Alector Corporate Overview

January 2025

Forward-Looking Statement

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potentially,” “predict,” “should,” “will” or the negative of these terms or other similar expressions. Forward-looking statements contained in this presentation also include, but are not limited to, statements regarding: our future financial condition, including the sufficiency of cash to fund operations through 2026; results of operations; business strategy and plans; the beneficial characteristics, safety, efficacy, and therapeutic effects of our product candidates; our plans, timelines and expectations related to our product candidates and our other clinical and pre-clinical programs, including with respect to the availability of data, the initiation of future clinical trials and plans and expectations regarding planned regulatory filings with respect to such programs; expectations regarding the timing and financial benefit of our collaborations; and objectives of management for future operations, as well as statements regarding industry trends.

We, Alector, Inc. (“Alector”), have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: Alector’s plans relating to its research programs, preclinical and clinical development programs and the development and manufacturing of its product candidates and blood-brain barrier technology platform; the ability of Alector’s clinical trials to demonstrate safety and efficacy of its product candidates, and other positive results; the timing and focus of Alector’s clinical trials, and the reporting of data from those trials, including the anticipated timing and detail regarding the release of data for INFRONT-3 and PROGRESS-AD; Alector's plans relating to commercializing its product candidates, if approved, including the geographic areas of focus and sales strategy; the expected potential benefits of strategic collaborations with third parties and Alector's ability to attract collaborators with development, regulatory and commercialization expertise; Alector’s estimates of the number of patients in the United States, the European Union and world-wide who suffer from the diseases it is targeting and the number of patients that will enroll in its clinical trials; the anticipated timing of enrollment in its clinical trials; the size of the market opportunity for Alector’s product candidates in each of the diseases it is targeting; Alector’s ability to expand its product candidates into additional indications and patient populations; the success of competing therapies that are or may become available; the beneficial characteristics, safety, efficacy, and therapeutic effects of Alector’s product candidates; the timing or likelihood of regulatory filings and approvals, including Alector’s expectation to seek special designations, such as orphan drug designation, for its product candidates for various diseases; Alector’s ability to obtain and maintain regulatory approval of its product candidates; Alector's plans relating to the further development and manufacturing of its product candidates, including additional indications that it may pursue; existing and future regulations and regulatory developments in the United States and other jurisdictions; Alector’s reliance on third parties to conduct clinical trials of its product candidates, and for the manufacture of its product candidates for preclinical studies and clinical trials; the impact of worldwide economic conditions, including macroeconomic downturns stemming from increased inflation, supply chain and other economic impacts of the coronavirus (COVID-19) pandemic and geopolitical events on our business; and the other risks, uncertainties and assumptions discussed in the public filings we have made and will make with the Securities and Exchange Commission (“SEC”). These risks are not exhaustive. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements.

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

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

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

Except as required by law, we undertake no obligation to update any statements in this presentation for any reason after the date of this presentation. We have filed Current Reports on Form 8-K, Quarterly Reports on Form 10-Q, Annual Reports on Form 10-K, and other documents with the SEC. You should read these documents for more complete information about us. You may obtain these documents for free by visiting EDGAR on the SEC website at www.sec.gov.

Alector Value Proposition

Bold Vision

A world where we made degenerative brain disorders history

Innovative Science

3R Strategy: Remove, Replace, Restore

Targeting 2 INDs in 2026

Novel Clinical Programs

Targeting Pivotal Ph 3 data in FTD Q4 2025

Targeting Ph 2 enrollment completion in AD in mid-2025

Advanced Technologies

Versatile Alector Brain Carrier (ABC) technology platform

Well Resourced

Experienced leadership and strong financial resources

Global Partnership

Profit-sharing collaboration with GSK for multiple PGRN product candidates

Innovative Science with 3R Strategy of Remove, Replace, Restore

Remove toxic proteins, **Replace** critical deficient proteins, and **Restore** immune and nerve cells to normal functioning

REMOVE

Abeta+ABC
Tau+ABC
Tau siRNA + ABC

REPLACE

Latozinemab
AL101
GCase+ABC

RESTORE

Reelin

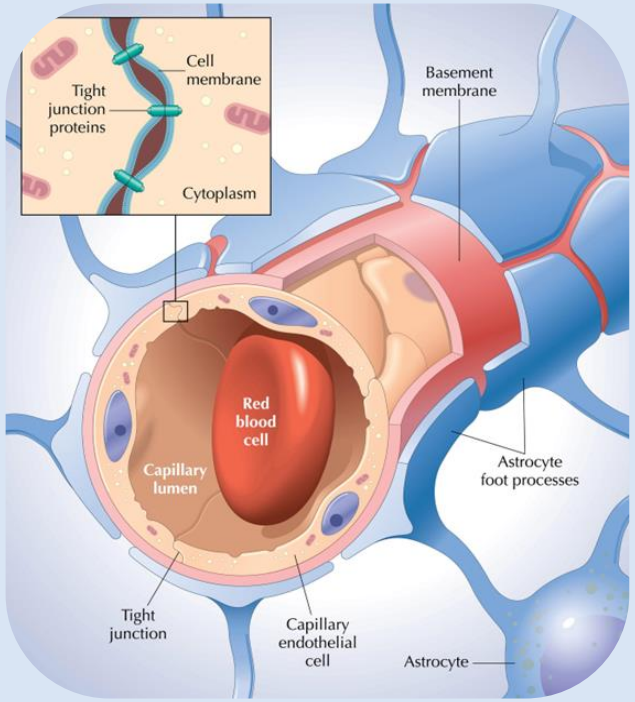
Leveraging our drug development expertise and proprietary technology to advance a curated portfolio of programs that **address genetically-validated targets.**

Alector Brain Carrier (ABC): Enhanced Delivery of Biologics Across the BBB

Supports portfolio of genetically validated programs for neurodegenerative diseases

Blood Brain Barrier (BBB)

- Maintains homeostasis and protects by restricting access
- Poses a challenge for how much drug gets into the brain



Alector Brain Carrier (ABC) is a proprietary, versatile BBB technology platform designed to overcome challenges of drug delivery to the CNS

- Selectively applied to our pipeline
- Aims to improve outcomes while reducing costs by enhancing delivery of therapeutics to achieve deeper brain penetration at lower doses
- Initial focus is on two key targets: transferrin receptor (TfR) and CD98hc
- Unique versatility and tunability may allow for the delivery of a range of cargos, including antibodies, proteins, enzymes, and nucleic acids
- May facilitate more convenient subcutaneous delivery

https://www.netterimages.com/the-blood-brain-barrier-labeled-hansen-physiology-1e-physiology-james-a-perkins-4921.html

Development Portfolio: Advancing Late-Stage Programs with Established Partner, Supported by Genetically Validated Research Portfolio and Proprietary ABC Platform

TARGET	CANDIDATE	RESEARCH	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	ALECTOR'S COMMERCIAL OWNERSHIP	RIGHTS
PGRN	Latozinemab	FTD-*GRN*					U.S. 50-50 profit share with co-promote. Tiered double-digit royalties ex-U.S.	GSK
	AL101	AD						GSK

Proprietary ABC Technology Selectively Applied

Aβ	ADP037-ABC	AD	alector
GCase	ADP050-ABC	PD, LBD	alector
Reelin	ADP056	AD	alector
Tau	ADP063-ABC	AD, FTD	alector
Tau	ADP064-ABC	AD, FTD	alector

IP portfolio across all programs contains 60+ patent families, which include 128 issued patents and >500 pending patent applications directed to more than 25 targets and/or technologies

$457.2 MILLION[1] IN CASH PROVIDES RUNWAY THROUGH 2026

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1. Cash, cash equivalents, and marketable securities as of September 30, 2024, were $457.2 million.

FTD-*GRN* = frontotemporal dementia with a progranulin gene mutation, AD = Alzheimer's disease, PD= Parkinson's disease, BD = Lewy body dementia, ABC = Alector Brain Carrier

