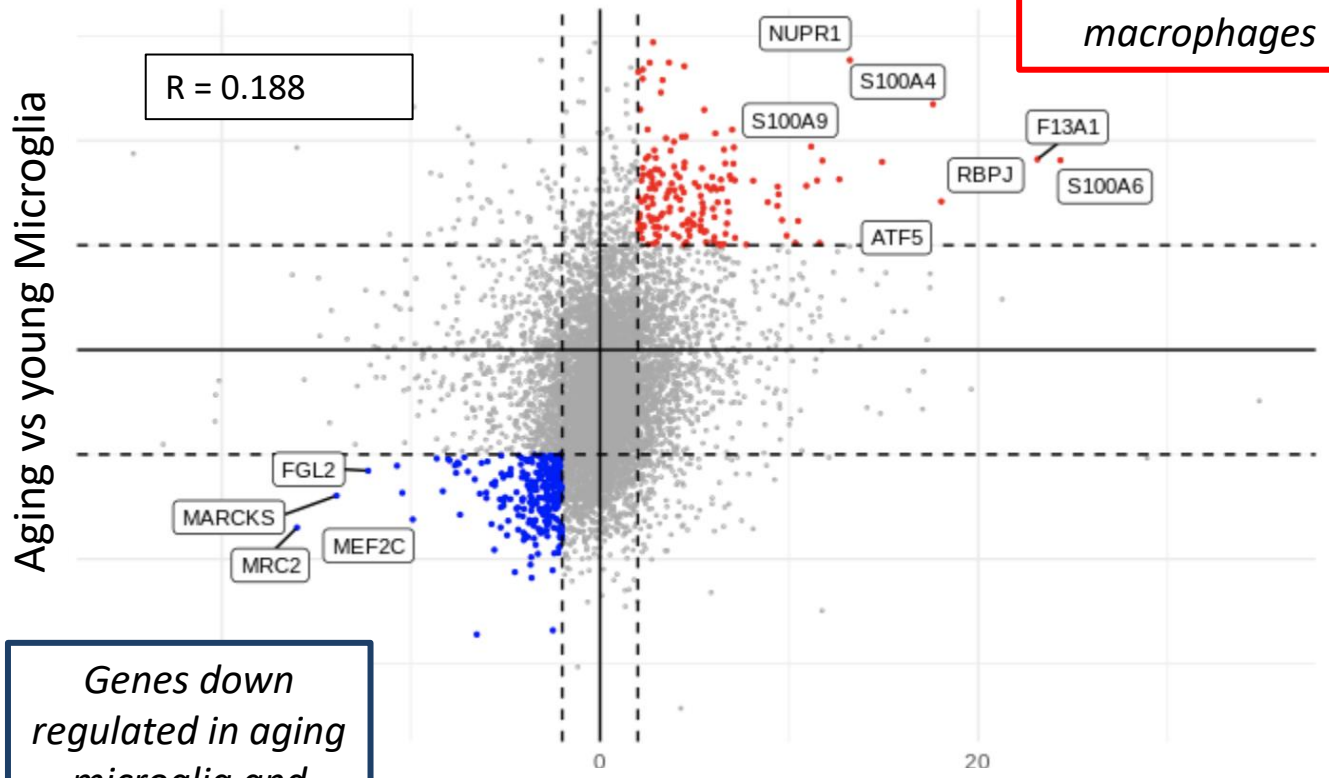
Aging Microglia

Reprogramming tumor associated macrophages (TAMs) to treat cancer

CANCER

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