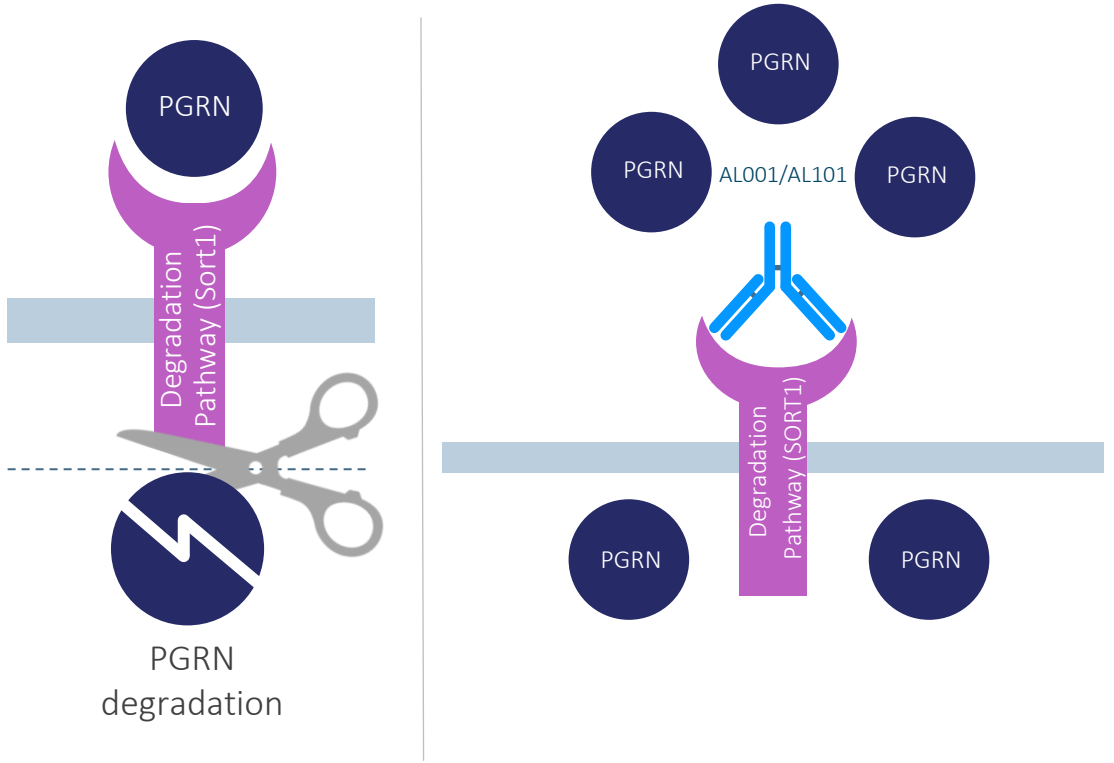
PGRN Programs

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

PGRN: Genetic and Biologic Rationale

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

Latozinemab and AL101: PGRN Elevating Program



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

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

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

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

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

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

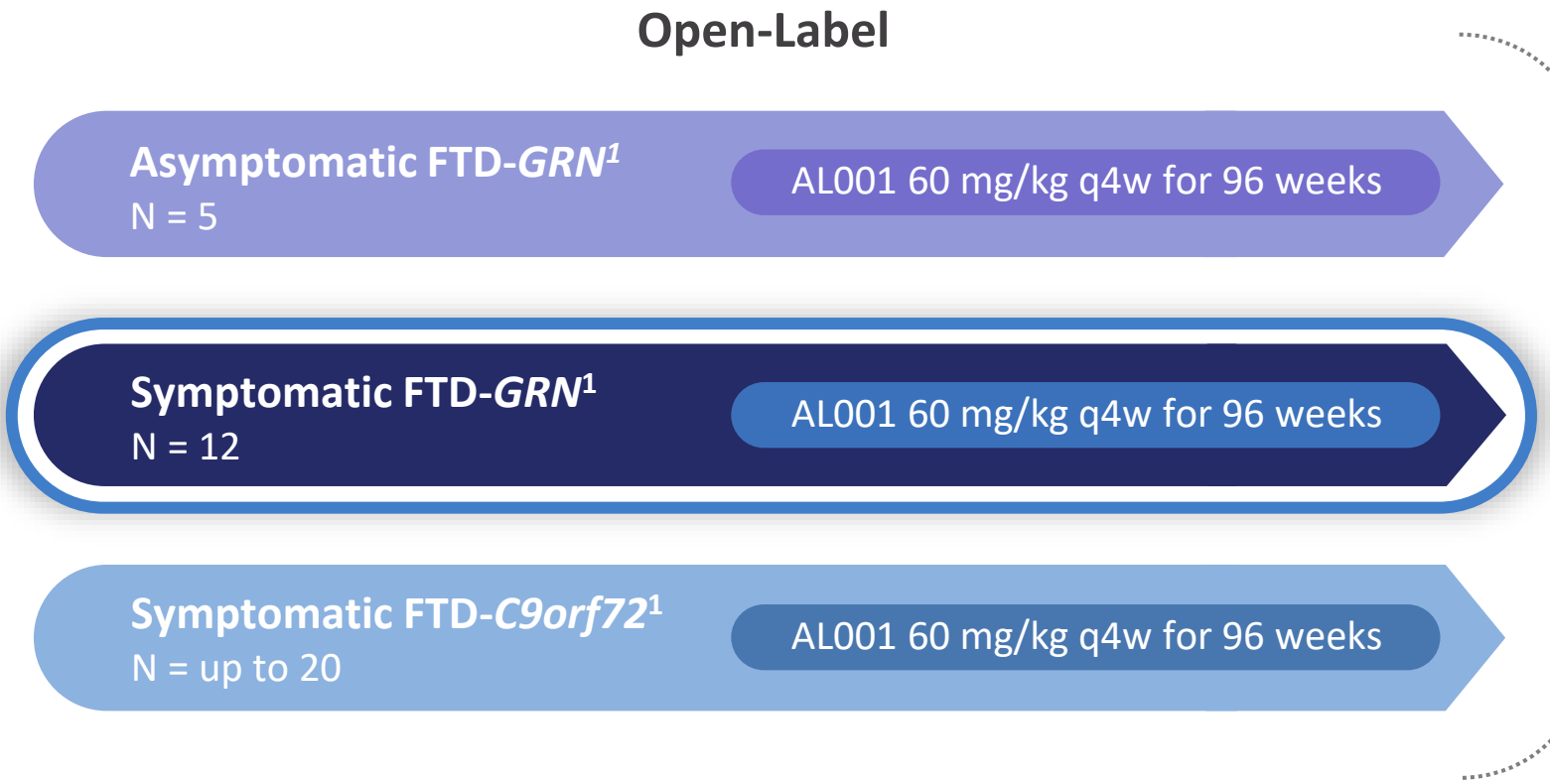
- **Diagnosis:**
  - Compulsive behavior, lack of restraint, apathy, anxiety, and aphasia
  - Symptoms typically begin between the ages of 45-64 years old
  - Frequently misdiagnosed as AD, depression, PD, or psychiatric condition

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

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

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

INFRONT-2: Phase 2 Trial with Latozinemab in FTD



PRIMARY ENDPOINT

Safety and Tolerability

SECONDARY ENDPOINT

PK, PD

EXPLORATORY ENDPOINTS

CSF and Plasma Biomarkers (Lysosomal, inflammation, neurodegeneration)

Volumetric MRI (vMRI)

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

AL001 = latozinemab

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)

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

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

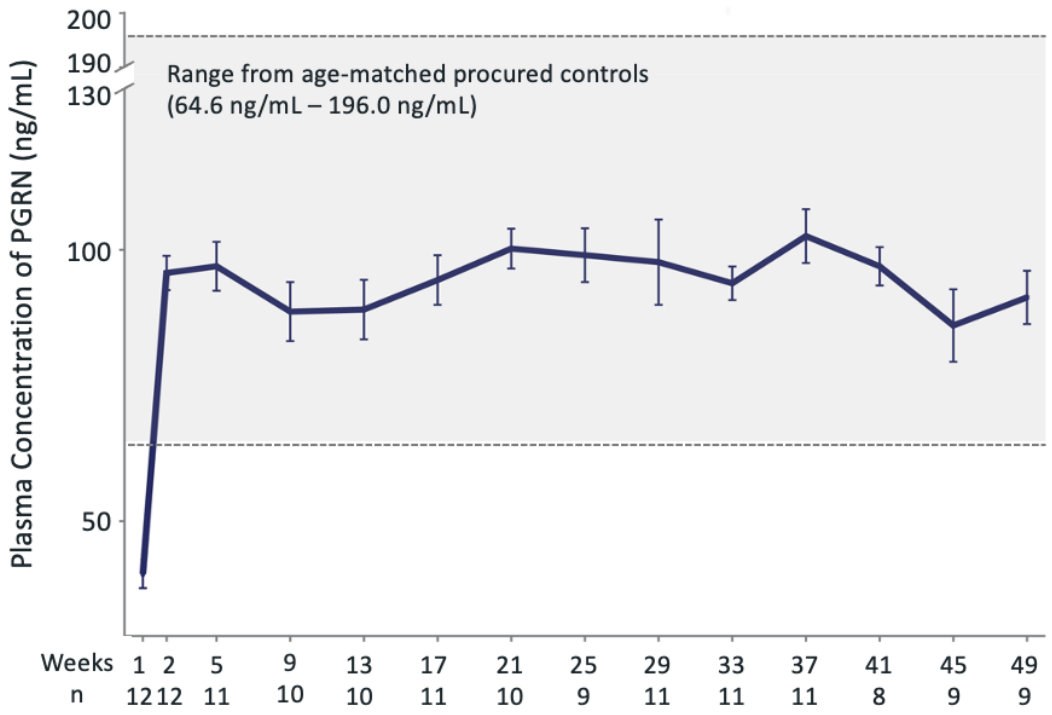
TARGET ENGAGEMENT	BIOMARKERS OF DISEASE ACTIVITY				CLINICAL BENEFIT
PGRN (Plasma and CSF)	Lysosomal Dysfunction	Inflammation	Brain Health	Brain Atrophy	Clinical Outcome Assessments
PGRN CSF and plasma PGRN levels	**e.g. CTSD, LAMP1** Dysfunctional lysosomes are hallmarks of FTD-*GRN*	**e.g. C1QB** Elevation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

CTSD = cathepsin D; LAMP1 = lysosomal associated membrane protein 1; C1QB = complement C1q B chain; GFAP = glial fibrillary acidic protein
CDR® plus NACC FTLD-SB = Clinical Dementia Rating (CDR) dementia staging instrument plus National Alzheimer's Coordinating Center (NACC) behavior and language domains frontotemporal lobar degeneration (FTLD) sum of boxes (SB)

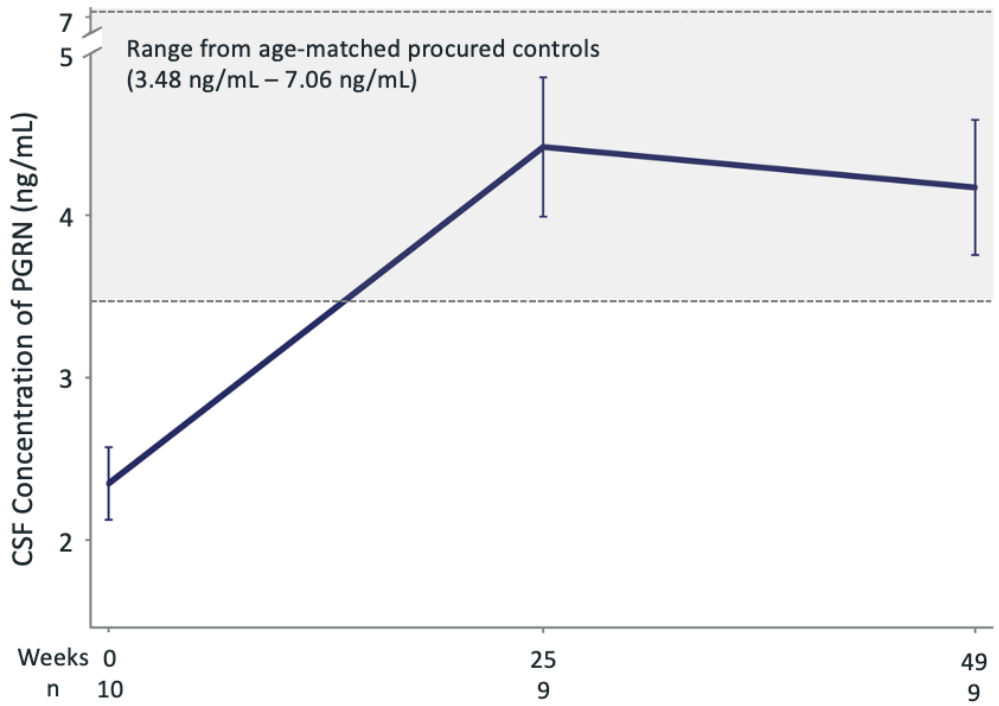
INFRONT-2: Latozinemab Restores PGRN in Plasma and CSF to Levels Seen in Healthy Volunteer Age-Matched Controls