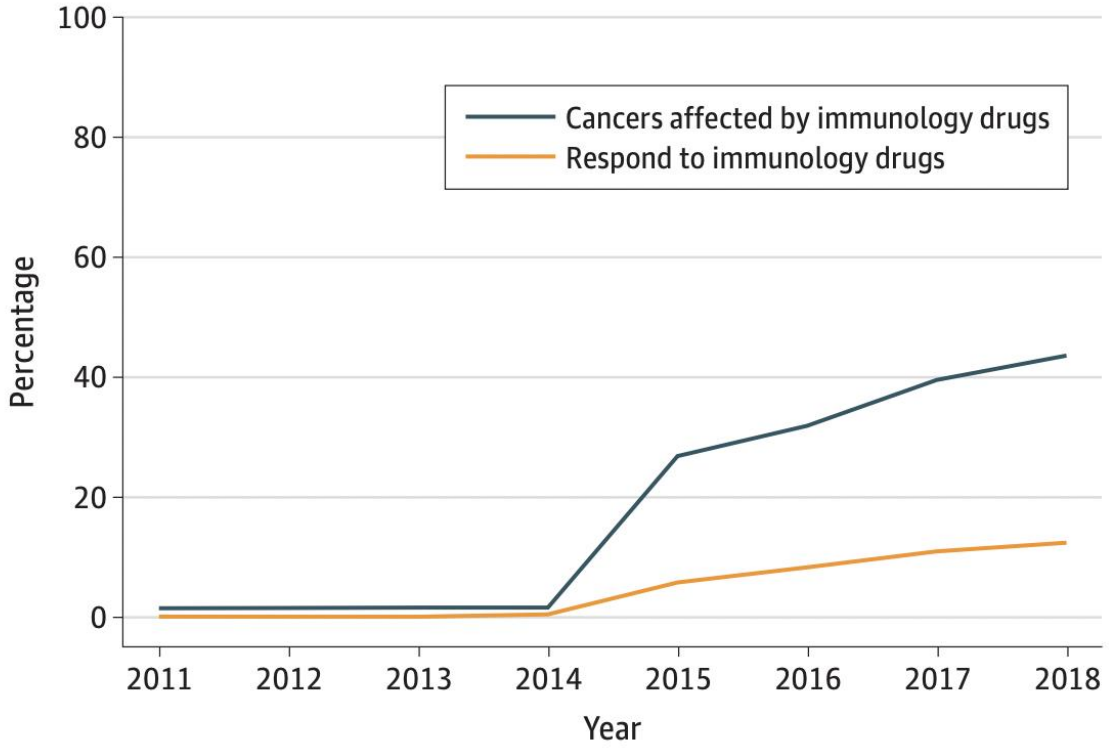
Genes upregulated in aging microglia and tumor macrophages



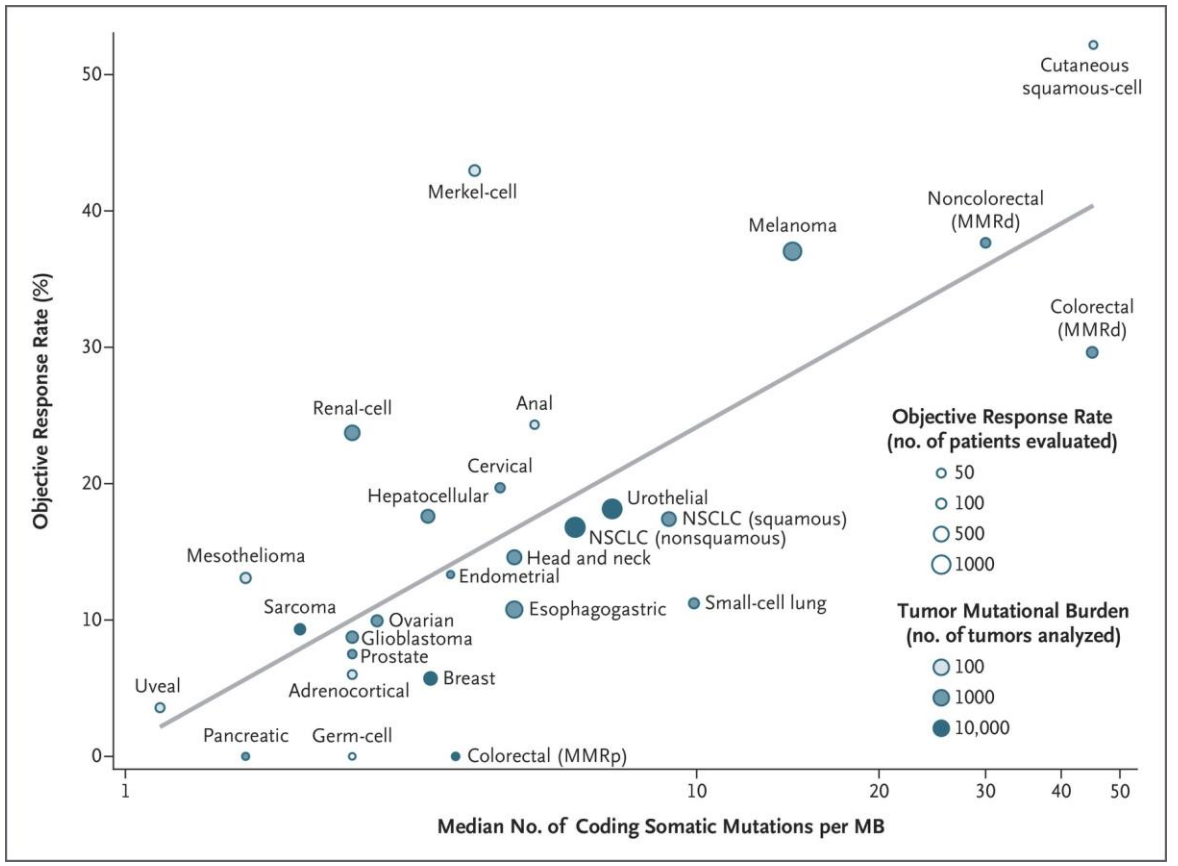
Genes down regulated in aging microglia and tumor macrophages

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

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



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



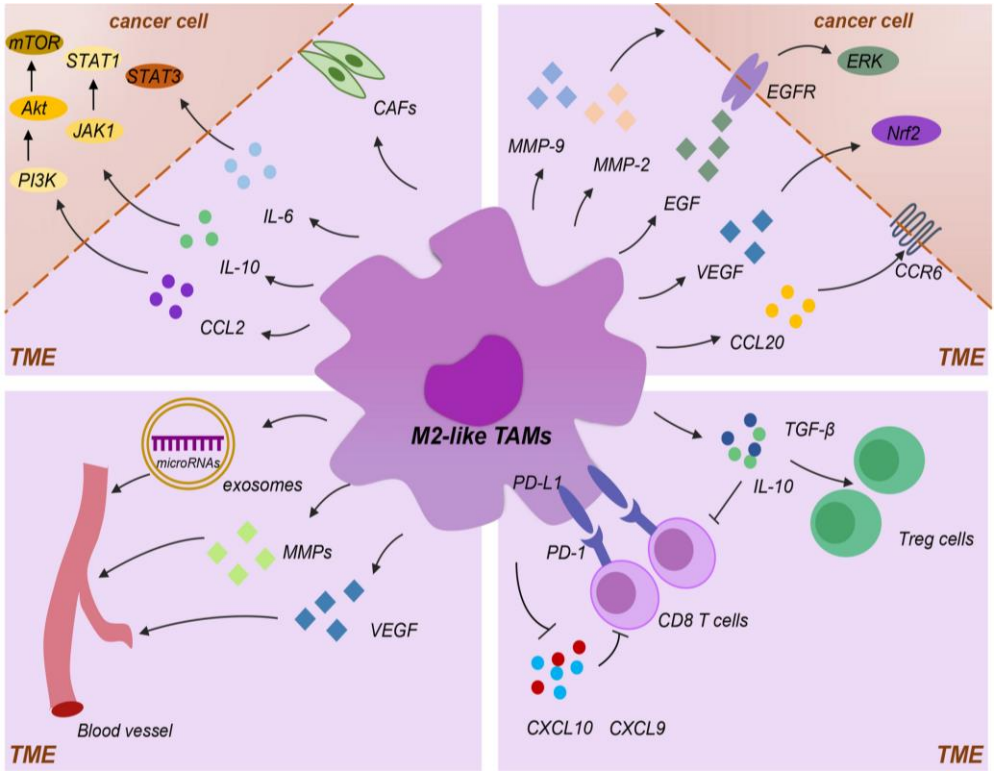
N Engl J Med 2017; 377:2500-2501

TAMs Lead to Poor Tumor Prognosis and Resistance to Immunotherapy in Cancer

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

Promote resistance to chemotherapy and radiotherapy

Promote tumor neo vascularization and growth



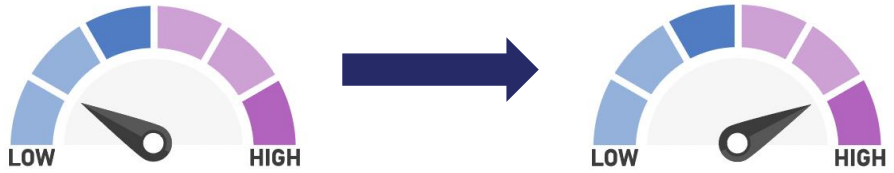
Promote tumor proliferation, invasion, migration and metastasis

Suppress infiltration, trafficking and activation of T-cell, stimulate resistance to CAR-T therapy

Alector's Therapeutic Strategy is to Reprogram TAMs (Rather Than Blocking or Killing Them) by Targeting Genetically Validated TAM Immune Checkpoints

Reprogramming TAMs to potentially cure cancer

Alector innate Immuno-oncology therapeutics reprogram TAMs



Immunosuppressive pro-tumorigenic

Immuno-promoting anti-tumorigenic

Expected activities of Alector's TAM checkpoint drugs

Untreated TAMs	Activities in the cancer micro-environment	Re-program TAMs
↓	*Stimulate anti tumor activity of T, B, natural killer, macrophages, dendritic cells*	↑
↓	*Suppress tumor growth, angiogenesis and metastasis*	↑
↓	*Augment T-cells checkpoint therapy, CAR-T, vaccine, chemo & radio-therapy*	↑

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