ACHIEVED PGRN RESTORATION IN FTD-*GRN* PARTICIPANTS

PGRN Plasma Concentration



PGRN CSF Concentration

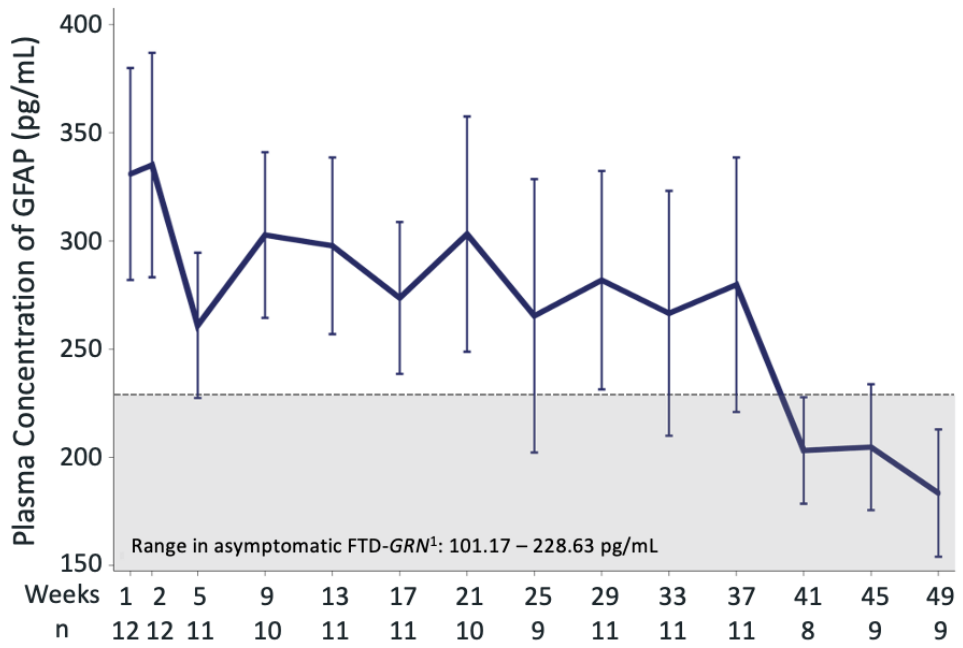


Data cut-off June 15, 2021
Mean +/- SEM
Source: AAIC 2021.

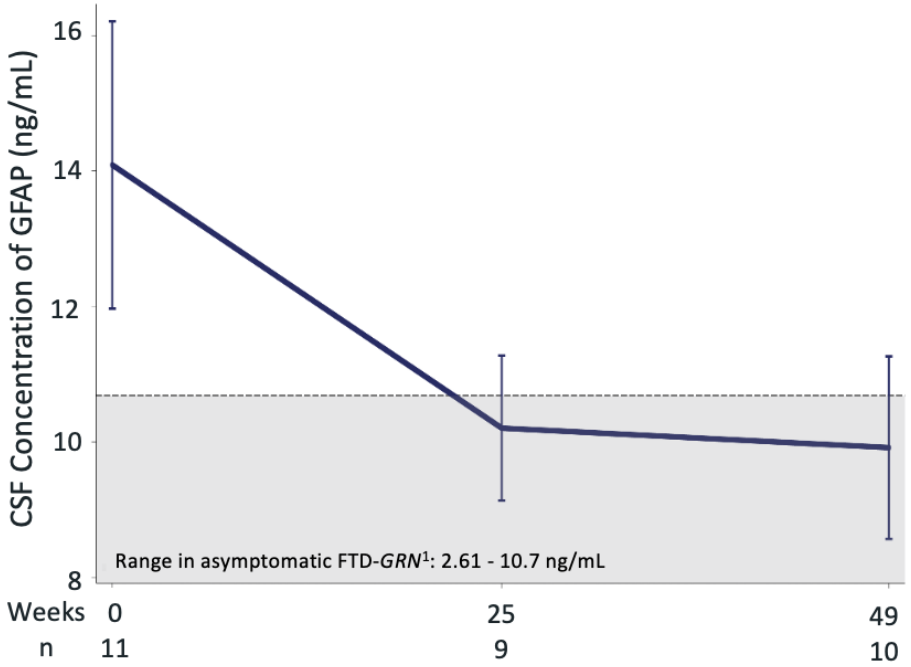
INFRONT-2: Latozinemab Treatment Decreases Glial Fibrillary Acidic Protein (GFAP) Levels Towards Range Seen in Asymptomatic Carriers of FTD-*GRN* Mutation

BIOMARKERS OF DISEASE ACTIVITY – ASTROGLIOSIS

GFAP Plasma Concentration



GFAP CSF Concentration



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

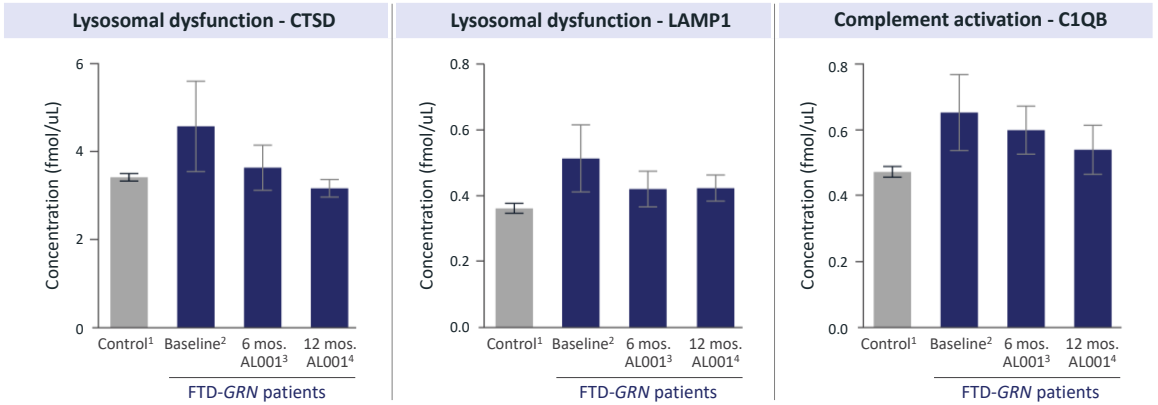
INFRONT-2: Encouraging Trends Across Biomarkers Of Disease Activity