Yang et al, Science Direct 2020

Alector's Pipeline of Myeloid Cell Cancer Therapeutic Programs

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

Program	Target	Discovery Biology	Target Validation	Lead Selection	IND Enabling	Phase 1
AL009	Multi Siglecs					
AL008	SIRP-α					
ADP020	Undisclosed					
ADP036	Undisclosed					
ADP042	Undisclosed					

Translating Scientific Insights into a Broad Portfolio of First-in-Class Programs

NOVEL APPROACH

Founded to pioneer a new field of research: **Immuno-neurology**

Informed by **neuroscience, human genetics and immunology**

Substantial IP portfolio established: *41 issued patents, 500+ patent applications*

MULTIPLE CLINICAL TRIALS

PGRN Phase 3 Program for FTD-GRN
TREM2 Phase 2 Program for Early AD

PGRN Phase 2 Program for FTD-C9orf72
MS4A Phase 1 Program for AD

Pre-Clinical Portfolio and Discovery Platform
Multiple immuno-neurology and oncology opportunities

WORLD CLASS PARTNERS

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

GSK

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

abbvie

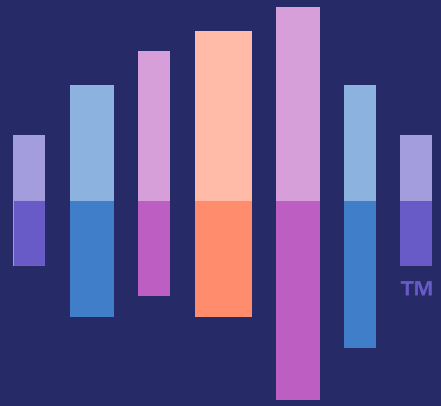
STRONG FINANCIALS

$758 MILLION IN CASH: RUNWAY THROUGH 2025

alector

FTD = Frontotemporal dementia, PD = Parkinson's Disease, AD = Alzheimer's Disease

Note: As of September 30, 2022, Alector's cash, cash equivalents and investments totaled $758.3 million.



Thank You