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

LYSOSOMAL AND INFLAMATORY BIOMARKERS

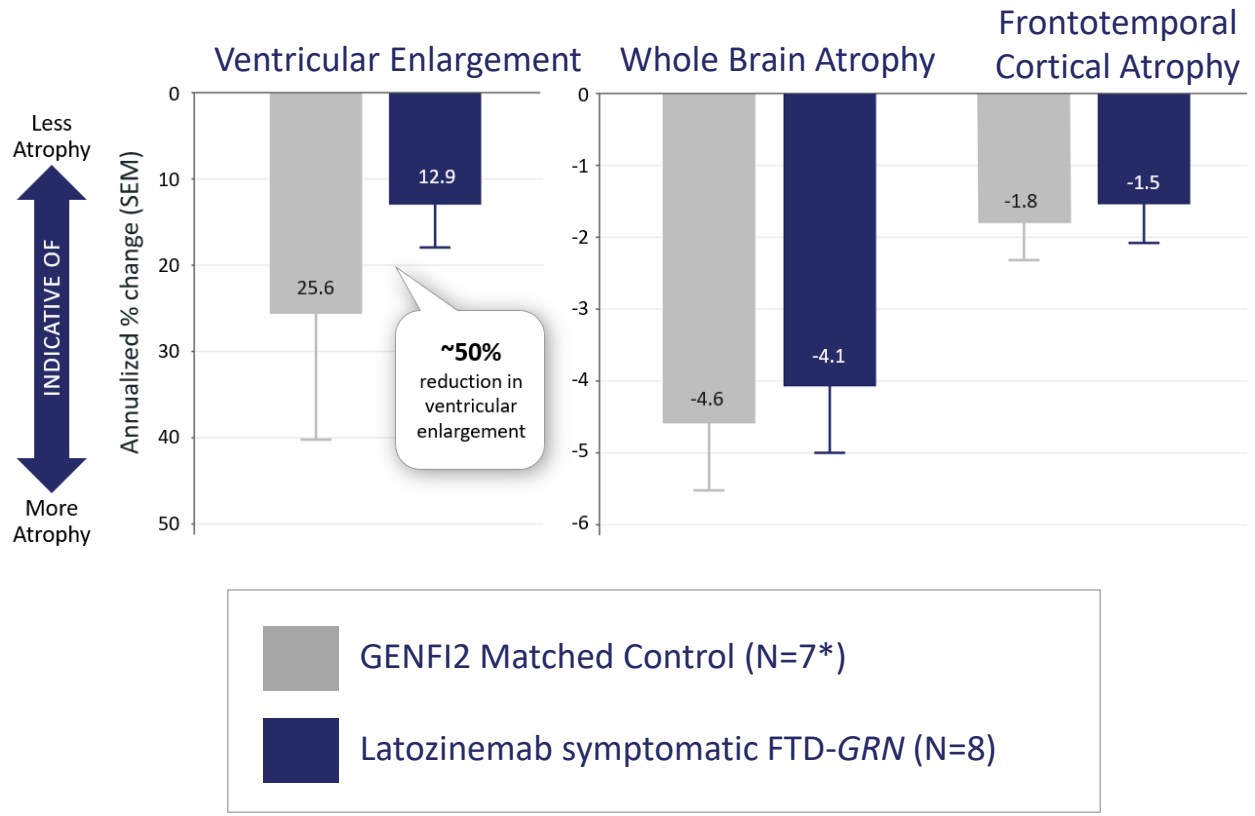
BRAIN VOLUME CHANGES BIOMARKERS

Normalization of lysosomal and inflammatory biomarkers



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

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



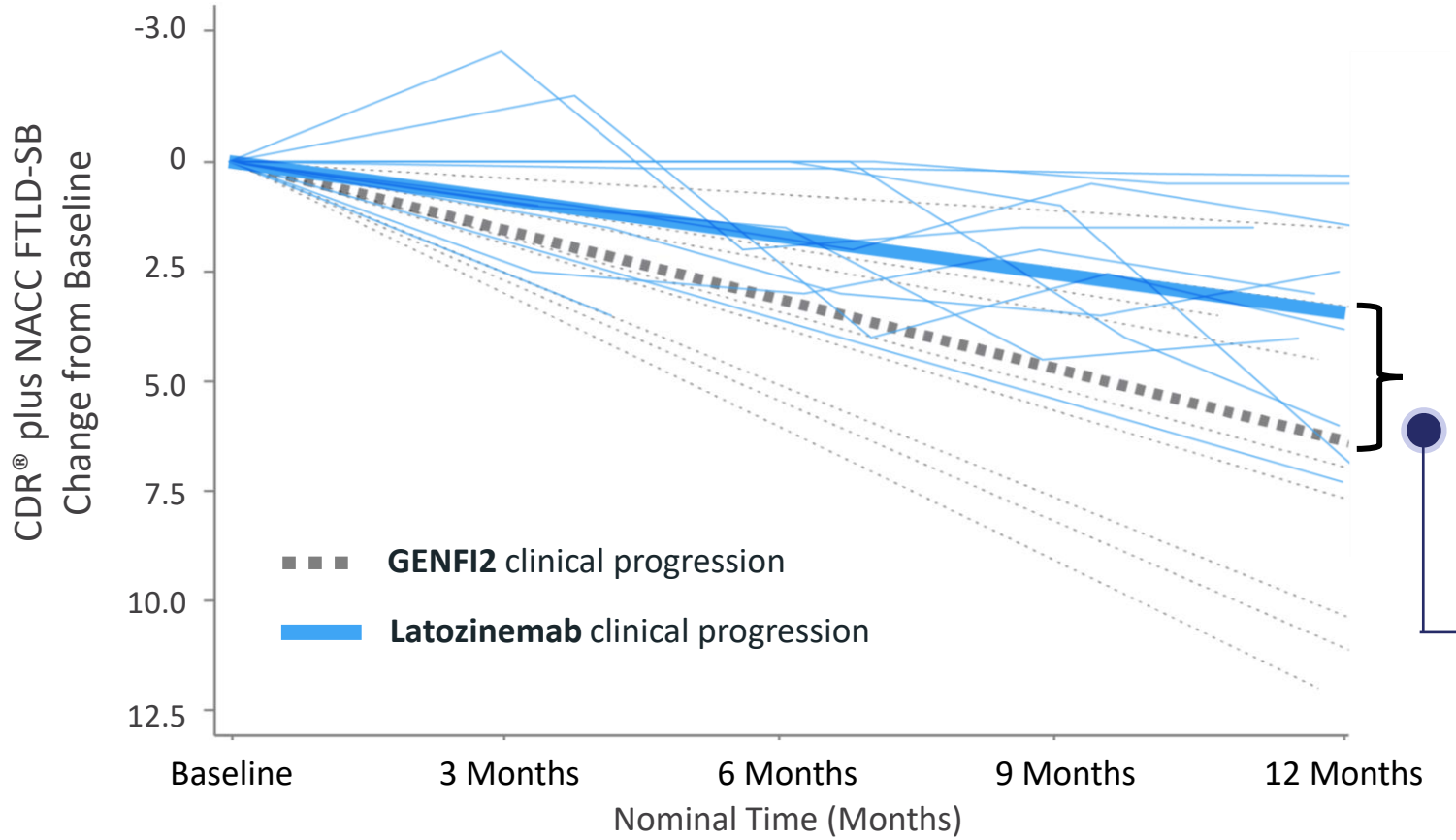
** n=8 for Whole Brain, n=7 for TBM measures (TBM measures were not available for one GENFI2 participant). One GENFI2 subject was excluded from the analysis as the patient displayed cortical volume increases (2.58% annual volume increase in the FT cortex) indicating image analysis artifact*

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

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

CLINICAL MEASURE

CDR® plus NACC FTLD-SB



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

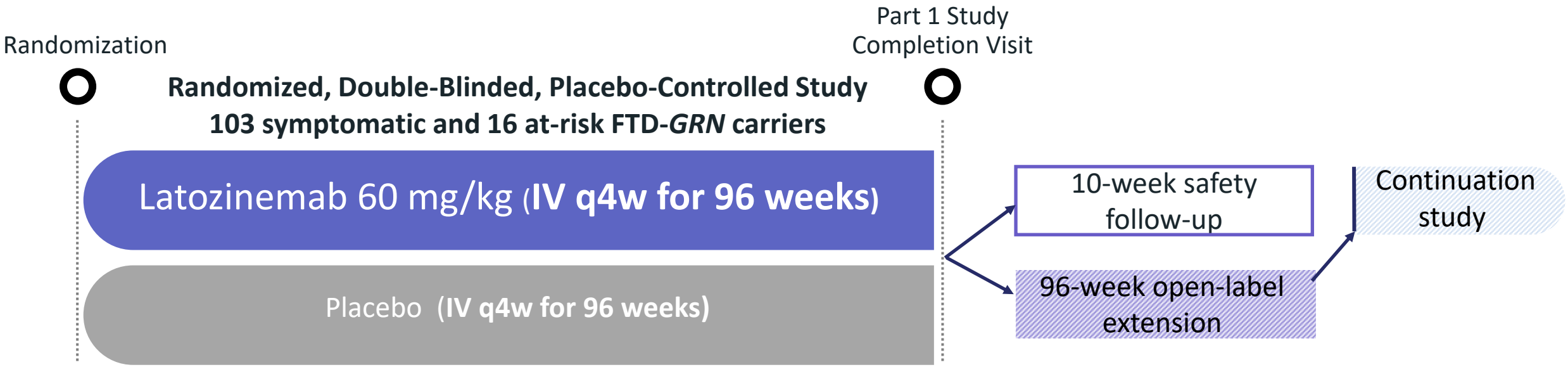
Estimated to slow annual disease progression by ~48% (3.1 point change)

1. Random Coefficient Model with Repeated Measurements including baseline & all available post-baseline measurements up to 12 months. Data cut-off Sep 8, 2021.
Phase 2 data presented at CTAD 2021 and ADPD 2022
NCT03987295

GENFI = The Genetic Frontotemporal Initiative
GENFI2 refers to the longitudinal FTD registry dataset

INFRONT-3: Ongoing Pivotal Phase 3 Study with Latozinemab

WE BELIEVE LATOZINEMAB IS THE MOST ADVANCED CANDIDATE IN DEVELOPMENT FOR FTD-*GRN*, WITH PIVOTAL DATA EXPECTED IN Q4 2025



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

"At risk" = GRN carriers who are pre-symptomatic and meet a pre-specified NfL threshold for enrollment in the Phase 3 trial;
CDR® plus NACC FTLD-SB = Clinical Dementia Rating Dementia Staging Instrument plus National Alzheimer's Disease Coordinating Center Frontotemporal Lobar Degeneration Behavior and Language Domains Sum of Boxes; CGI-S = Clinician's Global Impression-Severity; CGI-I = Clinician's Global Impression-Improvement; FRS = Frontotemporal Dementia Rating Scale;
RBANS = Repeatable Battery for the Assessment of Neuropsychological Status

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

INFRONT-3 Baseline Age

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

INFRONT-3 Baseline Clinical Characteristics[a]

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

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

Mean age of 63.7 years (SD: 8.8)

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

Mean plasma NfL geometric mean: 56.8 pg/mL

a. As of July 2024.

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

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

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

PGRN: Genetic and Biologic Rationale for AD

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

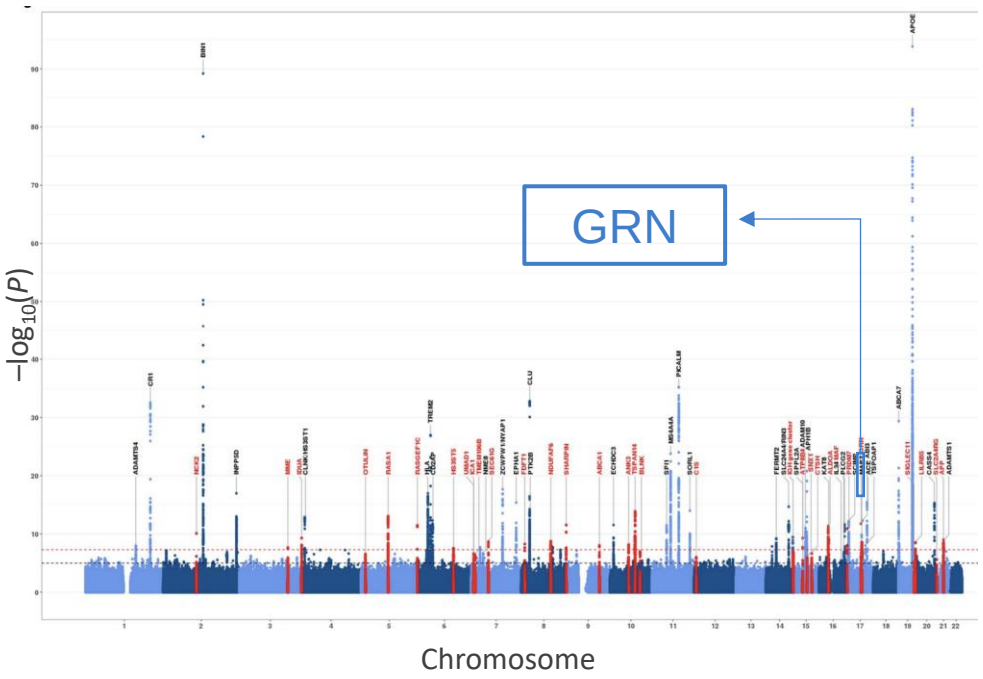
AL101/GSK4527226 AD Program

- **Phase 1:** Completed in healthy volunteers.
- **Phase 2:** Received IND clearance from FDA in AD.
- **Phase 2:** Reached approximately 75% of its target enrollment of 282 participants, with enrollment completion anticipated in mid-2025.

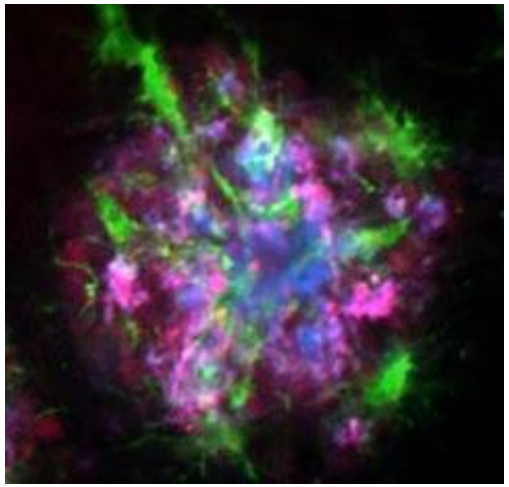
Mendsaikhan, A., et al. Characterization of lysosomal proteins Progranulin and Prosaposin and their interactions in Alzheimer's disease and aged brains: increased levels correlate with neuropathology. *acta neuropathol commun 7, 215 (2019). The breakdown of clinical diagnoses among ARTFL FTD mutations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

AL101/GSK4527226: Rationale for PGRN-Elevating Drugs in Alzheimer's Disease

PGRN is a Risk Gene for AD

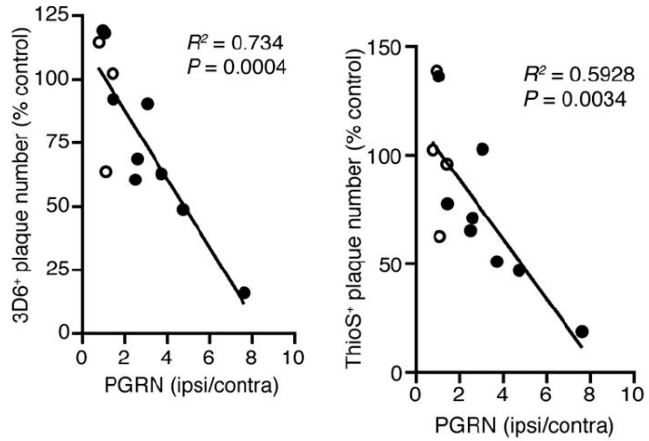


PGRN is Embedded in Aβ Plaques



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

PGRN is Protective in AD Model

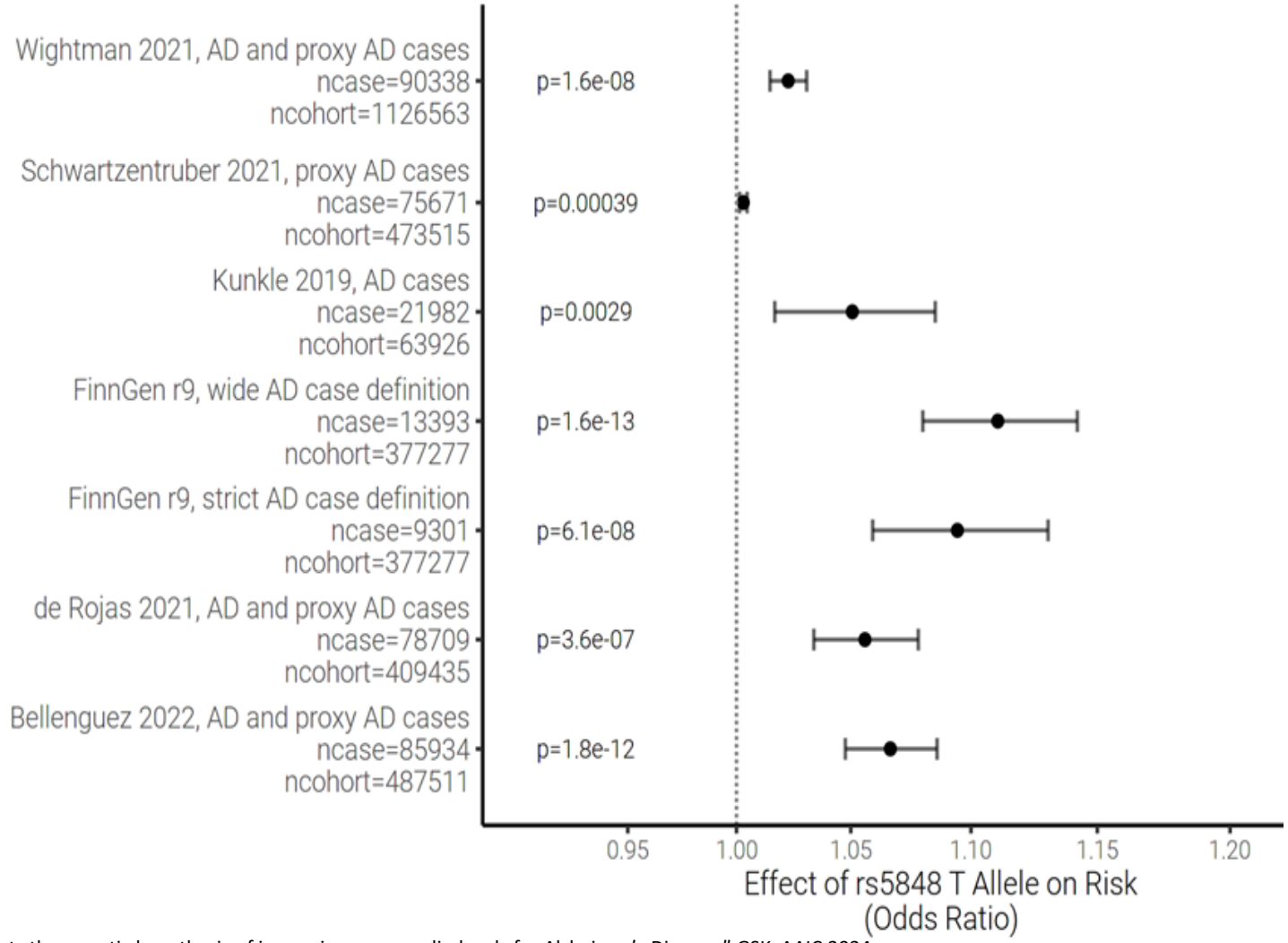


PGRN overexpression decreases Aβ plaque load in the dentate gyrus of AD mice

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

AL101/GSK4527226: Genetic Evidence Supports Increasing PGRN Levels in AD

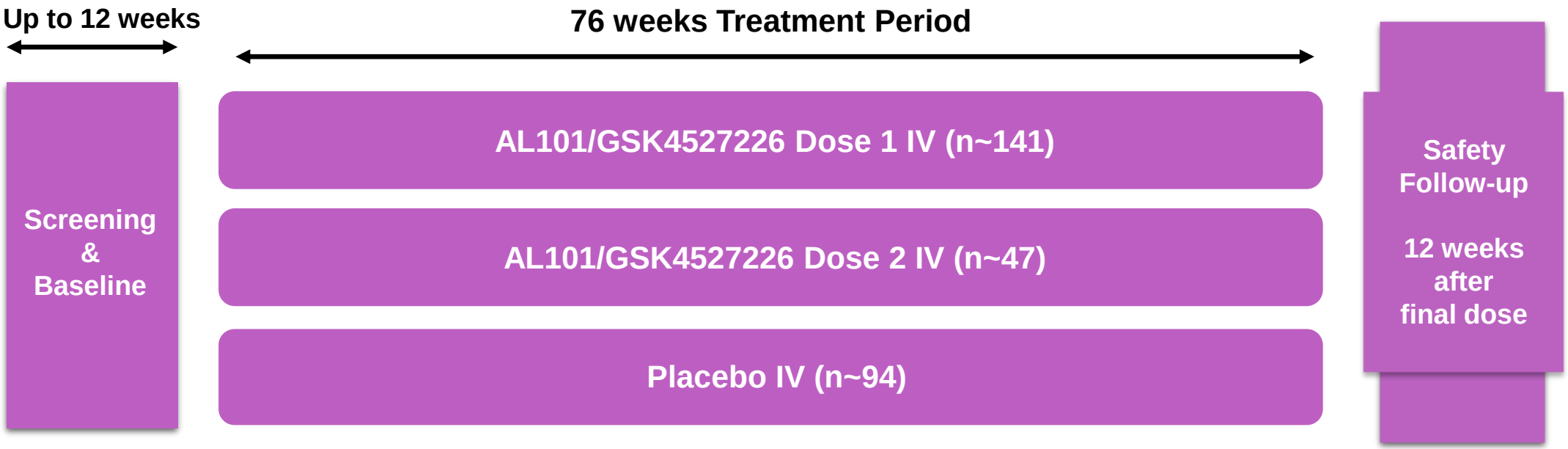
COMMON *GRN* VARIANT RS5848 T ALLELE IS ASSOCIATED WITH (A) AD RISK AND (B) DECREASED PGRN LEVELS IN CSF AND PLASMA



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

AL101/GSK4527226: PROGRESS-AD Study Design

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



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

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

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

Biomarkers: Amyloid PET, Tau PET, CSF and Plasma

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

GSK

Latozinemab and AL101

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

Latozinemab INFRONT-3 pivotal Phase 3 data anticipated by Q4 2025
AL101 PROGRESS-AD Phase 2 enrollment completion expected in mid-2025

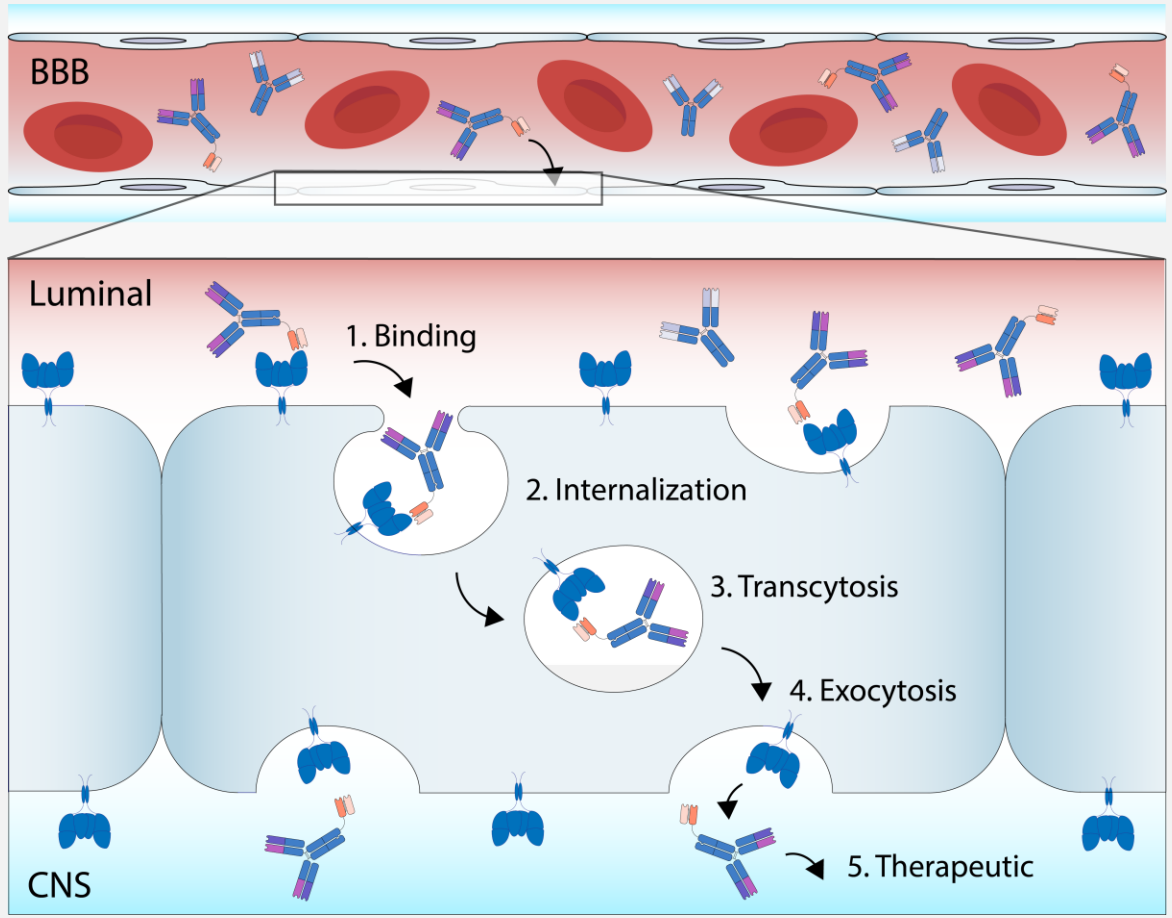
ABC Technology

Alector Brain Carrier (ABC): Designed for Effective Brain Delivery

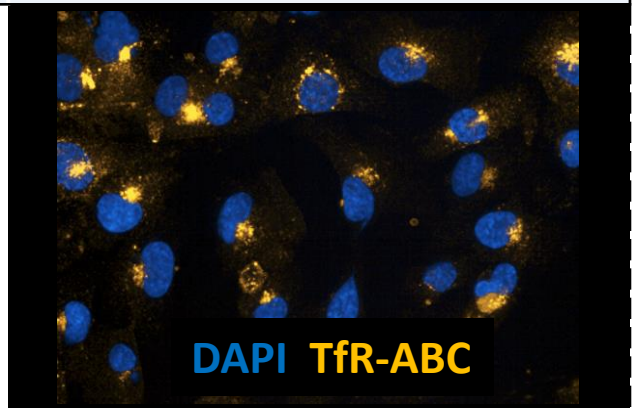
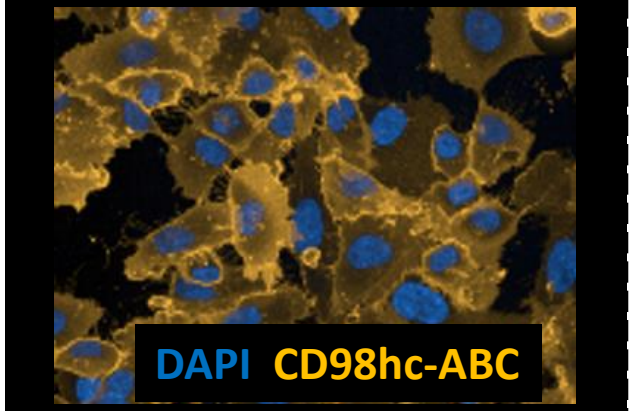
Alector Brain Carrier (ABC)

- Enables the potential to **widen the therapeutic window** while **lowering the costs of goods** and facilitating **convenient delivery** options
- **Versatile:** Tailored for a range of therapeutic cargos including antibodies, proteins, enzymes, and nucleic acids
- **Tunable:** Broad affinity toolbox for optimal therapeutic cargo-ABC pairing
- **Translatability:** Supports potential for rapid progression to the clinic

Receptor-Mediated Transcytosis



TfR and CD98hc: Offer Distinct Advantages for Cargo Selection

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

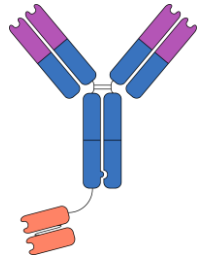
Therapeutic cargo will also impact target cell localization and trafficking

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

Alector data on file

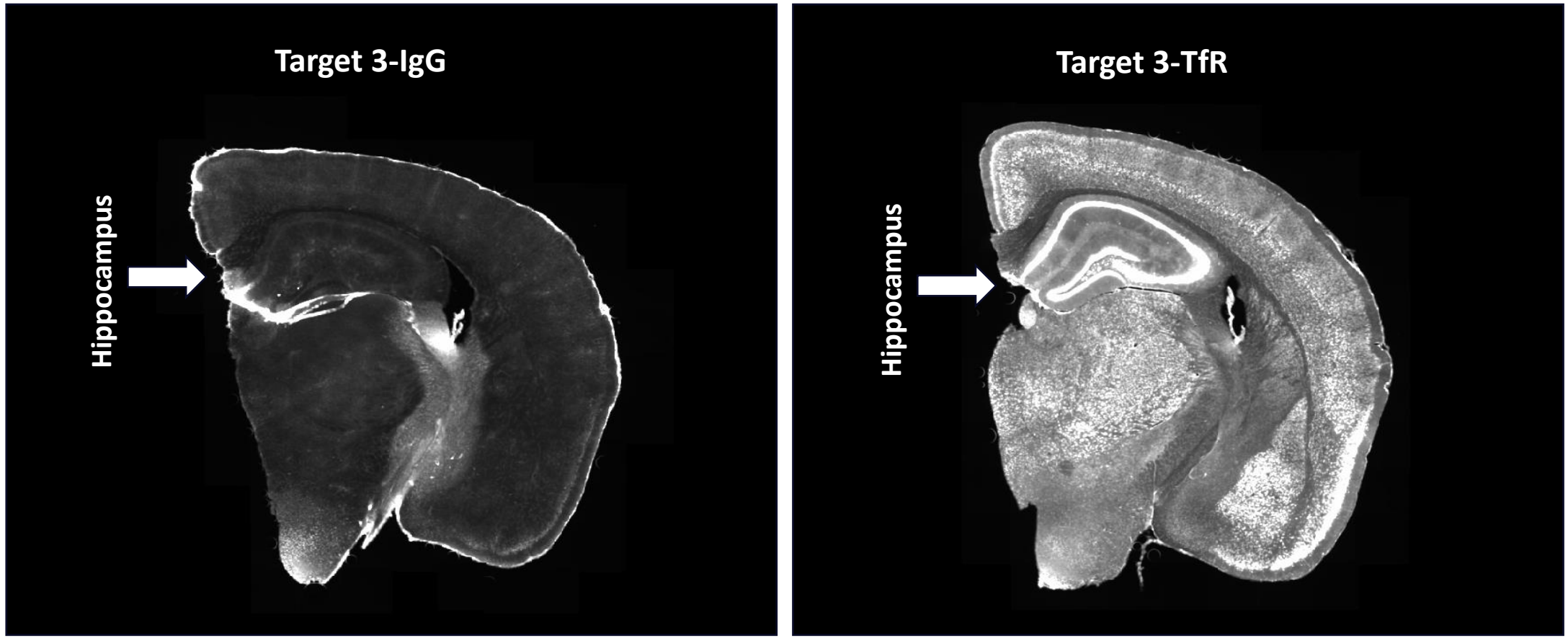
TfR-ABC: Drives Widespread Biodistribution in Mouse Brain

- Strong staining of neurons across brain regions due to combination of TfR and Target 3 binding
- Biodistribution of TfR-ABC molecule is highly cargo-dependent



Deep Brain Penetration with TfR-ABC

Treated without ABC	Treated with TfR-ABC



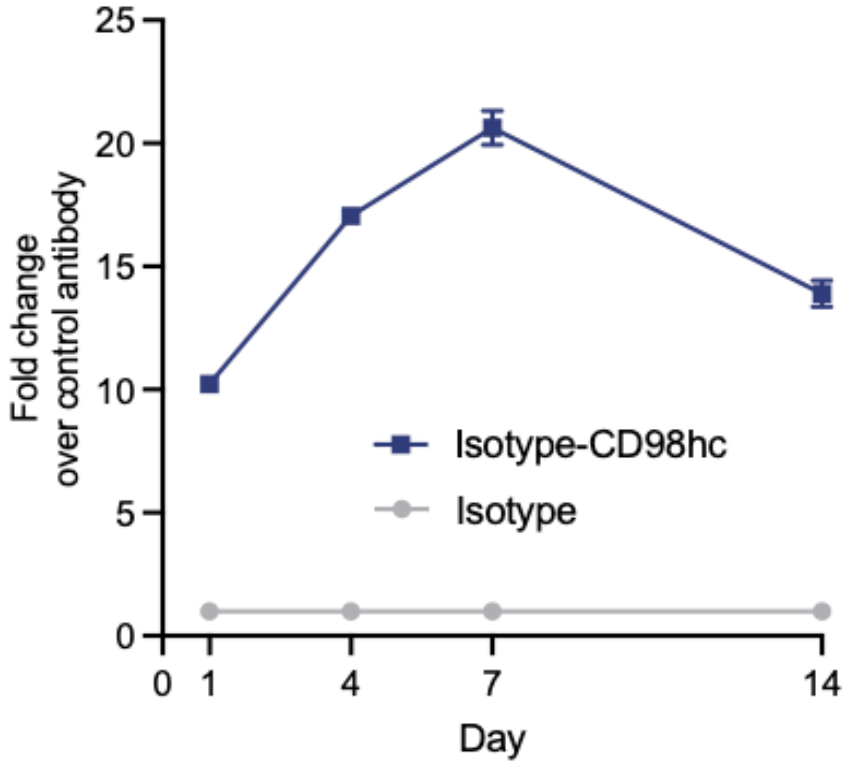
Anti-human antibody visualized post 50mg/kg iv dosing

alector

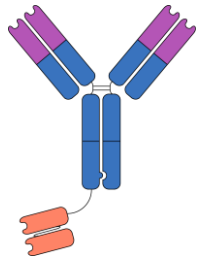
Alector data on file

CD98hc-ABC: Facilitates Brain Uptake to Parenchymal Fraction in hCD98hc ECD KI+/+ Mice

Antibody level in vessel-depleted brain fraction post 20mg/kg iv dose, n=3/group

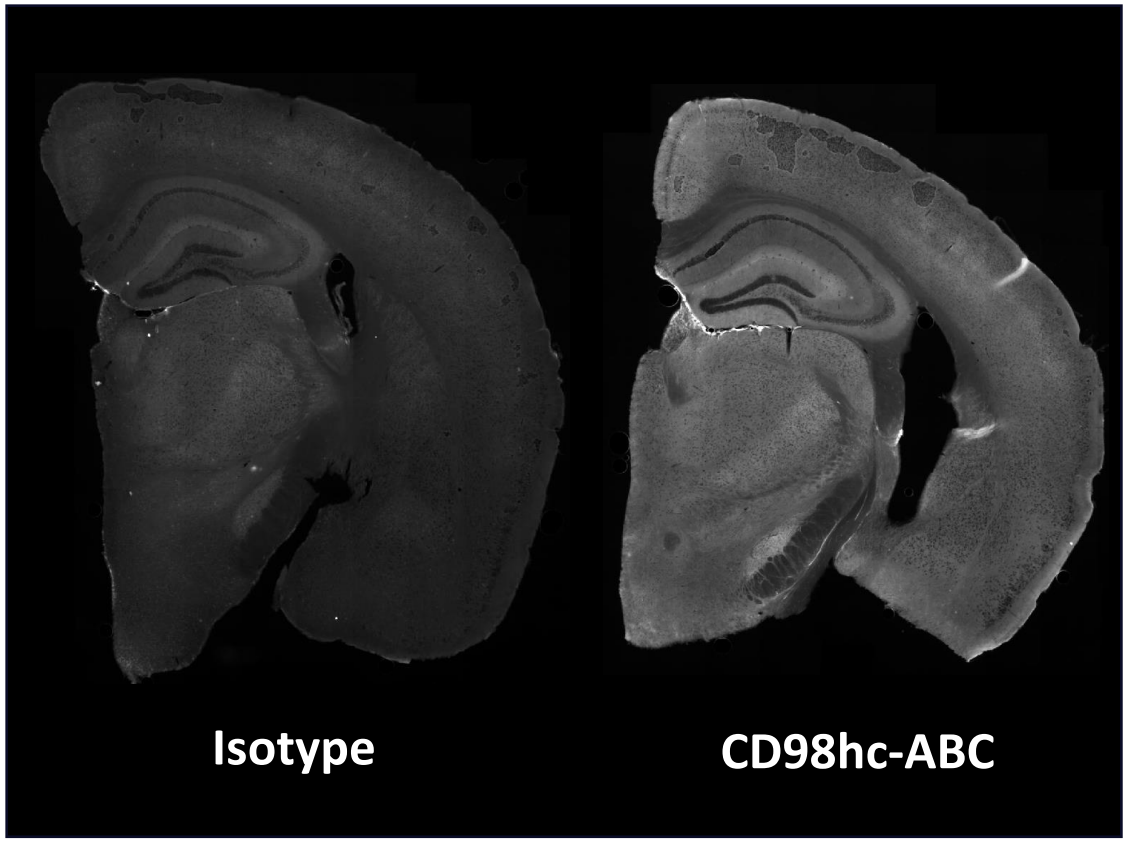


Isotype Fab



Anti-CD98hc scFv

Anti-human antibody visualized 7d post-iv dosing (20 mg/kg)



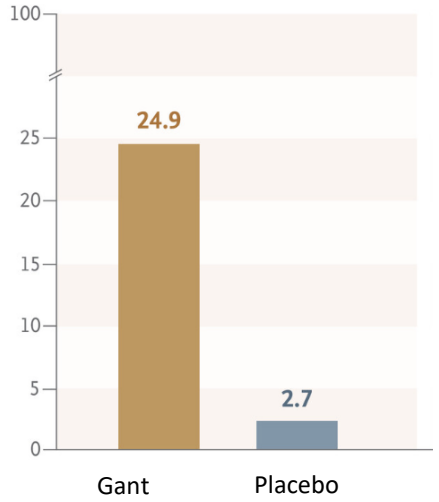
Proprietary Portfolio

ADP037-ABC: Brain-Penetrant Anti-Aβ Antibody

Vision	Combine Alector's anti-Aβ antibody with our proprietary ABC to facilitate rapid clearance of Aβ plaques with minimal ARIA and the potential for subcutaneous delivery.
Rationale and Strategy	• Current anti-Aβ antibodies are modestly effective, require high-doses to remove Aβ, and are associated with amyloid-related imaging abnormalities (ARIA) • Develop brain-penetrant antibody that specifically binds to a PyrGlu3 Aβ epitope • Demonstrate effective plaque binding and removal with minimal ARIA

ADDING BBB SHUTTLE REDUCED ARIA FOR ANTI-Aβ ANTIBODY

Gantenerumab in Early AD High ARIA Incidence



Trontinemab is the gantenerumab antibody with transferrin receptor BBB binding domain

Trontinemab in Early AD Low ARIA Incidence

	Completed[1]				*Not yet completed (interim data)*[1]	
	PART 1 (n=60)				PART 2 (n=95)	
Total number of participants with event (%)	**Cohort 1 0.2 mg/kg or Pbo (n = 14)**	**Cohort 2 0.6 mg/kg or Pbo (n = 14)**	**Cohort 3 1.8 mg/kg or Pbo (n = 16)**	**Cohort 4 3.6 mg/kg or Pbo (n = 16)**	**Cohort 3 1.8 mg/kg or Pbo (n = 60)**	**Cohort 4 3.6 mg/kg or Pbo (n = 35)**
ARIA-E[2]	0	0	1 (6.3%)	0	2 (3.3%)	0
ARIA-H	0	0	1 (6.3%)	0	4 (6.7%)	2 (5.7%)
Microhemorrhage	0	0	0	0	2 (3.3%)	2 (5.7%)
Superficial siderosis	0	0	1 (6.3%)	0	2 (3.3%)	0
Concurrent ARIA-E + ARIA-H	0	0	0	0	0	0

N Engl J Med 2023;389:1862-1876; Roche 30 October 2024 | CTAD 2024

ADP050-ABC: Brain-Penetrant GCase Replacement Therapy

Vision	Combine Alector-engineered GCase enzyme with our proprietary ABC for maximal GCase replacement in *GBA* mutation carriers with Parkinson's disease (PD) and Lewy body dementia (LBD).
Rationale and Strategy	• Natural GCase is unstable, short lived, difficult to manufacture, and unable to cross the BBB • Engineer an active, stable, developable, minimally immunogenetic GCase enzyme compatible with ABC format • Demonstrate increase in GCase levels/activity, reduction of alpha-synuclein, and effects on PD biomarkers in patients

GBA1 Gene Mutations Are a Major Risk Factor for Neurodegenerative Diseases

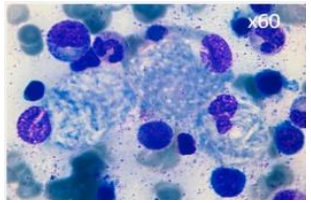
Parkinson's Disease (PD)[8]

- ~10 million patients worldwide[1]
- 5-15% are *GBA1* mutation carriers[2]
- Activity is reduced in non-carriers[2]
- Potential to use GCase ERT in sporadic PD

Lewy Body Dementia (LBD)[8]

- ~5-8 million patients worldwide[3]
- 3-30% are *GBA1* mutation carriers[4]
- Activity is reduced in non-carriers[4]
- Potential to use GCase ERT in sporadic LBD

Gaucher Disease (GD)[9]



- ~125,000 patients worldwide[5]
- *GBA1* mutations are causal
- GD type 1 have increased risk of PD[6]
- GD type 2 and 3 are neuronopathic[7]

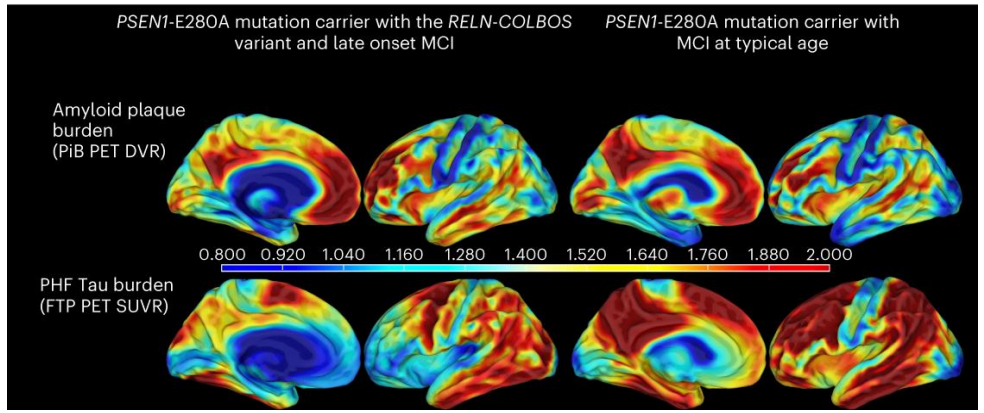
1. Parkinson's Foundation Statistics
2. Smith L, Schapira AHV. GBA Variants and Parkinson Disease: Mechanisms and Treatments. *Cells*. 2022 Apr 8;11(8):1261.
3. Alzheimer's Disease International, Dementia with Lewy Bodies
4. Nalls MA, et al. A multicenter study of glucocerebrosidase mutations in dementia with Lewy bodies. *JAMA Neurol*. 2013 Jun;70(6):727-35.
5. Meikle PJ, et al. Prevalence of lysosomal storage disorders. JAMA. 1999 Jan 20;281(3):249-54.
6. Bultron G, et al. The risk of Parkinson's disease in type 1 Gaucher disease. *J Inherit Metab Dis*. 2010 Apr;33(2):167-73.
7. National Gaucher Foundation, Gaucher Disease Types 2 and 3
8. Used with permission of Springer Nature BV, from Brain regions susceptible to alpha-synuclein spreading, Guo, YJ et al, 27, 1997; permission conveyed through Copyright Clearance Center, Inc.
9. Stirnemann J et al. Int J Mol Sci. 2017 Feb 17;18(2):441. (https://creativecommons.org/licenses/by/4.0/).

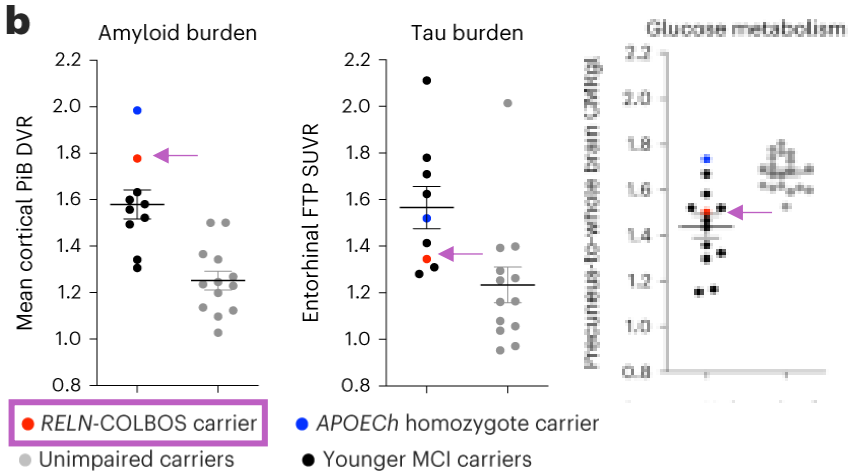
ADP056: Alector's Reelin Modulator

Vision	Develop a reelin modulator that replicates and exceeds the protective effects of the gene mutation.
Rationale and Strategy	• Reelin gain-of-function variant has been shown to protect against familial AD through a novel mechanism of action that uncouples Aβ pathology from tau pathology • Reelin is a large multimeric secreted protein consisting of 3,460 amino acids (~390kDa as a monomer), making it unsuitable for use as a drug • Develop a stable, long half-life reelin modulating drug that replicates the protective effects of the genetic variant

High brain amyloid and limited tau observed in individuals with protective reelin mutation and at risk for familial AD

RELN-H3447R=RELN-COLBOS



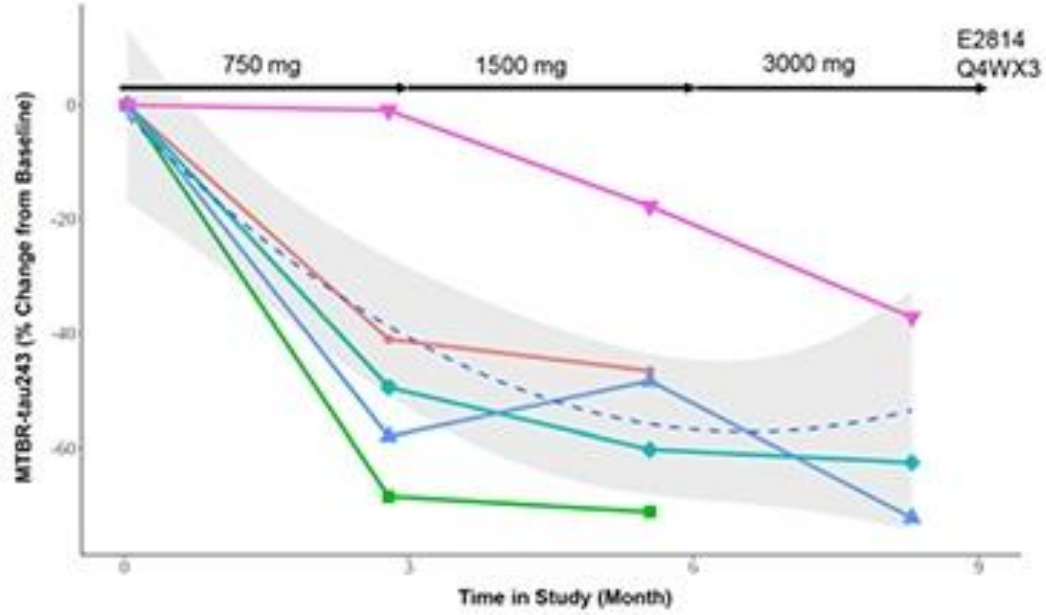


Lopera et al. *Nature Medicine* 2023

ADP063-ABC: Brain-Penetrant Anti-Tau Antibody

Vision	Combine Alector's anti-tau antibody in development with our proprietary ABC to block the spread of tau aggregates, with the potential for subcutaneous delivery and combination with anti-Aβ drugs.
Rationale and Strategy	• Pathological tau levels are directly associated with Alzheimer's disease • Tau mutations lead to frontotemporal dementia • The most promising anti-tau antibody targets the tau microtubule binding region (MTBR) and shows promising results in human trials (~60% reductions in MTBR-tau243, p-tau217) • Target a first-in-class therapeutic by developing anti-tau MTBR antibodies compatible with ABC to enable deep and effective brain penetration

CSF-MTBR-tau243 dropped by ~ 40% to 70% within the first three months in response to treatment with E2814 a naked anti-tau antibody in people with dominantly inherited AD



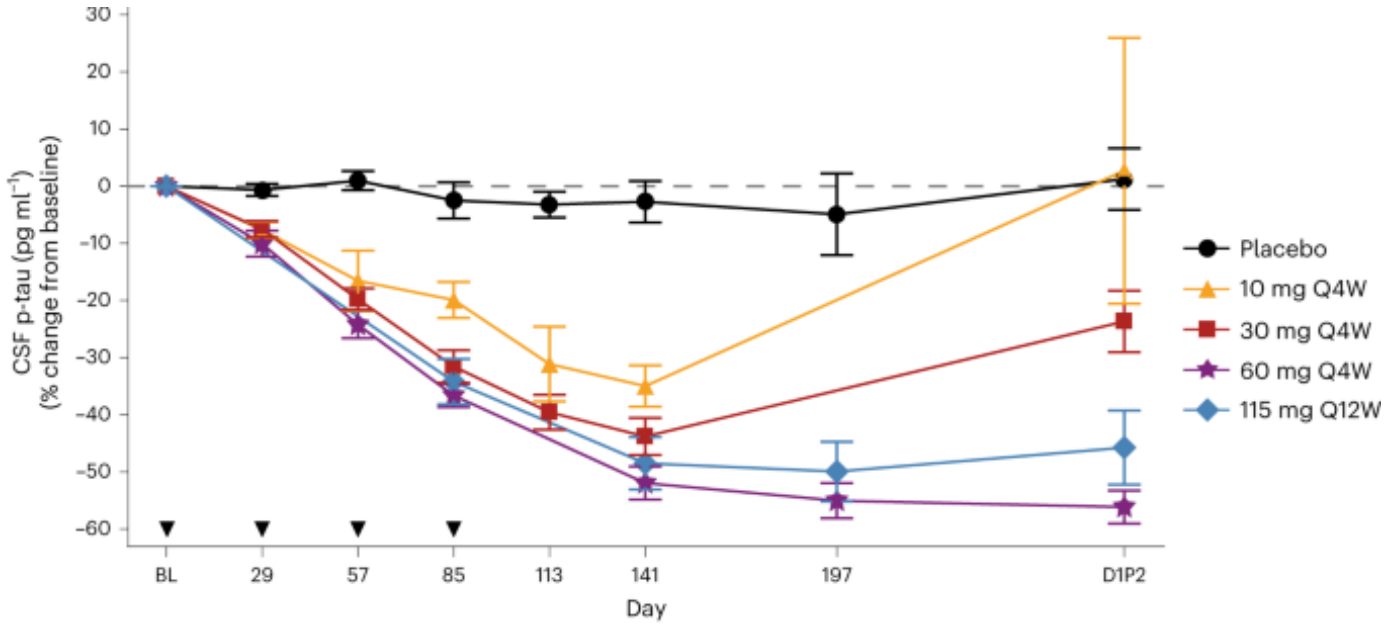
- Five participants with AD were treated with Eisai's anti-tau antibody E2814, with MTBR-tau-243 levels measured for each.
- Each colored line represents an individual participant.

"CSF MTBR-tau-243 Tracks Tangles, Plummets in Response to Antibody." *AlzForum*, 1 August 1 2023.

ADP064-ABC: Brain-Penetrant Tau siRNA

Vision	Combine potent anti-tau siRNA with our proprietary ABC to enable rapid blockade of tau mRNA synthesis, with the potential for peripheral delivery and combination with anti-Aβ drugs.
Rationale and Strategy	• Pathological tau levels are directly associated with Alzheimer's disease • Tau mutations lead to frontotemporal dementia • Intrathecally delivered tau ASO was shown to reduce CSF tau by 60% as well as tau tangles (ADPD 2023 BIIB080). • Develop tau-siRNA with ABC to enable deep and effective brain penetration and peripheral delivery

CSF concentrations of p-tau protein dropped by ~50% in response to Biogen's naked tau-targeting antisense oligonucleotide in people with mild AD



Mummery, C.J., et al. Tau-targeting antisense oligonucleotide MAPTRx in mild Alzheimer's disease: a phase 1b, randomized, placebo-controlled trial. *Nat Med* 29, 1437–1447 (2023).

Alector Value Proposition: Aims to Deliver Innovation That Makes Degenerative Brain Disorders History

Accomplishments to Date

Pioneering firsts for patients

- **Investigational latozinemab (AL001) first anti-SORT1** molecule in FTD-*GRN*[1]
- **Latozinemab granted Orphan Drug Designation** for FTD from FDA and EMA as well as **Breakthrough Therapy** and **Fast Track** designations for FTD-*GRN* from FDA
- **Enrollment ongoing** in AL101/ GSK4527226 AD Ph 2
- **Pipeline of first- and best-in-class** approaches for brain disorders[1]

Goals for Next 3 Years

Aim to deliver firsts for patients

- **Deliver data** for latozinemab FTD-*GRN* pivotal P3
- **Deliver data** for AL101/GSK4527226 AD P2
- **Deliver blood brain barrier** technology platform to enhance our novel programs
- **Deliver 4+ leads** for IND enabling studies and share initial clinical data to drive development progress

Goals for Next 3+ Years

Aim to make brain disorders history

- Obtain **regulatory approval** and **commercialize** latozinemab in FTD-*GRN**
- **Share P2 and P3 clinical data** for proprietary programs
- **Continue to advance our science** from research to the clinic with multiple INDs for genetically validated programs

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

1. Alector is not aware of any other PGRN-elevating candidates in a Phase 3 trial for FTD or in a Phase 2 or Phase 3 trial for AD as of Jan. 2025.
2. Cash, cash equivalents, and marketable securities as of September 30, 2024, were $457.2 million.
AL001 (latozinemab) and AL101 are investigational therapies.

*Assuming positive Phase 3 data

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Thank You